tion of an article of food that was the subject of a recall under section 350*l*(b) of this title or a public health advisory described in paragraph (1).

(Pub. L. 111–353, title II, § 206(f), Jan. 4, 2011, 124 Stat. 3943.)

Editorial Notes

REFERENCES IN TEXT

Subsection (a), referred to in par. (1), means subsec. (a) of section 206 of Pub. L. 111–353.

CODIFICATION

Section was enacted as part of the FDA Food Safety Modernization Act, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

Statutory Notes and Related Subsidiaries

CONSTRUCTION

Nothing in this section to be construed to alter jurisdiction and authorities established under certain other Acts or in a manner inconsistent with international agreements to which the United States is a party, see sections 2251 and 2252 of this title.

§ 350m. Requirements for critical food

(a) Notification of meaningful disruption for critical food

(1) In general

A manufacturer of a critical food (as defined in section 321(ss) of this title) shall notify the Secretary of a permanent discontinuance in the manufacture or an interruption of the manufacture of such food that is likely to lead to a meaningful disruption in the supply of such food in the United States, and the reasons for such discontinuance or interruption, as soon as practicable, but not later than 5 business days after such discontinuance or such interruption.

(2) Distribution of information

Not later than 5 calendar days after receiving a notification under paragraph (1), if the Secretary has determined that such discontinuance or interruption has resulted, or is likely to result, in a shortage of such critical food, the Secretary shall distribute, to the Secretary of Agriculture and to the maximum extent practicable to the appropriate entities, as determined by the Secretary through such means as the Secretary determines appropriate, information on such shortage.

(3) Confidentiality

Nothing in this subsection authorizes the Secretary to disclose any information that is a trade secret or confidential information subject to section 552(b)(4) of title 5 or section 1905 of title 18.

(4) Meaningful disruption

In this subsection, the term ''meaningful disruption''—

(A) means a change in production that is reasonably likely to lead to a significant reduction in the supply of a critical food by a manufacturer that affects the ability of the manufacturer to meet expected demand for its product; and

(B) does not include interruptions in manufacturing due to matters such as routine maintenance, changes or discontinuance of flavors, colors, or other insignificant formulation characteristics, or insignificant changes in manufacturing so long as the manufacturer expects to resume operations in a short period of time.

(b) Risk management plans

Each manufacturer of a critical food shall develop, maintain, and implement, as appropriate, a redundancy risk management plan that identifies and evaluates risks to the supply of the food, as applicable, for each establishment in which such food is manufactured. A risk management plan under this subsection—

(1) may identify and evaluate risks to the supply of more than one critical food, or critical food category, manufactured at the same establishment;

(2) may identify mechanisms by which the manufacturer would mitigate the impacts of a supply disruption through alternative production sites, alternative suppliers, stockpiling of inventory, or other means; and

(3) shall be subject to inspection and copying by the Secretary pursuant to an inspection under section 374 of this title.

(c) Failure to meet requirements

(1) In general

If a person fails to submit information required under, and in accordance with, subsection (a)—

(A) the Secretary shall issue a letter to such person informing such person of such failure; and

(B) not later than 45 calendar days after the issuance of a letter under subparagraph (A), subject to paragraph (2), the Secretary shall make available to the public on the website of the Food and Drug Administration, with appropriate redactions made to protect the information described in subsection (a)(3)—

(i) the letter issued under subparagraph (A); and

(ii) at the request of such person, any response to such letter such person submitted to the Secretary.

(2) Exception

If the Secretary determines that the letter under paragraph (1) was issued in error or, after review of such response, the person had a reasonable basis for not submitting a notification as required under subsection (a), the requirements of paragraph (1)(B) shall not apply.

(June 25, 1938, ch. 675, § 424, as added Pub. L. 117–328, div. FF, title III, § 3401(k), Dec. 29, 2022, 136 Stat. 5844.)

SUBCHAPTER V—DRUGS AND DEVICES

PART A—DRUGS AND DEVICES

§ 351. Adulterated drugs and devices

A drug or device shall be deemed to be adulterated—

(a) Poisonous, insanitary, etc., ingredients; adequate controls in manufacture

(1) If it consists in whole or in part of any filthy, putrid, or decomposed substance; or (2)(A) if it has been prepared, packed, or held under insanitary conditions whereby it may have been contaminated with filth, or whereby it may have been rendered injurious to health; or (B) if it is a drug and the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirements of this chapter as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess; or (C) if it is a compounded positron emission tomography drug and the methods used in, or the facilities and controls used for, its compounding, processing, packing, or holding do not conform to or are not operated or administered in conformity with the positron emission tomography compounding standards and the official monographs of the United States Pharmacopoeia to assure that such drug meets the requirements of this chapter as to safety and has the identity and strength, and meets the quality and purity characteristics, that it purports or is represented to possess; or (3) if its container is composed, in whole or in part, of any poisonous or deleterious substance which may render the contents injurious to health; or (4) if (A) it bears or contains, for purposes of coloring only, a color additive which is unsafe within the meaning of section 379e(a) of this title, or (B) it is a color additive the intended use of which in or on drugs or devices is for purposes of coloring only and is unsafe within the meaning of section 379e(a) of this title; or (5) if it is a new animal drug which is unsafe within the meaning of section 360b of this title; or (6) if it is an animal feed bearing or containing a new animal drug, and such animal feed is unsafe within the meaning of section 360b of this title.

(b) Strength, quality, or purity differing from official compendium

If it purports to be or is represented as a drug the name of which is recognized in an official compendium, and its strength differs from, or its quality or purity falls below, the standard set forth in such compendium. Such determination as to strength, quality, or purity shall be made in accordance with the tests or methods of assay set forth in such compendium, except that whenever tests or methods of assay have not been prescribed in such compendium, or such tests or methods of assay as are prescribed are, in the judgment of the Secretary, insufficient for the making of such determination, the Secretary shall bring such fact to the attention of the appropriate body charged with the revision of such compendium, and if such body fails within a reasonable time to prescribe tests or methods of assay which, in the judgment of the Secretary, are sufficient for purposes of this paragraph, then the Secretary shall promulgate regulations prescribing appropriate tests or methods of assay in accordance with which such determination as to strength, quality, or purity shall be made. No drug defined in an official compendium shall be deemed to be adulterated under this paragraph because it differs from the standard of strength, quality, or purity therefor set forth in such compendium, if its difference in strength, quality, or purity from such standard is plainly stated on its label. Whenever a drug is recognized in both the United States Pharmacopoeia and the Homoeopathic Pharmacopoeia of the United States it shall be subject to the requirements of the United States Pharmacopoeia unless it is labeled and offered for sale as a homoeopathic drug, in which case it shall be subject to the provisions of the Homoeopathic Pharmacopoeia of the United States and not to those of the United States Pharmacopoeia.

(c) Misrepresentation of strength, etc., where drug is unrecognized in compendium

If it is not subject to the provisions of paragraph (b) of this section and its strength differs from, or its purity or quality falls below, that which it purports or is represented to possess.

(d) Mixture with or substitution of another substance

If it is a drug and any substance has been (1) mixed or packed therewith so as to reduce its quality or strength or (2) substituted wholly or in part therefor.

(e) Devices not in conformity with performance standards

(1) If it is, or purports to be or is represented as, a device which is subject to a performance standard established under section 360d of this title unless such device is in all respects in conformity with such standard.

(2) If it is declared to be, purports to be, or is represented as, a device that is in conformity with any standard recognized under section 360d(c) of this title unless such device is in all respects in conformity with such standard.

(f) Certain class III devices

(1) If it is a class III device—

(A)(i) which is required by an order issued under subsection (b) of section 360e of this title to have an approval under such section of an application for premarket approval and which is not exempt from section 360e of this title under section 360j(g) of this title, and

(ii)(I) for which an application for premarket approval or a notice of completion of a product development protocol was not filed with the Secretary within the ninety-day period beginning on the date of the issuance of such order, or

(II) for which such an application was filed and approval of the application has been denied, suspended, or withdrawn, or such a notice was filed and has been declared not completed or the approval of the device under the protocol has been withdrawn;

(B)(i) which was classified under section 360c(f) of this title into class III, which under section 360e(a) of this title is required to have in effect an approved application for premarket approval, and which is not exempt from section 360e of this title under section 360j(g) of this title, and

(ii) which has an application which has been suspended or is otherwise not in effect; or

(C) which was classified under section 360j(*l*) of this title into class III, which under such section is required to have in effect an approved application under section 360e of this title, and which has an application which has been suspended or is otherwise not in effect.

(2)(A) In the case of a device classified under section 360c(f) of this title into class III and intended solely for investigational use, paragraph [1] (1)(B) shall not apply with respect to such device during the period ending on the ninetieth day after the date of the promulgation of the regulations prescribing the procedures and conditions required by section 360j(g)(2) of this title.

(B) In the case of a device subject to an order issued under subsection (b) of section 360e of this title, paragraph [1] (1) shall not apply with respect to such device during the period ending—

(i) on the last day of the thirtieth calendar month beginning after the month in which the classification of the device in class III became effective under section 360c of this title, or

(ii) on the ninetieth day after the date of the issuance of such order,

whichever occurs later.

(3) In the case of a device with respect to which a regulation was promulgated under section 360e(b) of this title prior to July 9, 2012, a reference in this subsection to an order issued under section 360e(b) of this title shall be deemed to include such regulation.

(g) Banned devices

If it is a banned device.

(h) Manufacture, packing, storage, or installation of device not in conformity with applicable requirements or conditions

If it is a device and the methods used in, or the facilities or controls used for, its manufacture, packing, storage, or installation are not in conformity with applicable requirements under section 360j(f)(1) of this title or an applicable condition prescribed by an order under section 360j(f)(2) of this title.

(i) Failure to comply with requirements under which device was exempted for investigational use

If it is a device for which an exemption has been granted under section 360j(g) of this title for investigational use and the person who was granted such exemption or any investigator who uses such device under such exemption fails to comply with a requirement prescribed by or under such section.

(j) Delayed, denied, or limited inspection; refusal to permit entry or inspection

If it is a drug or device and it has been manufactured, processed, packed, or held in any factory, warehouse, or establishment and the owner, operator, or agent of such factory, warehouse, or establishment delays, denies, or limits an inspection, or refuses to permit entry or inspection.

For purposes of paragraph (a)(2)(B), the term ''current good manufacturing practice'' includes the implementation of oversight and controls over the manufacture of drugs to ensure quality, including managing the risk of and establishing the safety of raw materials, materials used in the manufacturing of drugs, and finished drug products.

(June 25, 1938, ch. 675, § 501, 52 Stat. 1049; Pub. L. 86–618, title I, § 102(b)(1), July 12, 1960, 74 Stat. 398; Pub. L. 87–781, title I, § 101, Oct. 10, 1962, 76 Stat. 780; Pub. L. 90–399, § 101(a), July 13, 1968, 82 Stat. 343; Pub. L. 94–295, §§ 3(d), 9(b)(1), May 28, 1976, 90 Stat. 576, 583; Pub. L. 101–629, § 9(b), Nov. 28, 1990, 104 Stat. 4521; Pub. L. 102–571, title I, § 107(8), Oct. 29, 1992, 106 Stat. 4499; Pub. L. 105–115, title I, § 121(b)(1), title II, § 204(c), Nov. 21, 1997, 111 Stat. 2320, 2336; Pub. L. 112–144, title VI, § 608(b)(2), title VII, §§ 707(a), 711, July 9, 2012, 126 Stat. 1058, 1068, 1071; Pub. L. 115–52, title VII, § 702(c), Aug. 18, 2017, 131 Stat. 1056.)

Editorial Notes

AMENDMENTS

2017—Par. (j). Pub. L. 115–52 inserted ''or device'' after ''drug''.

2012—Pub. L. 112–144, § 711, inserted concluding provisions.

Par. (f)(1)(A)(i). Pub. L. 112–144, § 608(b)(2)(A)(i), substituted ''an order issued'' for ''a regulation promulgated''.

Par. (f)(1)(A)(ii)(I). Pub. L. 112–144, § 608(b)(2)(A)(ii), substituted ''issuance of such order'' for ''promulgation of such regulation''.

Par. (f)(2)(B). Pub. L. 112–144, § 608(b)(2)(B), substituted ''an order issued'' for ''a regulation promulgated'' in introductory provisions and ''issuance of such order'' for ''promulgation of such regulation'' in subcl. (ii).

Par. (f)(3). Pub. L. 112–144, § 608(b)(2)(C), added subpar. (3).

Par. (j). Pub. L. 112–144, § 707(a), added par. (j).

1997—Par. (a)(2)(C). Pub. L. 105–115, § 121(b)(1), inserted ''; or (C) if it is a compounded positron emission tomography drug and the methods used in, or the facilities and controls used for, its compounding, processing, packing, or holding do not conform to or are not operated or administered in conformity with the positron emission tomography compounding standards and the official monographs of the United States Pharmacopoeia to assure that such drug meets the requirements of this chapter as to safety and has the identity and strength, and meets the quality and purity characteristics, that it purports or is represented to possess;'' before ''or (3)''.

Par. (e). Pub. L. 105–115, § 204(c), designated existing provisions as subpar. (1) and added subpar. (2).

1992—Par. (a)(4). Pub. L. 102–571 substituted ''379e(a)'' for ''376(a)'' in cls. (A) and (B).

1990—Par. (f)(1). Pub. L. 101–629, § 9(b), which directed the amendment of subpars. (A) to (C) of par. (f), was executed by making the amendments in cls. (A) to (C) of subpar. (1) of par. (f) as follows to reflect the probable intent of Congress: in cl. (A)(ii)(II), substituted '', suspended, or withdrawn'' for ''or withdrawn''; in cl. (B)(ii), substituted ''which has an application which has been suspended or is otherwise not in effect'' for ''which does not have such an application in effect''; and in cl. (C), substituted ''which has an application which has been suspended or is otherwise not in effect'' for ''which does not have such an application in effect''.

1976—Par. (a). Pub. L. 94–295, § 9(b)(1), substituted ''(3) if its'' for ''(3) if it is a drug and its'' in cl. (3), substituted ''(4) if (A) it bears or contains'' for ''(4) if (A) it is a drug which bears or contains'' in cl. (4)(A), and substituted ''drugs or devices'' for ''drugs'' in cl. (4)(B).

Pars. (e) to (i). Pub. L. 94–295, § 3(d), added pars. (e) to (i).

[1] So in original. Probably should be ''subparagraph''.

1968—Par. (a). Pub. L. 90–399 added cls. (5) and (6).
1962—Par. (a). Pub. L. 87–781 designated existing provisions of cl. (2) as (A) and added (B).
1960—Par. (a). Pub. L. 86–618 substituted provisions in cl. (4) relating to unsafe color additives for provisions which related to a coal-tar color other than one from a batch that has been certified in accordance with regulations as provided by section 354 of this title.

Statutory Notes and Related Subsidiaries

EFFECTIVE AND TERMINATION DATES OF 1997 AMENDMENT

Pub. L. 105–115, title I, §121(b)(2), Nov. 21, 1997, 111 Stat. 2320, provided that: ''Section 501(a)(2)(C) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351(a)(2)(C)) shall not apply 4 years after the date of enactment of this Act [Nov. 21, 1997] or 2 years after the date on which the Secretary of Health and Human Services establishes the requirements described in subsection (c)(1)(B) [section 121(c)(1)(B) of Pub. L. 105–115, set out as a note under section 355 of this title], whichever is later.''

Amendment by Pub. L. 105–115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as an Effective Date of 1997 Amendment note under section 321 of this title.

EFFECTIVE DATE OF 1968 AMENDMENT

Amendment by Pub. L. 90–399 effective on first day of thirteenth calendar month after July 13, 1968, see section 108(a) of Pub. L. 90–399, set out as an Effective Date and Transitional Provisions note under section 360b of this title.

EFFECTIVE DATE OF 1962 AMENDMENT; EXCEPTIONS

Amendment by Pub. L. 87–781 effective on first day of seventh calendar month following October 1962, see section 107 of Pub. L. 87–781, set out as a note under section 321 of this title.

EFFECTIVE DATE OF 1960 AMENDMENT

Amendment by Pub. L. 86–618 effective July 12, 1960, subject to the provisions of section 203 of Pub. L. 86–618, see section 202 of Pub. L. 86–618, set out as a note under section 379e of this title.

EFFECTIVE DATE; POSTPONEMENT

Par. (a)(4) effective Jan. 1, 1940, see act June 23, 1939, ch. 242, 53 Stat. 853, set out as an Effective Date; Postponement in Certain Cases note under section 301 of this title.

APPROVAL BY REGULATION PRIOR TO JULY 9, 2012

Pub. L. 112–144, title VI, §608(b)(3), July 9, 2012, 126 Stat. 1059, provided that: ''The amendments made by this subsection [amending this section and section 360e of this title] shall have no effect on a regulation that was promulgated prior to the date of enactment of this Act [July 9, 2012] requiring that a device have an approval under section 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360e) of an application for premarket approval.''

GUIDANCE

Pub. L. 112–144, title VII, §707(b), July 9, 2012, 126 Stat. 1068, provided that: ''Not later than 1 year after the date of enactment of this section [July 9, 2012], the Secretary of Health and Human Services shall issue guidance that defines the circumstances that would constitute delaying, denying, or limiting inspection, or refusing to permit entry or inspection, for purposes of section 501(j) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 351(j)] (as added by subsection (a)).''

Executive Documents

TRANSFER OF FUNCTIONS

For transfer of functions of Federal Security Administrator to Secretary of Health, Education, and Welfare [now Health and Human Services], and of Food and Drug Administration in the Department of Agriculture to Federal Security Agency, see notes set out under section 321 of this title.

§ 352. Misbranded drugs and devices

A drug or device shall be deemed to be misbranded—

(a) False or misleading label

(1) If its labeling is false or misleading in any particular. Health care economic information provided to a payor, formulary committee, or other similar entity with knowledge and expertise in the area of health care economic analysis, carrying out its responsibilities for the selection of drugs or devices for coverage or reimbursement, shall not be considered to be false or misleading under this paragraph if the health care economic information relates to an indication approved under section 355, 360(k), 360c(f)(2), or 360e of this title or section 262 of title 42 for such drug or device, is based on competent and reliable scientific evidence, and includes, where applicable, a conspicuous and prominent statement describing any material differences between the health care economic information and the labeling approved for the drug or device under section 355, 360(k), 360c(f)(2), or 360e of this title or section 262 of title 42. The requirements set forth in section 355, 360(k), 360c(f)(2), or 360e of this title or section 262 of title 42 shall not apply to health care economic information provided to such a payor, committee, or entity in accordance with this paragraph. Information that is relevant to the substantiation of the health care economic information presented pursuant to this paragraph shall be made available to the Secretary upon request.

(2)(A) For purposes of this paragraph,[1] the term ''health care economic information'' means any analysis (including the clinical data, inputs, clinical or other assumptions, methods, results, and other components underlying or comprising the analysis) that identifies, measures, or describes the economic consequences, which may be based on the separate or aggregated clinical consequences of the represented health outcomes, of the use of a drug or device. Such analysis may be comparative to the use of another drug or device, to another health care intervention, or to no intervention.

(B) Such term does not include any analysis that relates only to an indication that is not approved under section 355, 360(k), 360c(f)(2), or 360e of this title or section 262 of title 42 for such drug or device.

(b) Package form; contents of label

If in package form unless it bears a label containing (1) the name and place of business of the manufacturer, packer, or distributor; and (2) an accurate statement of the quantity of the contents in terms of weight, measure, or numerical count: *Provided*, That under clause (2) of this paragraph reasonable variations shall be permitted, and exemptions as to small packages shall be established, by regulations prescribed by the Secretary.

[1] So in original. The term ''health care economic information'' appears only in par. (1).

(c) Prominence of information on label

If any word, statement, or other information required by or under authority of this chapter to appear on the label or labeling is not prominently placed thereon with such conspicuousness (as compared with other words, statements, designs, or devices, in the labeling) and in such terms as to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use.

(d) Repealed. Pub. L. 105–115, title I, § 126(b), Nov. 21, 1997, 111 Stat. 2327

(e) Designation of drugs or devices by established names

(1)(A) If it is a drug, unless its label bears, to the exclusion of any other nonproprietary name (except the applicable systematic chemical name or the chemical formula)—

(i) the established name (as defined in subparagraph (3)) of the drug, if there is such a name;

(ii) the established name and quantity or, if determined to be appropriate by the Secretary, the proportion of each active ingredient, including the quantity, kind, and proportion of any alcohol, and also including whether active or not the established name and quantity or if determined to be appropriate by the Secretary, the proportion of any bromides, ether, chloroform, acetanilide, acetophenetidin, amidopyrine, antipyrine, atropine, hyoscine, hyoscyamine, arsenic, digitalis, digitalis glucosides, mercury, ouabain, strophanthin, strychnine, thyroid, or any derivative or preparation of any such substances, contained therein, except that the requirement for stating the quantity of the active ingredients, other than the quantity of those specifically named in this subclause, shall not apply to nonprescription drugs not intended for human use; and

(iii) the established name of each inactive ingredient listed in alphabetical order on the outside container of the retail package and, if determined to be appropriate by the Secretary, on the immediate container, as prescribed in regulation promulgated by the Secretary, except that nothing in this subclause shall be deemed to require that any trade secret be divulged, and except that the requirements of this subclause with respect to alphabetical order shall apply only to nonprescription drugs that are not also cosmetics and that this subclause shall not apply to nonprescription drugs not intended for human use.

(B) For any prescription drug the established name of such drug or ingredient, as the case may be, on such label (and on any labeling on which a name for such drug or ingredient is used) shall be printed prominently and in type at least half as large as that used thereon for any proprietary name or designation for such drug or ingredient, except that to the extent that compliance with the requirements of subclause (ii) or (iii) of clause (A) or this clause is impracticable, exemptions shall be established by regulations promulgated by the Secretary.

(2) If it is a device and it has an established name, unless its label bears, to the exclusion of any other nonproprietary name, its established name (as defined in subparagraph (4)) prominently printed in type at least half as large as that used thereon for any proprietary name or designation for such device, except that to the extent compliance with the requirements of this subparagraph is impracticable, exemptions shall be established by regulations promulgated by the Secretary.

(3) As used in subparagraph (1), the term ''established name'', with respect to a drug or ingredient thereof, means (A) the applicable official name designated pursuant to section 358 of this title, or (B), if there is no such name and such drug, or such ingredient, is an article recognized in an official compendium, then the official title thereof in such compendium, or (C) if neither clause (A) nor clause (B) of this subparagraph applies, then the common or usual name, if any, of such drug or of such ingredient, except that where clause (B) of this subparagraph applies to an article recognized in the United States Pharmacopeia and in the Homoeopathic Pharmacopoeia under different official titles, the official title used in the United States Pharmacopeia shall apply unless it is labeled and offered for sale as a homoeopathic drug, in which case the official title used in the Homoeopathic Pharmacopoeia shall apply.

(4) As used in subparagraph (2), the term ''established name'' with respect to a device means (A) the applicable official name of the device designated pursuant to section 358 of this title, (B) if there is no such name and such device is an article recognized in an official compendium, then the official title thereof in such compendium, or (C) if neither clause (A) nor clause (B) of this subparagraph applies, then any common or usual name of such device.

(f) Directions for use and warnings on label

Unless its labeling bears (1) adequate directions for use; and (2) such adequate warnings against use in those pathological conditions or by children where its use may be dangerous to health, or against unsafe dosage or methods or duration of administration or application, in such manner and form, as are necessary for the protection of users, except that where any requirement of clause (1) of this paragraph, as applied to any drug or device, is not necessary for the protection of the public health, the Secretary shall promulgate regulations exempting such drug or device from such requirement. Required labeling for prescription devices intended for use in health care facilities or by a health care professional and required labeling for in vitro diagnostic devices intended for use by health care professionals or in blood establishments may be made available solely by electronic means, provided that the labeling complies with all applicable requirements of law, and that the manufacturer affords such users the opportunity to request the labeling in paper form, and after such request, promptly provides the requested information without additional cost.

(g) Representations as recognized drug; packing and labeling; inconsistent requirements for designation of drug

If it purports to be a drug the name of which is recognized in an official compendium, unless

it is packaged and labeled as prescribed therein. The method of packing may be modified with the consent of the Secretary. Whenever a drug is recognized in both the United States Pharmacopoeia and the Homoeopathic Pharmacopoeia of the United States, it shall be subject to the requirements of the United States Pharmacopoeia with respect to packaging and labeling unless it is labeled and offered for sale as a homoeopathic drug, in which case it shall be subject to the provisions of the Homoeopathic Pharmacopoeia of the United States, and not those of the United States Pharmacopoeia, except that in the event of inconsistency between the requirements of this paragraph and those of paragraph (e) as to the name by which the drug or its ingredients shall be designated, the requirements of paragraph (e) shall prevail.

(h) Deteriorative drugs; packing and labeling

If it has been found by the Secretary to be a drug liable to deterioration, unless it is packaged in such form and manner, and its label bears a statement of such precautions, as the Secretary shall by regulations require as necessary for the protection of the public health. No such regulation shall be established for any drug recognized in an official compendium until the Secretary shall have informed the appropriate body charged with the revision of such compendium of the need for such packaging or labeling requirements and such body shall have failed within a reasonable time to prescribe such requirements.

(i) Drug; misleading container; imitation; offer for sale under another name

(1) If it is a drug and its container is so made, formed, or filled as to be misleading; or (2) if it is an imitation of another drug; or (3) if it is offered for sale under the name of another drug.

(j) Health-endangering when used as prescribed

If it is dangerous to health when used in the dosage or manner, or with the frequency or duration prescribed, recommended, or suggested in the labeling thereof.

(k), (*l*) Repealed. Pub. L. 105–115, title I, § 125(a)(2)(B), (b)(2)(D), Nov. 21, 1997, 111 Stat. 2325

(m) Color additives; packing and labeling

If it is a color additive the intended use of which is for the purpose of coloring only, unless its packaging and labeling are in conformity with such packaging and labeling requirements applicable to such color additive, as may be contained in regulations issued under section 379e of this title.

(n) Prescription drug advertisements: established name; quantitative formula; side effects, contraindications, and effectiveness; prior approval; false advertising; labeling; construction of the Convention on Psychotropic Substances

In the case of any prescription drug distributed or offered for sale in any State, unless the manufacturer, packer, or distributor thereof includes in all advertisements and other descriptive printed matter issued or caused to be issued by the manufacturer, packer, or distributor with respect to that drug a true statement of (1) the established name as defined in paragraph (e), printed prominently and in type at least half as large as that used for any trade or brand name thereof, (2) the formula showing quantitatively each ingredient of such drug to the extent required for labels under paragraph (e), and (3) such other information in brief summary relating to side effects, contraindications, and effectiveness as shall be required in regulations which shall be issued by the Secretary in accordance with section 371(a) of this title, and in the case of published direct-to-consumer advertisements the following statement printed in conspicuous text: ''You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1–800-FDA-1088.'', except that (A) except in extraordinary circumstances, no regulation issued under this paragraph shall require prior approval by the Secretary of the content of any advertisement, and (B) no advertisement of a prescription drug, published after the effective date of regulations issued under this paragraph applicable to advertisements of prescription drugs, shall with respect to the matters specified in this paragraph or covered by such regulations, be subject to the provisions of sections 52 to 57 of title 15. This paragraph (n) shall not be applicable to any printed matter which the Secretary determines to be labeling as defined in section 321(m) of this title. Nothing in the Convention on Psychotropic Substances, signed at Vienna, Austria, on February 21, 1971, shall be construed to prevent drug price communications to consumers. In the case of an advertisement for a drug subject to section 353(b)(1) of this title presented directly to consumers in television or radio format and stating the name of the drug and its conditions of use, the major statement relating to side effects and contraindications shall be presented in a clear, conspicuous, and neutral manner.

(*o*) Drugs or devices from nonregistered establishments

If it was manufactured, prepared, propagated, compounded, or processed in an establishment not duly registered under section 360 of this title, if it is a drug and was imported or offered for import by a commercial importer of drugs not duly registered under section 381(s) of this title, if it was not included in a list required by section 360(j) of this title, if a notice or other information respecting it was not provided as required by such section or section 360(k) of this title, or if it does not bear such symbols from the uniform system for identification of devices prescribed under section 360(e) of this title as the Secretary by regulation requires.

(p) Packaging or labeling of drugs in violation of regulations

If it is a drug and its packaging or labeling is in violation of an applicable regulation issued pursuant to section 1472 or 1473 of title 15.

(q) Restricted devices using false or misleading advertising or used in violation of regulations

In the case of any restricted device distributed or offered for sale in any State, if (1) its adver-

tising is false or misleading in any particular, or (2) it is sold, distributed, or used in violation of regulations prescribed under section 360j(e) of this title.

(r) Restricted devices not carrying requisite accompanying statements in advertisements and other descriptive printed matter

In the case of any restricted device distributed or offered for sale in any State, unless the manufacturer, packer, or distributor thereof includes in all advertisements and other descriptive printed matter issued or caused to be issued by the manufacturer, packer, or distributor with respect to that device (1) a true statement of the device's established name as defined in subsection (e), printed prominently and in type at least half as large as that used for any trade or brand name thereof, and (2) a brief statement of the intended uses of the device and relevant warnings, precautions, side effects, and contraindications and, in the case of specific devices made subject to a finding by the Secretary after notice and opportunity for comment that such action is necessary to protect the public health, a full description of the components of such device or the formula showing quantitatively each ingredient of such device to the extent required in regulations which shall be issued by the Secretary after an opportunity for a hearing. Except in extraordinary circumstances, no regulation issued under this paragraph shall require prior approval by the Secretary of the content of any advertisement and no advertisement of a restricted device, published after the effective date of this paragraph shall, with respect to the matters specified in this paragraph or covered by regulations issued hereunder, be subject to the provisions of sections 52 through 55 of title 15. This paragraph shall not be applicable to any printed matter which the Secretary determines to be labeling as defined in section 321(m) of this title.

(s) Devices subject to performance standards not bearing requisite labeling

If it is a device subject to a performance standard established under section 360d of this title, unless it bears such labeling as may be prescribed in such performance standard.

(t) Devices for which there has been a failure or refusal to give required notification or to furnish required material or information

If it is a device and there was a failure or refusal (1) to comply with any requirement prescribed under section 360h of this title respecting the device, (2) to furnish any material or information required by or under section 360i of this title respecting the device, or (3) to comply with a requirement under section 360*l* of this title.

(u) Identification of manufacturer

(1) Subject to paragraph (2), if it is a reprocessed single-use device, unless it, or an attachment thereto, prominently and conspicuously bears the name of the manufacturer of the reprocessed device, a generally recognized abbreviation of such name, or a unique and generally recognized symbol identifying such manufacturer.

(2) If the original device or an attachment thereto does not prominently and conspicuously bear the name of the manufacturer of the original device, a generally recognized abbreviation of such name, or a unique and generally recognized symbol identifying such manufacturer, a reprocessed device may satisfy the requirements of paragraph (1) through the use of a detachable label on the packaging that identifies the manufacturer and is intended to be affixed to the medical record of a patient.

(v) Reprocessed single-use devices

If it is a reprocessed single-use device, unless all labeling of the device prominently and conspicuously bears the statement ''Reprocessed device for single use. Reprocessed by ____.'' The name of the manufacturer of the reprocessed device shall be placed in the space identifying the person responsible for reprocessing.

(w) New animal drugs

If it is a new animal drug—

(1) that is conditionally approved under section 360ccc of this title and its labeling does not conform with the approved application or section 360ccc(f) of this title, or that is not conditionally approved under section 360ccc of this title and its label bears the statement set forth in section 360ccc(f)(1)(A) of this title;

(2) that is indexed under section 360ccc–1 of this title and its labeling does not conform with the index listing under section 360ccc–1(e) of this title or 360ccc–1(h) of this title, or that has not been indexed under section 360ccc–1 of this title and its label bears the statement set forth in section 360ccc–1(h) of this title; or

(3) for which an application has been approved under section 360b of this title and the labeling of such drug does not include the application number in the format: ''Approved by FDA under (A)NADA # xxx–xxx'', except that this subparagraph shall not apply to representative labeling required under section 514.1(b)(3)(v)(b) of title 21, Code of Federal Regulations (or any successor regulation) for animal feed bearing or containing a new animal drug.

(x) Nonprescription drugs

If it is a nonprescription drug (as defined in section 379aa of this title) that is marketed in the United States, unless the label of such drug includes a domestic address or domestic phone number through which the responsible person (as described in section 379aa of this title) may receive a report of a serious adverse event (as defined in section 379aa of this title) with such drug.

(y) Drugs subject to approved risk evaluation and mitigation strategy

If it is a drug subject to an approved risk evaluation and mitigation strategy pursuant to section 355(p) of this title and the responsible person (as such term is used in section 355–1 of this title) fails to comply with a requirement of such strategy provided for under subsection (d), (e), or (f) of section 355–1 of this title.

(z) Postmarket studies and clinical trials; new safety information in labeling

If it is a drug, and the responsible person (as such term is used in section 355(*o*) of this title)

is in violation of a requirement established under paragraph (3) (relating to postmarket studies and clinical trials) or paragraph (4) (relating to labeling) of section 355(*o*) of this title with respect to such drug.

(aa) Unpaid fees; failure to submit identifying information

If it is a drug, or an active pharmaceutical ingredient, and it was manufactured, prepared, propagated, compounded, or processed in a facility for which fees have not been paid as required by section 379j–42(a)(4) of this title or for which identifying information required by section 379j–42(f) of this title has not been submitted, or it contains an active pharmaceutical ingredient that was manufactured, prepared, propagated, compounded, or processed in such a facility.

(bb) False or misleading advertisement or promotion of compounded drug

If the advertising or promotion of a compounded drug is false or misleading in any particular.

(cc) Failure to bear product identifier

If it is a drug and it fails to bear the product identifier as required by section 360eee–1 of this title.

(dd) Improper labeling of antimicrobial drugs

If it is an antimicrobial drug, as defined in section 360a–2(f) of this title, and its labeling fails to conform with the requirements under section 360a–2(d) of this title.

(ee) Nonprescription drug subject to regulation

If it is a nonprescription drug that is subject to section 355h of this title, is not the subject of an application approved under section 355 of this title, and does not comply with the requirements under section 355h of this title.

(ff) Drugs manufactured, prepared, propagated, compounded, or processed in facilities for which fees have not been paid

If it is a drug and it was manufactured, prepared, propagated, compounded, or processed in a facility for which fees have not been paid as required by section 379j–72 of this title.

(gg) Product information prior to approval

(1) Unless its labeling bears adequate directions for use in accordance with paragraph (f), except that (in addition to drugs or devices that conform with exemptions pursuant to such paragraph) no drug or device shall be deemed to be misbranded under such paragraph through the provision of truthful and not misleading product information to a payor, formulary committee, or other similar entity with knowledge and expertise in the area of health care economic analysis carrying out its responsibilities for the selection of drugs or devices for coverage or reimbursement if the product information relates to an investigational drug or device or investigational use of a drug or device that is approved, cleared, granted marketing authorization, or licensed under section 355, 360(k), 360c(f)(2), or 360e of this title or section 262 of title 42 (as applicable), provided—

(A) the product information includes—

(i) a clear statement that the investigational drug or device or investigational use of a drug or device has not been approved, cleared, granted marketing authorization, or licensed under section 355, 360(k), 360c(f)(2), or 360e of this title or section 262 of title 42 (as applicable) and that the safety and effectiveness of such drug or device for such use has not been established;

(ii) information related to the stage of development of the drug or device involved, such as—

(I) the status of any study or studies in which the investigational drug or device or investigational use is being investigated;

(II) how the study or studies relate to the overall plan for the development of the drug or device; and

(III) whether an application, premarket notification, or request for classification for the investigational drug or device or investigational use has been submitted to the Secretary and when such a submission is planned;

(iii) in the case of information that includes factual presentations of results from studies, which shall not be selectively presented, a description of—

(I) all material aspects of study design, methodology, and results; and

(II) all material limitations related to the study design, methodology, and results;

(iv) where applicable, a prominent statement disclosing the indication or indications for which the Secretary has approved, granted marketing authorization, cleared, or licensed the product pursuant to section 355, 360(k), 360c(f)(2), or 360e of this title or section 262 of title 42, and a copy of the most current required labeling; and

(v) updated information, if previously communicated information becomes materially outdated as a result of significant changes or as a result of new information regarding the product or its review status; and

(B) the product information does not include—

(i) information that represents that an unapproved product—

(I) has been approved, cleared, granted marketing authorization, or licensed under section 355, 360(k), 360c(f)(2), or 360e of this title or section 262 of title 42 (as applicable); or

(II) has otherwise been determined to be safe or effective for the purpose or purposes for which the drug or device is being studied; or

(ii) information that represents that an unapproved use of a drug or device that has been so approved, granted marketing authorization, cleared, or licensed—

(I) is so approved, granted marketing authorization, cleared, or licensed; or

(II) that the product is safe or effective for the use or uses for which the drug or device is being studied.

(2) For purposes of this paragraph, the term ''product information'' includes—

(A) information describing the drug or device (such as drug class, device description, and features);

(B) information about the indication or indications being investigated;

(C) the anticipated timeline for a possible approval, clearance, marketing authorization, or licensure pursuant to section 355, 360(k), 360c, or 360e of this title or section 262 of title 42;

(D) drug or device pricing information;

(E) patient utilization projections;

(F) product-related programs or services; and

(G) factual presentations of results from studies that do not characterize or make conclusions regarding safety or efficacy.

(June 25, 1938, ch. 675, § 502, 52 Stat. 1050; June 23, 1939, ch. 242, § 3, 53 Stat. 854; Dec. 22, 1941, ch. 613, § 2, 55 Stat. 851; July 6, 1945, ch. 281, § 2, 59 Stat. 463; Mar. 10, 1947, ch. 16, § 2, 61 Stat. 11; July 13, 1949, ch. 305, § 1, 63 Stat. 409; Aug. 5, 1953, ch. 334, § 1, 67 Stat. 389; Pub. L. 86–618, title I, § 102(b)(2), July 12, 1960, 74 Stat. 398; Pub. L. 87–781, title I, §§ 105(c), 112(a), (b), 131(a), title III, § 305, Oct. 10, 1962, 76 Stat. 785, 790, 791, 795; Pub. L. 90–399, § 105(a), July 13, 1968, 82 Stat. 352; Pub. L. 91–601, § 6(d), formerly § 7(d), Dec. 30, 1970, 84 Stat. 1673, renumbered Pub. L. 97–35, title XII, § 1205(c), Aug. 13, 1981, 95 Stat. 716; Pub. L. 94–295, §§ 3(e), 4(b)(2), 5(a), 9(b)(2), May 28, 1976, 90 Stat. 577, 580, 583; Pub. L. 95–633, title I, § 111, Nov. 10, 1978, 92 Stat. 3773; Pub. L. 102–300, § 3(a)(2), June 16, 1992, 106 Stat. 239; Pub. L. 102–571, title I, § 107(9), Oct. 29, 1992, 106 Stat. 4499; Pub. L. 103–80, § 3(m), Aug. 13, 1993, 107 Stat. 777; Pub. L. 105–115, title I, §§ 114(a), 125(a)(2)(B), (b)(2)(D), 126(b), title IV, § 412(c), Nov. 21, 1997, 111 Stat. 2312, 2325, 2327, 2375; Pub. L. 107–250, title II, § 206, title III, §§ 301(a), 302(a)(1), Oct. 26, 2002, 116 Stat. 1613, 1616; Pub. L. 108–214, § 2(b)(2)(B), Apr. 1, 2004, 118 Stat. 575; Pub. L. 108–282, title I, § 102(b)(5)(E), Aug. 2, 2004, 118 Stat. 902; Pub. L. 109–43, § 2(c)(1), Aug. 1, 2005, 119 Stat. 441; Pub. L. 109–462, § 2(d), Dec. 22, 2006, 120 Stat. 3472; Pub. L. 110–85, title IX, §§ 901(d)(3)(A), (6), 902(a), 906(a), Sept. 27, 2007, 121 Stat. 940, 942, 943, 949; Pub. L. 112–144, title III, § 306, title VII, §§ 702(a), 714(c), July 9, 2012, 126 Stat. 1024, 1065, 1074; Pub. L. 112–193, § 2(a), Oct. 5, 2012, 126 Stat. 1443; Pub. L. 113–54, title I, § 103(b), title II, § 206(b), Nov. 27, 2013, 127 Stat. 597, 639; Pub. L. 114–255, div. A, title III, §§ 3037, 3044(b)(2), Dec. 13, 2016, 130 Stat. 1105, 1121; Pub. L. 115–234, title III, § 303(a), Aug. 14, 2018, 132 Stat. 2436; Pub. L. 116–136, div. A, title III, § 3852, Mar. 27, 2020, 134 Stat. 454; Pub. L. 117–328, div. FF, title III, § 3630(a), Dec. 29, 2022, 136 Stat. 5893.)

Editorial Notes

AMENDMENTS

2022—Subsec. (a)(1). Pub. L. 117–328, § 3630(a)(1)–(3), substituted ''drugs or devices for coverage'' for ''drugs for coverage'', ''drug or device'' for ''drug'' in two places, ''under section 355 of this title or under section 262(a) of title 42'' for ''under section 355 of this title or under section 262(a) of title 42'', ''under section 355, 360(k), 360c(f)(2), or 360e of this title or section 262 of title 42'' for ''under section 355 of this title or under section 262 of title 42'', and ''in section 355, 360(k), 360c(f)(2), or 360e of this title or section 262 of title 42'' for ''in section 355(a) of this title or in subsections (a) and (k) of section 262 of title 42''.

Subsec. (a)(2)(A). Pub. L. 117–328, § 3630(a)(1)(B), substituted ''drug or device'' for ''drug'' in two places.

Subsec. (a)(2)(B). Pub. L. 117–328, § 3630(a)(1)(B), (2), substituted ''drug or device'' for ''drug'' and ''under section 355, 360(k), 360c(f)(2), or 360e of this title or section 262 of title 42'' for ''under section 355 of this title or under section 262 of title 42''.

Subsec. (gg). Pub. L. 117–328, § 3630(a)(4), added subsec. (gg).

2020—Subsecs. (ee), (ff). Pub. L. 116–136 added subsecs. (ee) and (ff).

2018—Subsec. (w)(3). Pub. L. 115–234 added par. (3).

2016—Subsec. (a). Pub. L. 114–255, § 3037, designated existing provisions as par. (1), substituted ''a payor, formulary committee, or other similar entity with knowledge and expertise in the area of health care economic analysis, carrying out its responsibilities for the selection of drugs for coverage or reimbursement'' for ''a formulary committee, or other similar entity, in the course of the committee or the entity carrying out its responsibilities for the selection of drugs for managed care or other similar organizations'', ''relates'' for ''directly relates'', and '', is based on competent and reliable scientific evidence, and includes, where applicable, a conspicuous and prominent statement describing any material differences between the health care economic information and the labeling approved for the drug under section 355 of this title or under section 262 of title 42. The requirements set forth in section 355(a) of this title or in subsections (a) and (k) of section 262 of title 42 shall not apply to health care economic information provided to such a payor, committee, or entity in accordance with this paragraph'' for ''and is based on competent and reliable scientific evidence. The requirements set forth in section 355(a) of this title or in section 262(a) of title 42 shall not apply to health care economic information provided to such a committee or entity in accordance with this paragraph'', struck out ''In this paragraph, the term 'health care economic information' means any analysis that identifies, measures, or compares the economic consequences, including the costs of the represented health outcomes, of the use of a drug to the use of another drug, to another health care intervention, or to no intervention.'' at end, and added par. (2).

Subsec. (dd). Pub. L. 114–255, § 3044(b)(2), added subsec. (dd).

2013—Par. (bb). Pub. L. 113–54, § 103(b), added par. (bb).

Par. (cc). Pub. L. 113–54, § 206(b), added par. (cc).

2012—Par. (*o*). Pub. L. 112–144, § 714(c), inserted ''if it is a drug and was imported or offered for import by a commercial importer of drugs not duly registered under section 381(s) of this title,'' after ''not duly registered under section 360 of this title,''.

Pub. L. 112–144, § 702(a), struck out ''in any State'' after ''establishment''.

Par. (aa). Pub. L. 112–193 substituted ''379j–42(a)(4)'' for ''379j–41(a)(4)''.

Pub. L. 112–144, § 306, added par. (aa).

2007—Par. (n). Pub. L. 110–85, § 906(a), inserted ''and in the case of published direct-to-consumer advertisements the following statement printed in conspicuous text: 'You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1–800-FDA-1088.','' after ''section 371(a) of this title,''.

Pub. L. 110–85, § 901(d)(6), substituted ''section 371(a) of this title'' for ''the procedure specified in section 371(e) of this title''.

Pub. L. 110–85, § 901(d)(3)(A), inserted at end ''In the case of an advertisement for a drug subject to section 353(b)(1) of this title presented directly to consumers in television or radio format and stating the name of the drug and its conditions of use, the major statement relating to side effects and contraindications shall be presented in a clear, conspicuous, and neutral manner.''

Pars. (y), (z). Pub. L. 110–85, § 902(a), added pars. (y) and (z).

2006—Par. (x). Pub. L. 109–462 added par. (x).

2005—Par. (u). Pub. L. 109–43 amended par. (u) generally. Prior to amendment, par. (u) read as follows: ''If it is a device, unless it, or an attachment thereto,

prominently and conspicuously bears the name of the manufacturer of the device, a generally recognized abbreviation of such name, or a unique and generally recognized symbol identifying such manufacturer, except that the Secretary may waive any requirement under this paragraph for the device if the Secretary determines that compliance with the requirement is not feasible for the device or would compromise the provision of reasonable assurance of the safety or effectiveness of the device.''

2004—Par. (f). Pub. L. 108–214, in last sentence, inserted ''or by a health care professional and required labeling for in vitro diagnostic devices intended for use by health care professionals or in blood establishments'' after ''in health care facilities'', inserted comma after ''means'', substituted ''requirements of law, and that the manufacturer affords such users the opportunity'' for ''requirements of law and, that the manufacturer affords health care facilities the opportunity'', and struck out ''the health care facility'' after ''promptly provides''.

Par. (w). Pub. L. 108–282 added par. (w).

2002—Par. (f). Pub. L. 107–250, §206, inserted at end ''Required labeling for prescription devices intended for use in health care facilities may be made available solely by electronic means provided that the labeling complies with all applicable requirements of law and, that the manufacturer affords health care facilities the opportunity to request the labeling in paper form, and after such request, promptly provides the health care facility the requested information without additional cost.''

Par. (u). Pub. L. 107–250, §301(a), which directed amendment of section by adding par. (u) at end, was executed by adding par. (u) before par. (v) to reflect the probable intent of Congress.

Par. (v). Pub. L. 107–250, §302(a)(1), added par. (v).

1997—Par. (a). Pub. L. 105–115, §114(a), inserted at end ''Health care economic information provided to a formulary committee, or other similar entity, in the course of the committee or the entity carrying out its responsibilities for the selection of drugs for managed care or other similar organizations, shall not be considered to be false or misleading under this paragraph if the health care economic information directly relates to an indication approved under section 355 of this title or under section 262(a) of title 42 for such drug and is based on competent and reliable scientific evidence. The requirements set forth in section 355(a) of this title or in section 262(a) of title 42 shall not apply to health care economic information provided to such a committee or entity in accordance with this paragraph. Information that is relevant to the substantiation of the health care economic information presented pursuant to this paragraph shall be made available to the Secretary upon request. In this paragraph, the term 'health care economic information' means any analysis that identifies, measures, or compares the economic consequences, including the costs of the represented health outcomes, of the use of a drug to the use of another drug, to another health care intervention, or to no intervention.''

Par. (d). Pub. L. 105–115, §126(b), struck out par. (d) which read as follows: ''If it is for use by man and contains any quantity of the narcotic or hypnotic substance alpha eucaine, barbituric acid, betaeucaine, bromal, cannabis, carbromal, chloral, coca, cocaine, codeine, heroin, marihuana, morphine, opium, paraldehyde, peyote, or sulphonmethane; or any chemical derivative of such substance, which derivative has been by the Secretary, after investigation, found to be, and by regulations designated as, habit forming; unless its label bears the name and quantity or proportion of such substance or derivative and in juxtaposition therewith the statement 'Warning—May be habit forming.' ''

Par. (e)(1). Pub. L. 105–115, §412(c), amended subpar. (1) generally. Prior to amendment, subpar. (1) read as follows: ''If it is a drug, unless (A) its label bears, to the exclusion of any other nonproprietary name (except the applicable systematic chemical name or the chemical formula), (i) the established name (as defined in subparagraph (3)) of the drug, if such there be, and (ii), in case it is fabricated from two or more ingredients, the established name and quantity of each active ingredient, including the quantity, kind, and proportion of any alcohol, and also including, whether active or not, the established name and quantity or proportion of any bromides, ether, chloroform, acetanilid, acetphenetidin, amidopyrine, antipyrine, atropine, hyoscine, hyoscyamine, arsenic, digitalis, digitalis glucosides, mercury ouabain strophanthin, strychnine, thyroid, or any derivative or preparation of any such substances, contained therein; *Provided*, That the requirement for stating the quantity of the active ingredients, other than the quantity of those specifically named in this paragraph, shall apply only to prescription drugs; and (B) for any prescription drug the established name of such drug or ingredient, as the case may be, on such label (and on any labeling on which a name for such drug or ingredient is used) is printed prominently and in type at least half as large as that used thereon for any proprietary name or designation for such drug or ingredient: *Provided*, That to the extent that compliance with the requirements of clause (A)(ii) or clause (B) of this subparagraph is impracticable, exemptions shall be established by regulations promulgated by the Secretary.''

Par. (k). Pub. L. 105–115, §125(a)(2)(B), struck out par. (k) which read as follows: ''If it is, or purports to be, or is represented as a drug composed wholly or partly of insulin, unless (1) it is from a batch with respect to which a certificate or release has been issued pursuant to section 356 of this title, and (2) such certificate or release is in effect with respect to such drug.''

Par. (*l*). Pub. L. 105–115, §125(b)(2)(D), struck out par. (*l*) which read as follows: ''If it is, or purports to be, or is represented as a drug (except a drug for use in animals other than man) composed wholly or partly of any kind of penicillin, streptomycin, chlortetracycline, chloramphenicol, bacitracin, or any other antibiotic drug, or any derivative thereof, unless (1) it is from a batch with respect to which a certificate or release has been issued pursuant to section 357 of this title, and (2) such certificate or release is in effect with respect to such drug: *Provided*, That this paragraph shall not apply to any drug or class of drugs exempted by regulations promulgated under section 357(c) or (d) of this title.''

1993—Par. (e)(3). Pub. L. 103–80, §3(m)(1), substituted ''of such ingredient, except that'' for ''of such ingredient: *Provided*, That''.

Par. (f). Pub. L. 103–80, §3(m)(2), substituted ''users, except that where'' for ''users: *Provided*, That where''.

Par. (g). Pub. L. 103–80, §3(m)(3), substituted ''prescribed therein. The method'' for ''prescribed therein: *Provided*, That the method'' and ''Pharmacopoeia, except that'' for ''Pharmacopoeia: *Provided further*, That,''.

Par. (n). Pub. L. 103–80, §3(m)(4), substituted '', except that (A)'' for '': *Provided*, That (A)''.

1992—Par. (m). Pub. L. 102–571 substituted ''379e'' for ''376''.

Par. (t)(3). Pub. L. 102–300 added cl. (3).

1978—Par. (n). Pub. L. 95–633 inserted provision relating to the construction of the Convention on Psychotropic Substances.

1976—Par. (e). Pub. L. 94–295, §5(a), substituted ''subparagraph (3)'' for ''subparagraph (2)'' in subpar. (1), added subpar. (2), redesignated former subpar. (2) as (3) and in subpar. (3) as so redesignated substituted ''subparagraph (1)'' for ''this paragraph (e)'', and added subpar. (4).

Par. (j). Pub. L. 94–295, §3(e)(2), substituted ''dosage or manner,'' for ''dosage,''.

Par. (m). Pub. L. 94–295, §9(b)(2), substituted ''the intended use of which is for'' for ''the intended use of which in or on drugs is for''.

Par. (*o*). Pub. L. 94–295, §4(b)(2), substituted ''If it was manufactured'' for ''If it is a drug and was manufac-

tured'' and inserted '', if it was not included in a list required by section 360(j) of this title, if a notice or other information respecting it was not provided as required by such section or section 360(k) of this title, or if it does not bear such symbols from the uniform system for identification of devices prescribed under section 360(e) of this title as the Secretary by regulation requires''.

Pars. (q) to (t). Pub. L. 94–295, § 3(e)(1), added pars. (q) to (t).

1970—Par. (p). Pub. L. 91–601 added par. (p).

1968—Par. (*l*). Pub. L. 90–399 inserted ''(except a drug for use in animals other than man)'' after ''represented as a drug''.

1962—Par. (e). Pub. L. 87–781, § 112(a), designated existing provisions as subpar. (1), substituted '', unless (A) its label bears, to the exclusion of any other nonproprietary name (except the applicable systematic chemical name or the chemical formula), (i) the established name (as defined in subparagraph (2) of this subsection) of the drug, if such there be, and (ii), in case it is fabricated from two or more ingredients, the established name and quantity'' for ''and is not designated solely by a name recognized in an official compendium unless its label bears (1) the common or usual name of the drug, if such there be; and (2), in case it is fabricated from two or more ingredients, the common or usual name'', and ''the established name'' for ''the name'', provided that the requirement for stating the quantity of active ingredients, other than those specified in this par., applies only to prescription drugs, and that the established name of a drug on a label is to be printed prominently and in type at least half as large as used for any proprietary designation, and added subpar. (2) defining ''established name''.

Par. (g). Pub. L. 87–781, § 112(b), provided that if there is an inconsistency between the provisions of this par. and those of par. (e), as to the name of a drug, the requirements of par. (e) should prevail.

Par. (*l*). Pub. L. 87–781, § 105(c), substituted ''bacitracin, or any other antibiotic drug'' for ''or bacitracin.''

Par. (n). Pub. L. 87–781, § 131(a), added par. (n).

Par. (*o*). Pub. L. 87–781, § 305, added par. (*o*).

1960—Par. (m). Pub. L. 86–618 added par. (m).

1953—Par. (*l*). Act Aug. 5, 1953, substituted ''chlortetracycline'' for ''aureomycin''.

1949—Par. (*l*). Act July 13, 1949, inserted '', aureomycin, chloramphenicol, or bacitracin'' after ''streptomycin''.

1947—Par. (*l*). Act Mar. 10, 1947, inserted ''or streptomycin'' after ''penicillin''.

1945—Par. (*l*). Act July 6, 1945, added par. (*l*).

1941—Par. (k). Act Dec. 22, 1941, added par. (k).

1939—Par. (d). Act June 29, 1939, substituted ''name, and quality or proportion'' for ''name, quantity, and percentage''.

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 2018 AMENDMENT

Pub. L. 115–234, title III, § 303(b), Aug. 14, 2018, 132 Stat. 2436, provided that: ''Section 502(w)(3) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 352(w)(3)], as added by subsection (a), shall apply beginning on September 30, 2023.''

EFFECTIVE DATE OF 2012 AMENDMENT

Amendment by section 306 of Pub. L. 112–144 effective Oct. 1, 2012, see section 305 of Pub. L. 112–144, set out as an Effective and Termination Dates note under section 379j–41 of this title.

EFFECTIVE DATE OF 2007 AMENDMENT

Amendment by Pub. L. 110–85 effective 180 days after Sept. 27, 2007, see section 909 of Pub. L. 110–85, set out as a note under section 331 of this title.

EFFECTIVE DATE OF 2006 AMENDMENT

Pub. L. 109–462, § 2(e)(1), (2), Dec. 22, 2006, 120 Stat. 3472, provided that:

''(1) IN GENERAL.—Except as provided in paragraph (2), the amendments made by this section [enacting section 379aa of this title and amending this section and section 331 of this title] shall take effect 1 year after the date of enactment of this Act [Dec. 22, 2006].

''(2) MISBRANDING.—Section 502(x) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 352(x)] (as added by this section) shall apply to any nonprescription drug (as defined in such section 502(x)) labeled on or after the date that is 1 year after the date of enactment of this Act [Dec. 22, 2006].''

EFFECTIVE DATE OF 2002 AMENDMENT

Pub. L. 107–250, title III, § 301(b), Oct. 26, 2002, 116 Stat. 1616, as amended by Pub. L. 108–214, § 2(c)(1), Apr. 1, 2004, 118 Stat. 575; Pub. L. 109–43, § 2(d), Aug. 1, 2005, 119 Stat. 441, provided that: ''Section 502(u) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 352(u)] (as amended by section 2(c) of the Medical Device User Fee Stabilization Act of 2005 [Pub. L. 109–43])—

''(1) shall be effective—

''(A) with respect to devices described under paragraph (1) of such section, 12 months after the date of enactment of the Medical Device User Fee Stabilization Act of 2005 [Aug. 1, 2005], or the date on which the original device first bears the name of the manufacturer of the original device, a generally recognized abbreviation of such name, or a unique and generally recognized symbol identifying such manufacturer, whichever is later; and

''(B) with respect to devices described under paragraph (2) of such section 502(u), 12 months after such date of enactment; and

''(2) shall apply only to devices reprocessed and introduced or delivered for introduction in interstate commerce after such applicable effective date.''

Pub. L. 107–250, title III, § 302(a)(2), Oct. 26, 2002, 116 Stat. 1616, provided that: ''The amendment made by paragraph (1) [amending this section] takes effect 15 months after the date of the enactment of this Act [Oct. 26, 2002], and only applies to devices introduced or delivered for introduction into interstate commerce after such effective date.''

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by sections 114(a), 126(b), and 412(c) of Pub. L. 105–115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as a note under section 321 of this title.

EFFECTIVE DATE OF 1978 AMENDMENT

Amendment by Pub. L. 95–633 effective on date the Convention on Psychotropic Substances enters into force in the United States [July 15, 1980], see section 112 of Pub. L. 95–633, set out as an Effective Date note under section 801a of this title.

EFFECTIVE DATE OF 1970 AMENDMENT

Amendment by Pub. L. 91–601 effective Dec. 30, 1970, and regulations establishing special packaging standards effective no sooner than 180 days or later than one year from date regulations are final, or an earlier date published in Federal Register, see section 8 of Pub. L. 91–601, set out as an Effective Date note under section 1471 of Title 15, Commerce and Trade.

EFFECTIVE DATE OF 1968 AMENDMENT

Amendment by Pub. L. 90–399 effective on first day of thirteenth calendar month after July 13, 1968, see section 108(a) of Pub. L. 90–399, set out as an Effective Date and Transitional Provisions note under section 360b of this title.

EFFECTIVE DATE OF 1962 AMENDMENT

Pub. L. 87–781, title I, § 112(c), Oct. 10, 1962, 76 Stat. 791, provided that: ''This section [amending this section] shall take effect on the first day of the seventh calendar month following the month in which this Act is enacted [October 1962].''

Pub. L. 87–781, title I, §131(b), Oct. 10, 1962, 76 Stat. 792, provided that: ''No drug which was being commercially distributed prior to the date of enactment of this Act [Oct. 10, 1962] shall be deemed to be misbranded under paragraph (n) of section 502 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 352(n)], as added by this section, until the earlier of the following dates: (1) the first day of the seventh month following the month in which this Act is enacted; or (2) the effective date of regulations first issued under clause (3) of such paragraph (n) in accordance with the procedure specified in section 701(e) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 371(e)].''

Amendment by Pub. L. 87–781 effective on first day of seventh calendar month following October 1962, see section 107 of Pub. L. 87–781, set out as a note under section 321 of this title.

EFFECTIVE DATE OF 1960 AMENDMENT

Amendment by Pub. L. 86–618 effective July 12, 1960, subject to the provisions of section 203 of Pub. L. 86–618, see section 202 of Pub. L. 86–618, set out as a note under section 379e of this title.

EFFECTIVE DATE; POSTPONEMENT

Pars. (b) and (d) to (h) effective Jan. 1, 1940, and such paragraphs effective July 1, 1940, as provided by regulations for certain lithographed labeling and containers bearing certain labeling, see act June 23, 1939, ch. 242, 53 Stat. 853, set out as an Effective Date: Postponement in Certain Cases note under section 301 of this title.

REGULATIONS

Pub. L. 110–85, title IX, §901(d)(3)(B), Sept. 27, 2007, 121 Stat. 940, provided that: ''Not later than 30 months after the date of the enactment of the Food and Drug Administration Amendments Act of 2007 [Sept. 27, 2007], the Secretary of Health and Human Services shall by regulation establish standards for determining whether a major statement relating to side effects and contraindications of a drug, described in section 502(n) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 352(n)) (as amended by subparagraph (A)) is presented in the manner required under such section.''

CONSTRUCTION OF 2016 AMENDMENT

Nothing in amendment by section 3044(b)(2) of Pub. L. 114–255 to be construed to restrict the prescribing of antimicrobial drugs or other products, including drugs approved under section 356(h) of this title, by health care professionals, or to limit the practice of health care, see section 3043 of Pub. L. 114–255, set out as a note under section 356 of this title.

PRESENTATION OF PRESCRIPTION DRUG BENEFIT AND RISK INFORMATION

Pub. L. 111–148, title III, §3507, Mar. 23, 2010, 124 Stat. 530, provided that:

''(a) IN GENERAL.—The Secretary of Health and Human Services (referred to in this section as the 'Secretary'), acting through the Commissioner of Food and Drugs, shall determine whether the addition of quantitative summaries of the benefits and risks of prescription drugs in a standardized format (such as a table or drug facts box) to the promotional labeling or print advertising of such drugs would improve health care decisionmaking by clinicians and patients and consumers.

''(b) REVIEW AND CONSULTATION.—In making the determination under subsection (a), the Secretary shall review all available scientific evidence and research on decisionmaking and social and cognitive psychology and consult with drug manufacturers, clinicians, patients and consumers, experts in health literacy, representatives of racial and ethnic minorities, and experts in women's and pediatric health.

''(c) REPORT.—Not later than 1 year after the date of enactment of this Act [Mar. 23, 2010], the Secretary shall submit to Congress a report that provides—

''(1) the determination by the Secretary under subsection (a); and

''(2) the reasoning and analysis underlying that determination.

''(d) AUTHORITY.—If the Secretary determines under subsection (a) that the addition of quantitative summaries of the benefits and risks of prescription drugs in a standardized format (such as a table or drug facts box) to the promotional labeling or print advertising of such drugs would improve health care decisionmaking by clinicians and patients and consumers, then the Secretary, not later than 3 years after the date of submission of the report under subsection (c), shall promulgate proposed regulations as necessary to implement such format.

''(e) CLARIFICATION.—Nothing in this section shall be construed to restrict the existing authorities of the Secretary with respect to benefit and risk information.''

GUIDANCE; MISBRANDED DEVICES

Pub. L. 109–43, §2(c)(2), Aug. 1, 2005, 119 Stat. 441, provided that: ''Not later than 180 days after the date of enactment of this Act [Aug. 1, 2005], the Secretary of Health and Human Services shall issue guidance to identify circumstances in which the name of the manufacturer of the original device, a generally recognized abbreviation of such name, or a unique and generally recognized symbol identifying such manufacturer, is not 'prominent and conspicuous', as used in section 502(u) of Federal Food, Drug, and Cosmetic Act [21 U.S.C. 352(u)] (as amended by paragraph (1)).''

STUDIES

Pub. L. 110–85, title IX, §906(b), Sept. 27, 2007, 121 Stat. 950, provided that:

''(1) IN GENERAL.—In the case of direct-to-consumer television advertisements, the Secretary of Health and Human Services, in consultation with the Advisory Committee on Risk Communication under section 567 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360bbb–6] (as added by section 917), shall, not later than 6 months after the date of the enactment of this Act [Sept. 27, 2007], conduct a study to determine if the statement in section 502(n) of such Act [21 U.S.C. 352(n)] (as added by subsection (a)) required with respect to published direct-to-consumer advertisements is appropriate for inclusion in such television advertisements.

''(2) CONTENT.—As part of the study under paragraph (1), such Secretary shall consider whether the information in the statement described in paragraph (1) would detract from the presentation of risk information in a direct-to-consumer television advertisement. If such Secretary determines the inclusion of such statement is appropriate in direct-to-consumer television advertisements, such Secretary shall issue regulations requiring the implementation of such statement in direct-to-consumer television advertisements, including determining a reasonable length of time for displaying the statement in such advertisements. The Secretary shall report to the appropriate committees of Congress the findings of such study and any plans to issue regulations under this paragraph.''

Pub. L. 108–173, title I, §107(f), Dec. 8, 2003, 117 Stat. 2171, directed the Secretary of Health and Human Services to undertake a study of how to make prescription pharmaceutical information, including drug labels and usage instructions, accessible to blind and visually-impaired individuals, and to submit a report to Congress not later than 18 months after Dec. 8, 2003.

Pub. L. 105–115, title I, §114(b), Nov. 21, 1997, 111 Stat. 2312, provided that: ''The Comptroller General of the United States shall conduct a study of the implementation of the provisions added by the amendment made by subsection (a) [amending this section]. Not later than 4 years and 6 months after the date of enactment of this Act [Nov. 21, 1997], the Comptroller General of the United States shall prepare and submit to Congress a report containing the findings of the study.''

COUNTERFEITING OF DRUGS; CONGRESSIONAL FINDINGS AND DECLARATION OF POLICY

Pub. L. 89–74, § 9(a), July 15, 1965, 79 Stat. 234, provided that: ''The Congress finds and declares that there is a substantial traffic in counterfeit drugs simulating the brand or other identifying mark or device of the manufacturer of the genuine article; that such traffic poses a serious hazard to the health of innocent consumers of such drugs because of the lack of proper qualifications, facilities, and manufacturing controls on the part of the counterfeiter, whose operations are clandestine; that, while such drugs are deemed misbranded within the meaning of section 502(i) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 352(i)], the controls for the suppression of the traffic in such drugs are inadequate because of the difficulty of determining the place of interstate origin of such drugs and, if that place is discovered, the fact that the implements for counterfeiting are not subject to seizure, and that these factors require enactment of additional controls with respect to such drugs without regard to their interstate or intrastate origins.''

Provisions as effective Feb. 1, 1966, see section 11 of Pub. L. 89–74, set out as an Effective Date of 1965 Amendment note under section 321 of this title.

Executive Documents

TRANSFER OF FUNCTIONS

For transfer of functions of Federal Security Administrator to Secretary of Health, Education, and Welfare [now Health and Human Services], and of Food and Drug Administration in the Department of Agriculture to Federal Security Agency, see notes set out under section 321 of this title.

§ 353. Exemptions and consideration for certain drugs, devices, and biological products

(a) Regulations for goods to be processed, labeled, or repacked elsewhere

The Secretary is directed to promulgate regulations exempting from any labeling or packaging requirement of this chapter drugs and devices which are, in accordance with the practice of the trade, to be processed, labeled, or repacked in substantial quantities at establishments other than those where originally processed or packed, on condition that such drugs and devices are not adulterated or misbranded under the provisions of this chapter upon removal from such processing, labeling, or repacking establishment.

(b) Prescription by physician; exemption from labeling and prescription requirements; misbranded drugs; compliance with narcotic and marihuana laws

(1) A drug intended for use by man which—

(A) because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, is not safe for use except under the supervision of a practitioner licensed by law to administer such drug; or

(B) is limited by an approved application under section 355 of this title to use under the professional supervision of a practitioner licensed by law to administer such drug;

shall be dispensed only (i) upon a written prescription of a practitioner licensed by law to administer such drug, or (ii) upon an oral prescription of such practitioner which is reduced promptly to writing and filed by the pharmacist, or (iii) by refilling any such written or oral prescription if such refilling is authorized by the prescriber either in the original prescription or by oral order which is reduced promptly to writing and filed by the pharmacist. The act of dispensing a drug contrary to the provisions of this paragraph shall be deemed to be an act which results in the drug being misbranded while held for sale.

(2) Any drug dispensed by filling or refilling a written or oral prescription of a practitioner licensed by law to administer such drug shall be exempt from the requirements of section 352 of this title, except paragraphs (a), (i)(2) and (3), (k), and (*l*), and the packaging requirements of paragraphs (g), (h), and (p), if the drug bears a label containing the name and address of the dispenser, the serial number and date of the prescription or of its filling, the name of the prescriber, and, if stated in the prescription, the name of the patient, and the directions for use and cautionary statements, if any, contained in such prescription. This exemption shall not apply to any drug dispensed in the course of the conduct of a business of dispensing drugs pursuant to diagnosis by mail, or to a drug dispensed in violation of paragraph (1) of this subsection.

(3) The Secretary may by regulation remove drugs subject to section 355 of this title from the requirements of paragraph (1) of this subsection when such requirements are not necessary for the protection of the public health.

(4)(A) A drug that is subject to paragraph (1) shall be deemed to be misbranded if at any time prior to dispensing the label of the drug fails to bear, at a minimum, the symbol ''Rx only''.

(B) A drug to which paragraph (1) does not apply shall be deemed to be misbranded if at any time prior to dispensing the label of the drug bears the symbol described in subparagraph (A).

(5) Nothing in this subsection shall be construed to relieve any person from any requirement prescribed by or under authority of law with respect to drugs now included or which may hereafter be included within the classifications stated in sections 4721, 6001, and 6151 of title 26, or to marihuana as defined in section 4761 of title 26.

(c) Sales restrictions

(1) No person may sell, purchase, or trade or offer to sell, purchase, or trade any drug sample. For purposes of this paragraph and subsection (d), the term ''drug sample'' means a unit of a drug, subject to subsection (b), which is not intended to be sold and is intended to promote the sale of the drug. Nothing in this paragraph shall subject an officer or executive of a drug manufacturer or distributor to criminal liability solely because of a sale, purchase, trade, or offer to sell, purchase, or trade in violation of this paragraph by other employees of the manufacturer or distributor.

(2) No person may sell, purchase, or trade, offer to sell, purchase, or trade, or counterfeit any coupon. For purposes of this paragraph, the term ''coupon'' means a form which may be redeemed, at no cost or at a reduced cost, for a drug which is prescribed in accordance with subsection (b).

(3)(A) No person may sell, purchase, or trade, or offer to sell, purchase, or trade, any drug—

(i) which is subject to subsection (b), and

(ii)(I) which was purchased by a public or private hospital or other health care entity, or

(II) which was donated or supplied at a reduced price to a charitable organization described in section 501(c)(3) of title 26.

(B) Subparagraph (A) does not apply to—

(i) the purchase or other acquisition by a hospital or other health care entity which is a member of a group purchasing organization of a drug for its own use from the group purchasing organization or from other hospitals or health care entities which are members of such organization,

(ii) the sale, purchase, or trade of a drug or an offer to sell, purchase, or trade a drug by an organization described in subparagraph (A)(ii)(II) to a nonprofit affiliate of the organization to the extent otherwise permitted by law,

(iii) a sale, purchase, or trade of a drug or an offer to sell, purchase, or trade a drug among hospitals or other health care entities which are under common control,

(iv) a sale, purchase, or trade of a drug or an offer to sell, purchase, or trade a drug for emergency medical reasons, or

(v) a sale, purchase, or trade of a drug, an offer to sell, purchase, or trade a drug, or the dispensing of a drug pursuant to a prescription executed in accordance with subsection (b).

For purposes of this paragraph, the term ''entity'' does not include a wholesale distributor of drugs or a retail pharmacy licensed under State law and the term ''emergency medical reasons'' includes transfers of a drug between health care entities or from a health care entity to a retail pharmacy undertaken to alleviate temporary shortages of the drug arising from delays in or interruptions of regular distribution schedules.

(d) Distribution of drug samples

(1) Except as provided in paragraphs (2) and (3), no person may distribute any drug sample. For purposes of this subsection, the term ''distribute'' does not include the providing of a drug sample to a patient by a—

(A) practitioner licensed to prescribe such drug,

(B) health care professional acting at the direction and under the supervision of such a practitioner, or

(C) pharmacy of a hospital or of another health care entity that is acting at the direction of such a practitioner and that received such sample pursuant to paragraph (2) or (3).

(2)(A) The manufacturer or authorized distributor of record of a drug subject to subsection (b) may, in accordance with this paragraph, distribute drug samples by mail or common carrier to practitioners licensed to prescribe such drugs or, at the request of a licensed practitioner, to pharmacies of hospitals or other health care entities. Such a distribution of drug samples may only be made—

(i) in response to a written request for drug samples made on a form which meets the requirements of subparagraph (B), and

(ii) under a system which requires the recipient of the drug sample to execute a written receipt for the drug sample upon its delivery and the return of the receipt to the manufacturer or authorized distributor of record.

(B) A written request for a drug sample required by subparagraph (A)(i) shall contain—

(i) the name, address, professional designation, and signature of the practitioner making the request,

(ii) the identity of the drug sample requested and the quantity requested,

(iii) the name of the manufacturer of the drug sample requested, and

(iv) the date of the request.

(C) Each drug manufacturer or authorized distributor of record which makes distributions by mail or common carrier under this paragraph shall maintain, for a period of 3 years, the request forms submitted for such distributions and the receipts submitted for such distributions and shall maintain a record of distributions of drug samples which identifies the drugs distributed and the recipients of the distributions. Forms, receipts, and records required to be maintained under this subparagraph shall be made available by the drug manufacturer or authorized distributor of record to Federal and State officials engaged in the regulation of drugs and in the enforcement of laws applicable to drugs.

(3) The manufacturer or authorized distributor of record of a drug subject to subsection (b) may, by means other than mail or common carrier, distribute drug samples only if the manufacturer or authorized distributor of record makes the distributions in accordance with subparagraph (A) and carries out the activities described in subparagraphs (B) through (F) as follows:

(A) Drug samples may only be distributed—

(i) to practitioners licensed to prescribe such drugs if they make a written request for the drug samples, or

(ii) at the written request of such a licensed practitioner, to pharmacies of hospitals or other health care entities.

A written request for drug samples shall be made on a form which contains the practitioner's name, address, and professional designation, the identity of the drug sample requested, the quantity of drug samples requested, the name of the manufacturer or authorized distributor of record of the drug sample, the date of the request and signature of the practitioner making the request.

(B) Drug manufacturers or authorized distributors of record shall store drug samples under conditions that will maintain their stability, integrity, and effectiveness and will assure that the drug samples will be free of contamination, deterioration, and adulteration.

(C) Drug manufacturers or authorized distributors of record shall conduct, at least annually, a complete and accurate inventory of all drug samples in the possession of representatives of the manufacturer or authorized distributor of record. Drug manufacturers or authorized distributors of record shall maintain lists of the names and address of each of their representatives who distribute drug samples and of the sites where drug sam-

ples are stored. Drug manufacturers or authorized distributors of record shall maintain records for at least 3 years of all drug samples distributed, destroyed, or returned to the manufacturer or authorized distributor of record, of all inventories maintained under this subparagraph, of all thefts or significant losses of drug samples, and of all requests made under subparagraph (A) for drug samples. Records and lists maintained under this subparagraph shall be made available by the drug manufacturer or authorized distributor of record to the Secretary upon request.

(D) Drug manufacturers or authorized distributors of record shall notify the Secretary of any significant loss of drug samples and any known theft of drug samples.

(E) Drug manufacturers or authorized distributors of record shall report to the Secretary any conviction of their representatives for violations of subsection (c)(1) or a State law because of the sale, purchase, or trade of a drug sample or the offer to sell, purchase, or trade a drug sample.

(F) Drug manufacturers or authorized distributors of record shall provide to the Secretary the name and telephone number of the individual responsible for responding to a request for information respecting drug samples.

(4) In this subsection, the term ''authorized distributors of record'' means those distributors with whom a manufacturer has established an ongoing relationship to distribute such manufacturer's products.

(e) Licensing and reporting requirements for wholesale distributors; fees; definitions

(1) REQUIREMENT.—Subject to section 360eee–2 of this title:

(A) IN GENERAL.—No person may engage in wholesale distribution of a drug subject to subsection (b)(1) in any State unless such person—

(i)(I) is licensed by the State from which the drug is distributed; or

(II) if the State from which the drug is distributed has not established a licensure requirement, is licensed by the Secretary; and

(ii) if the drug is distributed interstate, is licensed by the State into which the drug is distributed if the State into which the drug is distributed requires the licensure of a person that distributes drugs into the State.

(B) STANDARDS.—Each Federal and State license described in subparagraph (A) shall meet the standards, terms, and conditions established by the Secretary under section 360eee–2 of this title.

(2) REPORTING AND DATABASE.—

(A) REPORTING.—Beginning January 1, 2015, any person who owns or operates an establishment that engages in wholesale distribution shall—

(i) report to the Secretary, on an annual basis pursuant to a schedule determined by the Secretary—

(I) each State by which the person is licensed and the appropriate identification number of each such license; and

(II) the name, address, and contact information of each facility at which, and all trade names under which, the person conducts business; and

(ii) report to the Secretary within a reasonable period of time and in a reasonable manner, as determined by the Secretary, any significant disciplinary actions, such as the revocation or suspension of a wholesale distributor license, taken by a State or the Federal Government during the reporting period against the wholesale distributor.

(B) DATABASE.—Not later than January 1, 2015, the Secretary shall establish a database of authorized wholesale distributors. Such database shall—

(i) identify each authorized wholesale distributor by name, contact information, and each State where such wholesale distributor is appropriately licensed to engage in wholesale distribution;

(ii) be available to the public on the Internet Web site of the Food and Drug Administration; and

(iii) be regularly updated on a schedule determined by the Secretary.

(C) COORDINATION.—The Secretary shall establish a format and procedure for appropriate State officials to access the information provided pursuant to subparagraph (A) in a prompt and secure manner.

(D) CONFIDENTIALITY.—Nothing in this paragraph shall be construed as authorizing the Secretary to disclose any information that is a trade secret or confidential information subject to section 552(b)(4) of title 5 or section 1905 of title 18.

(3) COSTS.—

(A) AUTHORIZED FEES OF SECRETARY.—If a State does not establish a licensing program for persons engaged in the wholesale distribution of a drug subject to subsection (b), the Secretary shall license a person engaged in wholesale distribution located in such State and may collect a reasonable fee in such amount necessary to reimburse the Secretary for costs associated with establishing and administering the licensure program and conducting periodic inspections under this section. The Secretary shall adjust fee rates as needed on an annual basis to generate only the amount of revenue needed to perform this service. Fees authorized under this paragraph shall be collected and available for obligation only to the extent and in the amount provided in advance in appropriations Acts. Such fees are authorized to remain available until expended. Such sums as may be necessary may be transferred from the Food and Drug Administration salaries and expenses appropriation account without fiscal year limitation to such appropriation account for salaries and expenses with such fiscal year limitation.

(B) STATE LICENSING FEES.—Nothing in this chapter shall prohibit States from collecting fees from wholesale distributors in connection with State licensing of such distributors.

(4) For the purposes of this subsection and subsection (d), the term ''wholesale distribution'' means the distribution of a drug subject to subsection (b) to a person other than a consumer or

patient, or receipt of a drug subject to subsection (b) by a person other than the consumer or patient, but does not include—

(A) intracompany distribution of any drug between members of an affiliate or within a manufacturer;

(B) the distribution of a drug, or an offer to distribute a drug among hospitals or other health care entities which are under common control;

(C) the distribution of a drug or an offer to distribute a drug for emergency medical reasons, including a public health emergency declaration pursuant to section 319 of the Public Health Service Act [42 U.S.C. 247d], except that, for purposes of this paragraph, a drug shortage not caused by a public health emergency shall not constitute an emergency medical reason;

(D) the dispensing of a drug pursuant to a prescription executed in accordance with subsection (b)(1);

(E) the distribution of minimal quantities of drug by a licensed retail pharmacy to a licensed practitioner for office use;

(F) the distribution of a drug or an offer to distribute a drug by a charitable organization to a nonprofit affiliate of the organization to the extent otherwise permitted by law;

(G) the purchase or other acquisition by a dispenser, hospital, or other health care entity of a drug for use by such dispenser, hospital, or other health care entity;

(H) the distribution of a drug by the manufacturer of such drug;

(I) the receipt or transfer of a drug by an authorized third-party logistics provider provided that such third-party logistics provider does not take ownership of the drug;

(J) a common carrier that transports a drug, provided that the common carrier does not take ownership of the drug;

(K) the distribution of a drug, or an offer to distribute a drug by an authorized repackager that has taken ownership or possession of the drug and repacks it in accordance with section 360eee–1(e) of this title;

(L) salable drug returns when conducted by a dispenser;

(M) the distribution of a collection of finished medical devices, which may include a product or biological product, assembled in kit form strictly for the convenience of the purchaser or user (referred to in this subparagraph as a ''medical convenience kit'') if—

(i) the medical convenience kit is assembled in an establishment that is registered with the Food and Drug Administration as a device manufacturer in accordance with section 360(b)(2) of this title;

(ii) the medical convenience kit does not contain a controlled substance that appears in a schedule contained in the Comprehensive Drug Abuse Prevention and Control Act of 1970 [21 U.S.C. 801 et seq.];

(iii) in the case of a medical convenience kit that includes a product, the person that manufacturers the kit—

(I) purchased such product directly from the pharmaceutical manufacturer or from a wholesale distributor that purchased the product directly from the pharmaceutical manufacturer; and

(II) does not alter the primary container or label of the product as purchased from the manufacturer or wholesale distributor; and

(iv) in the case of a medical convenience kit that includes a product, the product is—

(I) an intravenous solution intended for the replenishment of fluids and electrolytes;

(II) a product intended to maintain the equilibrium of water and minerals in the body;

(III) a product intended for irrigation or reconstitution;

(IV) an anesthetic;

(V) an anticoagulant;

(VI) a vasopressor; or

(VII) a sympathomimetic;

(N) the distribution of an intravenous drug that, by its formulation, is intended for the replenishment of fluids and electrolytes (such as sodium, chloride, and potassium) or calories (such as dextrose and amino acids);

(O) the distribution of an intravenous drug used to maintain the equilibrium of water and minerals in the body, such as dialysis solutions;

(P) the distribution of a drug that is intended for irrigation, or sterile water, whether intended for such purposes or for injection;

(Q) the distribution of medical gas, as defined in section 360ddd of this title;

(R) facilitating the distribution of a product by providing solely administrative services, including processing of orders and payments; or

(S) the transfer of a product by a hospital or other health care entity, or by a wholesale distributor or manufacturer operating at the direction of the hospital or other health care entity, to a repackager described in section 360eee(16)(B) of this title and registered under section 360 of this title for the purpose of repackaging the drug for use by that hospital, or other health care entity and other health care entities that are under common control, if ownership of the drug remains with the hospital or other health care entity at all times.

(5) THIRD-PARTY LOGISTICS PROVIDERS.—Notwithstanding paragraphs (1) through (4), each entity that meets the definition of a third-party logistics provider under section 360eee(22) of this title shall obtain a license as a third-party logistics provider as described in section 360eee–3(a) of this title and is not required to obtain a license as a wholesale distributor if the entity never assumes an ownership interest in the product it handles.

(6) AFFILIATE.—For purposes of this subsection, the term ''affiliate'' means a business entity that has a relationship with a second business entity if, directly or indirectly—

(A) one business entity controls, or has the power to control, the other business entity; or

(B) a third party controls, or has the power to control, both of the business entities.

(f) Veterinary prescription drugs

(1)(A) A drug intended for use by animals other than man, other than a veterinary feed di-

rective drug intended for use in animal feed or an animal feed bearing or containing a veterinary feed directive drug, which—

(i) because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary for its use, is not safe for animal use except under the professional supervision of a licensed veterinarian, or

(ii) is limited by an approved application under subsection (b) of section 360b of this title, a conditionally-approved application under section 360ccc of this title, or an index listing under section 360ccc–1 of this title to use under the professional supervision of a licensed veterinarian,

shall be dispensed only by or upon the lawful written or oral order of a licensed veterinarian in the course of the veterinarian's professional practice.

(B) For purposes of subparagraph (A), an order is lawful if the order—

(i) is a prescription or other order authorized by law,

(ii) is, if an oral order, promptly reduced to writing by the person lawfully filling the order, and filed by that person, and

(iii) is refilled only if authorized in the original order or in a subsequent oral order promptly reduced to writing by the person lawfully filling the order, and filed by that person.

(C) The act of dispensing a drug contrary to the provisions of this paragraph shall be deemed to be an act which results in the drug being misbranded while held for sale.

(2) Any drug when dispensed in accordance with paragraph (1) of this subsection—

(A) shall be exempt from the requirements of section 352 of this title, except subsections (a), (g), (h), (i)(2), (i)(3), and (p) of such section, and

(B) shall be exempt from the packaging requirements of subsections (g), (h), and (p) of such section, if—

(i) when dispensed by a licensed veterinarian, the drug bears a label containing the name and address of the practitioner and any directions for use and cautionary statements specified by the practitioner, or

(ii) when dispensed by filling the lawful order of a licensed veterinarian, the drug bears a label containing the name and address of the dispenser, the serial number and date of the order or of its filling, the name of the licensed veterinarian, and the directions for use and cautionary statements, if any, contained in such order.

The preceding sentence shall not apply to any drug dispensed in the course of the conduct of a business of dispensing drugs pursuant to diagnosis by mail.

(3) The Secretary may by regulation exempt drugs for animals other than man subject to section 360b, 360ccc, or 360ccc–1 of this title from the requirements of paragraph (1) when such requirements are not necessary for the protection of the public health.

(4) A drug which is subject to paragraph (1) shall be deemed to be misbranded if at any time prior to dispensing its label fails to bear the statement ''Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.''. A drug to which paragraph (1) does not apply shall be deemed to be misbranded if at any time prior to dispensing its label bears the statement specified in the preceding sentence.

(g) Regulation of combination products

(1)(A) The Secretary shall, in accordance with this subsection, assign a primary agency center to regulate products that constitute a combination of a drug, device, or biological product.

(B) The Secretary shall conduct the premarket review of any combination product under a single application, whenever appropriate.

(C) For purposes of this subsection, the term ''primary mode of action'' means the single mode of action of a combination product expected to make the greatest contribution to the overall intended therapeutic effects of the combination product.

(D) The Secretary shall determine the primary mode of action of the combination product. If the Secretary determines that the primary mode of action is that of—

(i) a drug (other than a biological product), the agency center charged with premarket review of drugs shall have primary jurisdiction;

(ii) a device, the agency center charged with premarket review of devices shall have primary jurisdiction; or

(iii) a biological product, the agency center charged with premarket review of biological products shall have primary jurisdiction.

(E) In determining the primary mode of action of a combination product, the Secretary shall not determine that the primary mode of action is that of a drug or biological product solely because the combination product has any chemical action within or on the human body.

(F) If a sponsor of a combination product disagrees with the determination under subparagraph (D)—

(i) such sponsor may request, and the Secretary shall provide, a substantive rationale to such sponsor that references scientific evidence provided by the sponsor and any other scientific evidence relied upon by the Secretary to support such determination; and

(ii)(I) the sponsor of the combination product may propose one or more studies (which may be nonclinical, clinical, or both) to establish the relevance, if any, of the chemical action in achieving the primary mode of action of such product;

(II) if the sponsor proposes any such studies, the Secretary and the sponsor of such product shall collaborate and seek to reach agreement, within a reasonable time of such proposal, not to exceed 90 calendar days, on the design of such studies; and

(III) if an agreement is reached under subclause (II) and the sponsor conducts one or more of such studies, the Secretary shall consider the data resulting from any such study when reevaluating the determination of the primary mode of action of such product, and unless and until such reevaluation has occurred and the Secretary issues a new determination, the determination of the Secretary under subparagraph (D) shall remain in effect.

(2)(A)[1](i) To establish clarity and certainty for the sponsor, the sponsor of a combination product may request a meeting on such combination product. If the Secretary concludes that a determination of the primary mode of action pursuant to paragraph (1)(D) is necessary, the sponsor may request such meeting only after the Secretary makes such determination. If the sponsor submits a written meeting request, the Secretary shall, not later than 75 calendar days after receiving such request, meet with the sponsor of such combination product.

(ii) A meeting under clause (i) may—

(I) address the standards and requirements for market approval or clearance of the combination product;

(II) address other issues relevant to such combination product, such as requirements related to postmarket modification of such combination product and good manufacturing practices applicable to such combination product; and

(III) identify elements under subclauses (I) and (II) that may be more appropriate for discussion and agreement with the Secretary at a later date given that scientific or other information is not available, or agreement is otherwise not feasible regarding such elements, at the time a request for such meeting is made.

(iii) Any agreement under this subparagraph shall be in writing and made part of the administrative record by the Secretary.

(iv) Any such agreement shall remain in effect, except—

(I) upon the written agreement of the Secretary and the sponsor or applicant; or

(II) pursuant to a decision by the director of the reviewing division of the primary agency center, or a person more senior than such director, in consultation with consulting centers and the Office, as appropriate, that an issue essential to determining whether the standard for market clearance or other applicable standard under this chapter or the Public Health Service Act [42 U.S.C. 201 et seq.] applicable to the combination product has been identified since the agreement was reached, or that deviating from the agreement is otherwise justifiable based on scientific evidence, for public health reasons.

(3) For purposes of conducting the premarket review of a combination product that contains an approved constituent part described in paragraph (4), the Secretary may require that the sponsor of such combination product submit to the Secretary only data or information that the Secretary determines is necessary to meet the standard for clearance or approval, as applicable, under this chapter or the Public Health Service Act, including any incremental risks and benefits posed by such combination product, using a risk-based approach and taking into account any prior finding of safety and effectiveness or substantial equivalence for the approved constituent part relied upon by the applicant in accordance with paragraph (5).

(4) For purposes of paragraph (3), an approved constituent part is—

(A) a drug constituent part of a combination product being reviewed in a single application or request under section 360e, 360(k), or 360c(f)(2) of this title (submitted in accordance with paragraph (5)), that is an approved drug, provided such application or request complies with paragraph (5);

(B) a device constituent part approved under section 360e of this title that is referenced by the sponsor and that is available for use by the Secretary under section 360j(h)(4) of this title; or

(C) any constituent part that was previously approved, cleared, or classified under section 355, 360(k), 360c(f)(2), or 360e of this title for which the sponsor has a right of reference or any constituent part that is a nonprescription drug, as defined in section 379aa(a)(2) of this title.

(5)(A) If an application is submitted under section 360e or 360(k) of this title or a request is submitted under section 360c(f)(2) of this title, consistent with any determination made under paragraph (1)(D), for a combination product containing as a constituent part an approved drug—

(i) the application or request shall include the certification or statement described in section 355(b)(2) of this title; and

(ii) the applicant or requester shall provide notice as described in section 355(b)(3) of this title.

(B) For purposes of this paragraph and paragraph (4), the term ''approved drug'' means an active ingredient—

(i) that was in an application previously approved under section 355(c) of this title;

(ii) where such application is relied upon by the applicant submitting the application or request described in subparagraph (A);

(iii) for which full reports of investigations that have been made to show whether such drug is safe for use and whether such drug is effective in use were not conducted by or for the applicant submitting the application or request described in subparagraph (A); and

(iv) for which the applicant submitting the application or request described in subparagraph (A) has not obtained a right of reference or use from the person by or for whom the investigations described in clause (iii) were conducted.

(C) The following provisions shall apply with respect to an application or request described in subparagraph (A) to the same extent and in the same manner as if such application or request were an application described in section 355(b)(2) of this title that referenced the approved drug:

(i) Subparagraphs (A), (B), (C), and (D) of section 355(c)(3) of this title.

(ii) Clauses (ii), (iii), and (iv) of section 355(c)(3)(E) of this title.

(iii) Subsections (b) and (c) of section 355a of this title.

(iv) Section 355f(a) of this title.

(v) Section 360cc(a) of this title.

(D) Notwithstanding any other provision of this subsection, an application or request for classification for a combination product described in subparagraph (A) shall be considered

[1] So in original. No subpar. (B) has been enacted.

an application submitted under section 355(b)(2) of this title for purposes of section 271(e)(2)(A) of title 35.

(6) Nothing in this subsection shall be construed as prohibiting a sponsor from submitting separate applications for the constituent parts of a combination product, unless the Secretary determines that a single application is necessary.

(7) Nothing in this subsection shall prevent the Secretary from using any agency resources of the Food and Drug Administration necessary to ensure adequate review of the safety, effectiveness, or substantial equivalence of an article.

(8)(A) Not later than 60 days after October 26, 2002, the Secretary shall establish within the Office of the Commissioner of Food and Drugs an office to ensure the prompt assignment of combination products to agency centers, the timely and effective premarket review of such products, and consistent and appropriate postmarket regulation of like products subject to the same statutory requirements to the extent permitted by law. Additionally, the office shall, in determining whether a product is to be designated a combination product, consult with the component within the Office of the Commissioner of Food and Drugs that is responsible for such determinations. Such office (referred to in this paragraph as the ''Office'') shall have appropriate scientific and medical expertise, and shall be headed by a director.

(B) In carrying out this subsection, the Office shall, for each combination product, promptly assign an agency center with primary jurisdiction in accordance with paragraph (1) for the premarket review of such product.

(C)(i) In carrying out this subsection, the Office shall help to ensure timely and effective premarket review that involves more than one agency center by coordinating such reviews, overseeing the timeliness of such reviews, and overseeing the alignment of feedback regarding such reviews.

(ii) In order to ensure the timeliness and alignment of the premarket review of a combination product, the agency center with primary jurisdiction for the product, and the consulting agency center, shall be responsible to the Office with respect to the timeliness and alignment of the premarket review.

(iii) The Office shall ensure that, with respect to a combination product, a designated person or persons in the primary agency center is the primary point or points of contact for the sponsor of such combination product. The Office shall also coordinate communications to and from any consulting center involved in such premarket review, if requested by such primary agency center or any such consulting center. Agency communications and commitments, to the extent consistent with other provisions of law and the requirements of all affected agency centers, from the primary agency center shall be considered as communication from the Secretary on behalf of all agency centers involved in the review.

(iv) The Office shall, with respect to the premarket review of a combination product—

(I) ensure that any meeting between the Secretary and the sponsor of such product is attended by each agency center involved in the review, as appropriate;

(II) ensure that each consulting agency center has completed its premarket review and provided the results of such review to the primary agency center in a timely manner; and

(III) ensure that each consulting center follows the guidance described in clause (vi) and advises, as appropriate, on other relevant regulations, guidances, and policies.

(v) In seeking agency action with respect to a combination product, the sponsor of such product—

(I) shall identify the product as a combination product; and

(II) may request in writing the participation of representatives of the Office in meetings related to such combination product, or to have the Office otherwise engage on such regulatory matters concerning the combination product.

(vi) Not later than 4 years after December 13, 2016, and after a public comment period of not less than 60 calendar days, the Secretary shall issue a final guidance that describes—

(I) the structured process for managing presubmission interactions with sponsors developing combination products;

(II) the best practices for ensuring that the feedback in such pre-submission interactions represents the Agency's best advice based on the information provided during such pre-submission interactions;[2]

(III) the information that is required to be submitted with a meeting request under paragraph (2), how such meetings relate to other types of meetings in the Food and Drug Administration, and the form and content of any agreement reached through a meeting under such paragraph (2);[3]

(D) In carrying out this subsection, the Office shall ensure the consistency and appropriateness of postmarket regulation of like products subject to the same statutory requirements to the extent permitted by law.

(E)(i) Any dispute regarding the timeliness of the premarket review of a combination product may be presented to the Office for resolution, unless the dispute is clearly premature.

(ii) During the review process, any dispute regarding the substance of the premarket review may be presented to the Commissioner of Food and Drugs after first being considered by the agency center with primary jurisdiction of the premarket review, under the scientific dispute resolution procedures for such center. The Commissioner of Food and Drugs shall consult with the Director of the Office in resolving the substantive dispute.

(F) The Secretary, acting through the Office, shall review each agreement, guidance, or practice of the Secretary that is specific to the assignment of combination products to agency centers and shall determine whether the agreement, guidance, or practice is consistent with the requirements of this subsection. In carrying out such review, the Secretary shall consult

[2] So in original. The word ''and'' probably should appear.

[3] So in original. The semicolon probably should be a period.

with stakeholders and the directors of the agency centers. After such consultation, the Secretary shall determine whether to continue in effect, modify, revise, or eliminate such agreement, guidance, or practice, and shall publish in the Federal Register a notice of the availability of such modified or revised agreement, guidance or practice. Nothing in this paragraph shall be construed as preventing the Secretary from following each agreement, guidance, or practice until continued, modified, revised, or eliminated.

(G) Not later than one year after October 26, 2002 (except with respect to clause (iv), beginning not later than one year after December 13, 2016), and annually thereafter, the Secretary shall report to the appropriate committees of Congress on the activities and impact of the Office. The report shall include provisions—

(i) describing the numbers and types of combination products under review and the timeliness in days of such assignments, reviews, and dispute resolutions;

(ii) identifying the number of premarket reviews of such products that involved a consulting agency center;

(iii) describing improvements in the consistency of postmarket regulation of combination products; and

(iv) identifying the percentage of combination products for which a dispute resolution, with respect to premarket review, was requested by the combination product's sponsor.

(H) Nothing in this paragraph shall be construed to limit the regulatory authority of any agency center.

(9) As used in this subsection:

(A) The term ''agency center'' means a center or alternative organizational component of the Food and Drug Administration.

(B) The term ''biological product'' has the meaning given the term in section 351(i) of the Public Health Service Act (42 U.S.C. 262(i)).

(C) The term ''market clearance'' includes—

(i) approval of an application under section 355, 357,[4] 360e, or 360j(g) of this title;

(ii) a finding of substantial equivalence under this part;

(iii) approval of a biologics license application under subsection (a) of section 351 of the Public Health Service Act (42 U.S.C. 262); and

(iv) de novo classification under section 360c(a)(1) of this title.

(D) The terms ''premarket review'' and ''reviews'' include all activities of the Food and Drug Administration conducted prior to approval or clearance of an application, notification, or request for classification submitted under section 355, 360(k), 360c(f)(2), 360e, or 360j of this title or under section 351 of the Public Health Service Act [42 U.S.C. 262], including with respect to investigational use of the product.

(h) Regulation of certain products as drugs

(1) Any contrast agent, radioactive drug, or OTC monograph drug shall be deemed to be a drug under section 321(g) of this title and not a device under section 321(h) of this title.

(2) For purposes of this subsection:

(A) The term ''contrast agent'' means an article that is intended for use in conjunction with a medical imaging device, and—

(i) is a diagnostic radiopharmaceutical, as defined in sections 315.2 and 601.31 of title 21, Code of Federal Regulations (or any successor regulations); or

(ii) is a diagnostic agent that improves the visualization of structure or function within the body by increasing the relative difference in signal intensity within the target tissue, structure, or fluid.

(B) The term ''radioactive drug'' has the meaning given such term in section 310.3(n) of title 21, Code of Federal Regulations (or any successor regulations), except that such term does not include—

(i) an implant or article similar to an implant;

(ii) an article that applies radiation from outside of the body; or

(iii) the radiation source of an article described in clause (i) or (ii).

(C) The term ''OTC monograph drug'' has the meaning given such term in section 379j–71 of this title.

(3) Nothing in this subsection shall be construed as allowing for the classification of a product as a drug (as defined in section 321(g) of this title) if such product—

(A) is not described in paragraph (1); and

(B) meets the definition of a device under section 321(h) of this title,

unless another provision of this chapter otherwise indicates a different classification.

(4) The Secretary shall waive the application fee under sections 379h and 379j–42 of this title for applications for drugs that are—

(A) on September 30, 2022, legally marketed as devices; and

(B) deemed drugs pursuant to paragraph (1)[5]

(June 25, 1938, ch. 675, §503, 52 Stat. 1051; Oct. 26, 1951, ch. 578, §1, 65 Stat. 648; Pub. L. 87–781, title I, §104(e)(2), Oct. 10, 1962, 76 Stat. 785; Pub. L. 91–601, §6(e), formerly §7(e), Dec. 30, 1970, 84 Stat. 1673, renumbered Pub. L. 97–35, title XII, §1205(c), Aug. 13, 1981, 95 Stat. 716; Pub. L. 100–293, §§4–6, Apr. 22, 1988, 102 Stat. 96–98; Pub. L. 100–670, title I, §105, Nov. 16, 1988, 102 Stat. 3983; Pub. L. 101–629, §16(a), Nov. 28, 1990, 104 Stat. 4526; Pub. L. 102–108, §2(d), Aug. 17, 1991, 105 Stat. 550; Pub. L. 102–300, §6(d), June 16, 1992, 106 Stat. 240; Pub. L. 102–353, §§2(a)–(c), 4, Aug. 26, 1992, 106 Stat. 941, 942; Pub. L. 104–250, §5(a), Oct. 9, 1996, 110 Stat. 3155; Pub. L. 105–115, title I, §§123(e), 126(a), (c)(1), (2), Nov. 21, 1997, 111 Stat. 2324, 2327, 2328; Pub. L. 107–250, title II, §204, Oct. 26, 2002, 116 Stat. 1611; Pub. L. 108–282, title I, §102(b)(5)(F), Aug. 2, 2004, 118 Stat. 903; Pub. L. 113–54, title II, §204(a)(1)–(4), (b), Nov. 27, 2013, 127 Stat. 630–635; Pub. L. 114–255, div. A, title III, §3038(a), Dec. 13, 2016, 130 Stat. 1105; Pub. L. 117–328, div. FF, title III, §3621, Dec. 29, 2022, 136 Stat. 5877.)

[4] See References in Text note below.

[5] So in original. Probably should be followed by a period.

Editorial Notes

REFERENCES IN TEXT

The Comprehensive Drug Abuse Prevention and Control Act of 1970, referred to in subsec. (e)(4)(M)(ii), is Pub. L. 91–513, Oct. 27, 1970, 84 Stat. 1236, which is classified principally to chapter 13 (§ 801 et seq.) of this title. For complete classification of this Act to the Code, see Short Title note set out under section 801 of this title and Tables.

The Public Health Service Act, referred to in subsec. (g)(2)(A)(iv)(II), (3), is act July 1, 1944, ch. 373, 58 Stat. 682, which is classified generally to chapter 6A (§ 201 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 201 of Title 42 and Tables.

Section 357 of this title, referred to in subsec. (g)(9)(C)(i), was repealed by Pub. L. 105–115, title I, § 125(b)(1), Nov. 21, 1997, 111 Stat. 2325.

CODIFICATION

In subsec. (b)(5), ''sections 4721, 6001, and 6151 of title 26'' and ''section 4761 of title 26'' substituted for ''section 3220 of the Internal Revenue Code (26 U.S.C. 3220)'' and ''section 3238(b) of the Internal Revenue Code (26 U.S.C. 3238(b))'', respectively, on authority of section 7852(b) of Title 26, Internal Revenue Code.

AMENDMENTS

2022—Subsec. (h). Pub. L. 117–328 added subsec. (h).

2016—Subsec. (g)(1). Pub. L. 114–255, § 3038(a)(4), added par. (1) and struck out former par. (1) which read as follows: ''The Secretary shall in accordance with this subsection assign an agency center to regulate products that constitute a combination of a drug, device, or biological product. The Secretary shall determine the primary mode of action of the combination product. If the Secretary determines that the primary mode of action is that of—

''(A) a drug (other than a biological product), the agency center charged with premarket review of drugs shall have primary jurisdiction,

''(B) a device, the agency center charged with premarket review of devices shall have primary jurisdiction, or

''(C) a biological product, the agency center charged with premarket review of biological products shall have primary jurisdiction.''

Subsec. (g)(2). Pub. L. 114–255, § 3038(a)(4), added par. (2). Former par. (2) redesignated (7).

Subsec. (g)(3). Pub. L. 114–255, § 3038(a)(1), (4), added par. (3) and struck out former par. (3) which read as follows: ''The Secretary shall promulgate regulations to implement market clearance procedures in accordance with paragraphs (1) and (2) not later than 1 year after November 28, 1990.''

Subsec. (g)(4) to (6). Pub. L. 114–255, § 3038(a)(4), added pars. (4) to (6). Former pars. (4) and (5) redesignated (8) and (9), respectively.

Subsec. (g)(7). Pub. L. 114–255, § 3038(a)(2), redesignated par. (2) as (7).

Subsec. (g)(8). Pub. L. 114–255, § 3038(a)(3), redesignated par. (4) as (8).

Subsec. (g)(8)(C)(i). Pub. L. 114–255, § 3038(a)(5)(A)(i), amended cl. (i) generally. Prior to amendment, cl. (i) read as follows: ''In carrying out this subsection, the Office shall ensure timely and effective premarket reviews by overseeing the timeliness of and coordinating reviews involving more than one agency center.''

Subsec. (g)(8)(C)(ii). Pub. L. 114–255, § 3038(a)(5)(A)(ii), inserted ''and alignment'' after ''the timeliness'' in two places.

Subsec. (g)(8)(C)(iii) to (vi). Pub. L. 114–255, § 3038(a)(5)(A)(iii), added cls. (iii) to (vi).

Subsec. (g)(8)(G). Pub. L. 114–255, § 3038(a)(5)(B)(i), inserted ''(except with respect to clause (iv), beginning not later than one year after December 13, 2016)'' after ''October 26, 2002'' in introductory provisions.

Subsec. (g)(8)(G)(iv). Pub. L. 114–255, § 3038(a)(5)(B)(ii)–(iv), added cl. (iv).

Subsec. (g)(9). Pub. L. 114–255, § 3038(a)(3), redesignated par. (5) as (9).

Subsec. (g)(9)(C). Pub. L. 114–255, § 3038(a)(6)(A), substituted semicolon for comma at end of cl. (i), semicolon for '', and'' at end of cl. (ii), and ''; and'' for period at end of cl. (iii), and added cl. (iv).

Subsec. (g)(9)(D). Pub. L. 114–255, § 3038(a)(6)(B), added subpar. (D).

2013—Subsec. (d)(4). Pub. L. 113–54, § 204(b), added par. (4).

Subsec. (e). Pub. L. 113–54, § 204(a)(1)–(4), added pars. (1) to (6) and struck out former pars. (1) to (3). Prior to amendment, pars. (1) to (3) set out certain disclosure and licensing requirements for wholesale distributors and defined ''authorized distributors of record'' and ''wholesale distribution''.

2004—Subsec. (f)(1)(A)(ii). Pub. L. 108–282, § 102(b)(5)(F)(i), substituted ''360b of this title, a conditionally-approved application under section 360ccc of this title, or an index listing under section 360ccc–1 of this title'' for ''360b of this title''.

Subsec. (f)(3). Pub. L. 108–282, § 102(b)(5)(F)(ii), substituted ''section 360b, 360ccc, or 360ccc–1'' for ''section 360b''.

2002—Subsec. (g)(1). Pub. L. 107–250, § 204(1)(A), substituted ''shall in accordance with this subsection assign an agency center'' for ''shall designate a component of the Food and Drug Administration'' in first sentence of introductory provisions.

Subsec. (g)(1)(A) to (C). Pub. L. 107–250, § 204(1)(B), substituted ''the agency center charged'' for ''the persons charged''.

Subsec. (g)(4). Pub. L. 107–250, § 204(3), added par. (4). Former par. (4) redesignated (5).

Subsec. (g)(5). Pub. L. 107–250, § 204(2), (4), redesignated par. (4) as (5), added subpar. (A), and redesignated former subpars. (A) and (B) as (B) and (C), respectively.

1997—Subsec. (b)(1)(A) to (C). Pub. L. 105–115, § 126(c)(1), redesignated subpars. (B) and (C) as (A) and (B), respectively, and struck out former subpar. (A), which read as follows: ''is a habit-forming drug to which section 352(d) of this title applies; or''.

Subsec. (b)(3). Pub. L. 105–115, § 126(c)(2), struck out reference to section 352(d) of this title before ''355''.

Subsec. (b)(4). Pub. L. 105–115, § 126(a), amended par. (4) generally. Prior to amendment, par. (4) read as follows: ''A drug which is subject to paragraph (1) of this subsection shall be deemed to be misbranded if at any time prior to dispensing its label fails to bear the statement 'Caution: Federal law prohibits dispensing without prescription'. A drug to which paragraph (1) of this subsection does not apply shall be deemed to be misbranded if at any time prior to dispensing its label bears the caution statement quoted in the preceding sentence.''

Subsec. (g)(4)(A). Pub. L. 105–115, § 123(e)(1), substituted ''section 351(i)'' for ''section 351(a)'' and ''262(i)'' for ''262(a)''.

Subsec. (g)(4)(B)(iii). Pub. L. 105–115, § 123(e)(2), substituted ''biologics license application under subsection (a)'' for ''product or establishment license under subsection (a) or (d)''.

1996—Subsec. (f)(1)(A). Pub. L. 104–250 inserted '', other than a veterinary feed directive drug intended for use in animal feed or an animal feed bearing or containing a veterinary feed directive drug,'' after ''other than man'' in introductory provisions.

1992—Subsec. (d)(1). Pub. L. 102–353, § 4(1), amended par. (1) generally. Prior to amendment, par. (1) read as follows: ''Except as provided in paragraphs (2) and (3), no representative of a drug manufacturer or distributor may distribute any drug sample.''

Subsec. (d)(2). Pub. L. 102–353, § 4(2), substituted ''authorized distributor of record'' for ''distributor'' wherever appearing.

Subsec. (d)(3). Pub. L. 102–353, § 4(2), substituted ''authorized distributor of record'' for ''distributor'' and ''authorized distributors of record'' for ''distributors'' wherever appearing.

Subsec. (e)(1). Pub. L. 102–353, § 4(3), amended par. (1) generally. Prior to amendment, par. (1) read as follows: ''Each person who is engaged in the wholesale distribution of drugs subject to subsection (b) of this section and who is not an authorized distributor of record of such drugs shall provide to each wholesale distributor of such drugs a statement identifying each sale of the drug (including the date of the sale) before the sale to such wholesale distributor. Each manufacturer shall maintain at its corporate offices a current list of such authorized distributors.''

Subsec. (e)(2)(A). Pub. L. 102–353, § 2(a), (d), temporarily inserted ''or has registered with the Secretary in accordance with paragraph (3)''. See Termination Date of 1992 Amendment note below.

Subsec. (e)(3). Pub. L. 102–353, § 2(b), (d), temporarily added par. (3). Former par. (3) redesignated (4). See Termination Date of 1992 Amendment note below.

Subsec. (e)(4). Pub. L. 102–353, § 4(4), inserted ''and subsection (d) of this section'' after ''For the purposes of this subsection''.

Pub. L. 102–353, § 2(b), (d), temporarily redesignated par. (3) as (4). See Termination Date of 1992 Amendment note below.

Subsec. (f)(1)(B). Pub. L. 102–353, § 2(c), which directed the substitution of ''an order'' for ''and order'', could not be executed because ''and order'' did not appear in subpar. (B).

Subsec. (g)(3). Pub. L. 102–300 substituted ''clearance'' for ''approval''.

1991—Subsec. (c). Pub. L. 102–108, § 2(d)(3), redesignated subsec. (c), relating to veterinary prescription drugs, as (f). Former subsec. (f) redesignated (g).

Subsec. (c)(2), (3)(B)(v). Pub. L. 102–108, § 2(d)(1), made technical amendment to reference to subsection (b) of this section involving corresponding provision of original act.

Subsec. (d)(3)(E). Pub. L. 102–108, § 2(d)(2), made technical amendment to reference to subsection (c)(1) of this section involving corresponding provision of original act.

Subsec. (f). Pub. L. 102–108, § 2(d)(4), redesignated subsec. (f), relating to regulation of combination products, as (g).

Pub. L. 102–108, § 2(d)(3), redesignated subsec. (c), relating to veterinary prescription drugs, as (f).

Subsec. (g). Pub. L. 102–108, § 2(d)(4), redesignated subsec. (f), relating to regulation of combination products, as (g).

1990—Pub. L. 101–629, § 16(a)(1), substituted ''Exemptions and consideration for certain drugs, devices, and biological products'' for ''Exemptions in case of drugs and devices'' in section catchline.

Subsec. (f). Pub. L. 101–629, § 16(a)(2), added subsec. (f).

1988—Subsec. (c). Pub. L. 100–670 added subsec. (c) relating to veterinary prescription drugs.

Pub. L. 100–293, § 4, added subsec. (c) relating to sales restrictions.

Subsec. (d). Pub. L. 100–293, § 5, added subsec. (d).

Subsec. (e). Pub. L. 100–293, § 6, added subsec. (e).

1970—Subsec. (b)(2). Pub. L. 91–601 included exemption from packaging requirements of subsec. (p) of section 352 of this title.

1962—Subsec. (b)(1)(C). Pub. L. 87–781 substituted ''approved'' for ''effective''.

1951—Subsec. (b). Act Oct. 26, 1951, amended subsec. (b) generally to protect the public from abuses in the sale of potent prescription drugs, and to relieve retail pharmacists and the public from unnecessary restrictions on the dispensation of drugs that are safe to use without supervision of a doctor.

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 2013 AMENDMENT

Pub. L. 113–54, title II, § 204(c), Nov. 27, 2013, 127 Stat. 636, provided that: ''The amendments made by subsections (a) and (b) [enacting section 360eee–2 of this title and amending this section] shall take effect on January 1, 2015.''

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by Pub. L. 105–115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as a note under section 321 of this title.

TERMINATION DATE OF 1992 AMENDMENT

Pub. L. 102–353, § 2(d), Aug. 26, 1992, 106 Stat. 941, provided that: ''Effective September 14, 1994, the amendments made by subsections (a) and (b) [amending this section] shall no longer be in effect.''

EFFECTIVE DATE OF 1988 AMENDMENT

Pub. L. 100–293, § 8, Apr. 22, 1988, 102 Stat. 100, provided that:

''(a) GENERAL RULE.—Except as provided in subsection (b), this Act and the amendments made by this Act [amending this section and sections 331, 333, and 381 of this title and enacting provisions set out as notes under this section and section 301 of this title] shall take effect upon the expiration of 90 days after the date of the enactment of this Act [Apr. 22, 1988].

''(b) EXCEPTION.—

''(1) Section 503(d) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 353(d)] (as added by section 5 of this Act) shall take effect upon the expiration of 180 days after the date of the enactment of this Act [Apr. 22, 1988].

''(2) The Secretary of Health and Human Services shall by regulation issue the guidelines required by section 503(e)(2)(B) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 353(e)(2)(B)] (as added by section 6 of this Act) not later than 180 days after the date of the enactment of this Act. Section 503(e)(2)(A) of such Act shall take effect upon the expiration of 2 years after the date such regulations are promulgated and take effect.''

EFFECTIVE DATE OF 1970 AMENDMENT

Amendment by Pub. L. 91–601 effective Dec. 30, 1970, and regulations establishing special packaging standards effective no sooner than 180 days or later than one year from date regulations are final, or an earlier date published in Federal Register, see section 8 of Pub. L. 91–601, set out as an Effective Date note under section 1471 of Title 15, Commerce and Trade.

EFFECTIVE DATE OF 1962 AMENDMENT

Amendment by Pub. L. 87–781 effective Oct. 10, 1962, see section 107 of Pub. L. 87–781, set out as a note under section 321 of this title.

EFFECTIVE DATE OF 1951 AMENDMENT

Amendment by act Oct. 26, 1951, effective six months after Oct. 26, 1951, see section 3 of act Oct. 26, 1951, set out as a note under section 333 of this title.

EFFECTIVE MEDICATION GUIDES

Pub. L. 104–180, title VI, § 601, Aug. 6, 1996, 110 Stat. 1593, provided that:

''(a) IN GENERAL.—Not later than 30 days after the date of enactment of this Act [Aug. 6, 1996], the Secretary of the Department of Health and Human Services shall request that national organizations representing health care professionals, consumer organizations, voluntary health agencies, the pharmaceutical industry, drug wholesalers, patient drug information database companies, and other relevant parties collaborate to develop a long-range comprehensive action plan to achieve goals consistent with the goals of the proposed rule of the Food and Drug Administration on 'Prescription Drug Product Labeling: Medication Guide Requirements' (60 Fed. Reg. 44182; relating to the provision of oral and written prescription information to consumers).

''(b) GOALS.—Goals consistent with the proposed rule described in subsection (a) are the distribution of useful written information to 75 percent of individuals re-

ceiving new precriptions [sic] by the year 2000 and to 95 percent by the year 2006.

''(c) PLAN.—The plan described in subsection (a) shall—

''(1) identify the plan goals;

''(2) assess the effectiveness of the current private-sector approaches used to provide oral and written prescription information to consumers;

''(3) develop guidelines for providing effective oral and written prescription information consistent with the findings of any such assessment;

''(4) contain elements necessary to ensure the transmittal of useful information to the consuming public, including being scientifically accurate, non-promotional in tone and content, sufficiently specific and comprehensive as to adequately inform consumers about the use of the product, and in an understandable, legible format that is readily comprehensible and not confusing to consumers expected to use the product.[;]

''(5) develop a mechanism to assess periodically the quality of the oral and written prescription information and the frequency with which the information is provided to consumers; and

''(6) provide for compliance with relevant State board regulations.

''(d) LIMITATION ON THE AUTHORITY OF THE SECRETARY.—The Secretary of the Department of Health and Human Services shall have no authority to implement the proposed rule described in subsection (a), or to develop any similar regulation, policy statement, or other guideline specifying a uniform content or format for written information voluntarily provided to consumers about prescription drugs if, (1) not later than 120 days after the date of enactment of this Act [Aug. 6, 1996], the national organizations described in subsection (a) develop and submit to the Secretary for Health and Human Services a comprehensive, long-range action plan (as described in subsection (a)) which shall be acceptable to the Secretary of Health and Human Services; (2) the aforementioned plan is submitted to the Secretary of Health and Human Services for review and acceptance: *Provided*, That the Secretary shall give due consideration to the submitted plan and that any such acceptance shall not be arbitrarily withheld; and (3) the implementation of (a) a plan accepted by the Secretary commences within 30 days of the Secretary's acceptance of such plan, or (b) the plan submitted to the Secretary commences within 60 days of the submission of such plan if the Secretary fails to take any action on the plan within 30 days of the submission of the plan. The Secretary shall accept, reject or suggest modifications to the plan submitted within 30 days of its submission. The Secretary may confer with and assist private parties in the development of the plan described in subsections (a) and (b).

''(e) SECRETARY REVIEW.—Not later than January 1, 2001, the Secretary of the Department of Health and Human Services shall review the status of private-sector initiatives designed to achieve the goals of the plan described in subsection (a), and if such goals are not achieved, the limitation in subsection (d) shall not apply, and the Secretary shall seek public comment on other initiatives that may be carried out to meet such goals.''

CONGRESSIONAL FINDINGS

Pub. L. 100–293, §2, Apr. 22, 1988, 102 Stat. 95, provided that: ''The Congress finds the following:

''(1) American consumers cannot purchase prescription drugs with the certainty that the products are safe and effective.

''(2) The integrity of the distribution system for prescription drugs is insufficient to prevent the introduction and eventual retail sale of substandard, ineffective, or even counterfeit drugs.

''(3) The existence and operation of a wholesale submarket, commonly known as the 'diversion market', prevents effective control over or even routine knowledge of the true sources of prescription drugs in a significant number of cases.

''(4) Large amounts of drugs are being reimported to the United States as American goods returned. These imports are a health and safety risk to American consumers because they may have become subpotent or adulterated during foreign handling and shipping.

''(5) The ready market for prescription drug reimports has been the catalyst for a continuing series of frauds against American manufacturers and has provided the cover for the importation of foreign counterfeit drugs.

''(6) The existing system of providing drug samples to physicians through manufacturer's representatives has been abused for decades and has resulted in the sale to consumers of misbranded, expired, and adulterated pharmaceuticals.

''(7) The bulk resale of below wholesale priced prescription drugs by health care entities, for ultimate sale at retail, helps fuel the diversion market and is an unfair form of competition to wholesalers and retailers that must pay otherwise prevailing market prices.

''(8) The effect of these several practices and conditions is to create an unacceptable risk that counterfeit, adulterated, misbranded, subpotent, or expired drugs will be sold to American consumers.''

Executive Documents

TRANSFER OF FUNCTIONS

For transfer of functions of Federal Security Administrator to Secretary of Health, Education, and Welfare [now Health and Human Services], and of Food and Drug Administration in the Department of Agriculture to Federal Security Agency, see notes set out under section 321 of this title.

§ 353a. Pharmacy compounding

(a) In general

Sections 351(a)(2)(B), 352(f)(1), and 355 of this title shall not apply to a drug product if the drug product is compounded for an identified individual patient based on the receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient, if the drug product meets the requirements of this section, and if the compounding—

(1) is by—

(A) a licensed pharmacist in a State licensed pharmacy or a Federal facility, or

(B) a licensed physician,

on the prescription order for such individual patient made by a licensed physician or other licensed practitioner authorized by State law to prescribe drugs; or

(2)(A) is by a licensed pharmacist or licensed physician in limited quantities before the receipt of a valid prescription order for such individual patient; and

(B) is based on a history of the licensed pharmacist or licensed physician receiving valid prescription orders for the compounding of the drug product, which orders have been generated solely within an established relationship between—

(i) the licensed pharmacist or licensed physician; and

(ii)(I) such individual patient for whom the prescription order will be provided; or

(II) the physician or other licensed practitioner who will write such prescription order.

(b) Compounded drug

(1) Licensed pharmacist and licensed physician

A drug product may be compounded under subsection (a) if the licensed pharmacist or licensed physician—

(A) compounds the drug product using bulk drug substances, as defined in regulations of the Secretary published at section 207.3(a)(4) of title 21 of the Code of Federal Regulations—

(i) that—

(I) comply with the standards of an applicable United States Pharmacopoeia or National Formulary monograph, if a monograph exists, and the United States Pharmacopoeia chapter on pharmacy compounding;

(II) if such a monograph does not exist, are drug substances that are components of drugs approved by the Secretary; or

(III) if such a monograph does not exist and the drug substance is not a component of a drug approved by the Secretary, that appear on a list developed by the Secretary through regulations issued by the Secretary under subsection (c);

(ii) that are manufactured by an establishment that is registered under section 360 of this title (including a foreign establishment that is registered under section 360(i) of this title); and

(iii) that are accompanied by valid certificates of analysis for each bulk drug substance;

(B) compounds the drug product using ingredients (other than bulk drug substances) that comply with the standards of an applicable United States Pharmacopoeia or National Formulary monograph, if a monograph exists, and the United States Pharmacopoeia chapter on pharmacy compounding;

(C) does not compound a drug product that appears on a list published by the Secretary in the Federal Register of drug products that have been withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective; and

(D) does not compound regularly or in inordinate amounts (as defined by the Secretary) any drug products that are essentially copies of a commercially available drug product.

(2) Definition

For purposes of paragraph (1)(D), the term ''essentially a copy of a commercially available drug product'' does not include a drug product in which there is a change, made for an identified individual patient, which produces for that patient a significant difference, as determined by the prescribing practitioner, between the compounded drug and the comparable commercially available drug product.

(3) Drug product

A drug product may be compounded under subsection (a) only if—

(A) such drug product is not a drug product identified by the Secretary by regulation as a drug product that presents demonstrable difficulties for compounding that reasonably demonstrate an adverse effect on the safety or effectiveness of that drug product; and

(B) such drug product is compounded in a State—

(i) that has entered into a memorandum of understanding with the Secretary which addresses the distribution of inordinate amounts of compounded drug products interstate and provides for appropriate investigation by a State agency of complaints relating to compounded drug products distributed outside such State; or

(ii) that has not entered into the memorandum of understanding described in clause (i) and the licensed pharmacist, licensed pharmacy, or licensed physician distributes (or causes to be distributed) compounded drug products out of the State in which they are compounded in quantities that do not exceed 5 percent of the total prescription orders dispensed or distributed by such pharmacy or physician.

The Secretary shall, in consultation with the National Association of Boards of Pharmacy, develop a standard memorandum of understanding for use by the States in complying with subparagraph (B)(i).

(c) Regulations

(1) In general

The Secretary shall issue regulations to implement this section. Before issuing regulations to implement subsections (b)(1)(A)(i)(III), (b)(1)(C), or (b)(3)(A), the Secretary shall convene and consult an advisory committee on compounding unless the Secretary determines that the issuance of such regulations before consultation is necessary to protect the public health. The advisory committee shall include representatives from the National Association of Boards of Pharmacy, the United States Pharmacopoeia, pharmacy, physician, and consumer organizations, and other experts selected by the Secretary.

(2) Limiting compounding

The Secretary, in consultation with the United States Pharmacopoeia Convention, Incorporated, shall promulgate regulations identifying drug substances that may be used in compounding under subsection (b)(1)(A)(i)(III) for which a monograph does not exist or which are not components of drug products approved by the Secretary. The Secretary shall include in the regulation the criteria for such substances, which shall include historical use, reports in peer reviewed medical literature, or other criteria the Secretary may identify.

(d) Application

This section shall not apply to—

(1) compounded positron emission tomography drugs as defined in section 321(ii) of this title; or

(2) radiopharmaceuticals.

(e) "Compounding" defined

As used in this section, the term ''compounding'' does not include mixing, recon-

stituting, or other such acts that are performed in accordance with directions contained in approved labeling provided by the product's manufacturer and other manufacturer directions consistent with that labeling.

(June 25, 1938, ch. 675, § 503A, as added Pub. L. 105–115, title I, § 127(a), Nov. 21, 1997, 111 Stat. 2328; amended Pub. L. 113–54, title I, § 106(a), Nov. 27, 2013, 127 Stat. 598.)

Editorial Notes

AMENDMENTS

2013—Subsec. (a). Pub. L. 113–54, § 106(a)(1), struck out ''unsolicited'' before ''receipt of a valid prescription'' in introductory provisions.

Subsec. (b)(1)(A)(i)(III). Pub. L. 113–54, § 106(a)(4), substituted ''subsection (c)'' for ''subsection (d)''.

Subsecs. (c) to (f). Pub. L. 113–54, § 106(a)(2), (3), redesignated subsecs. (d) to (f) as (c) to (e), respectively, and struck out former subsec. (c). Prior to amendment, subsec. (c) read as follows: ''A drug may be compounded under subsection (a) of this section only if the pharmacy, licensed pharmacist, or licensed physician does not advertise or promote the compounding of any particular drug, class of drug, or type of drug. The pharmacy, licensed pharmacist, or licensed physician may advertise and promote the compounding service provided by the licensed pharmacist or licensed physician.''

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE

Pub. L. 105–115, title I, § 127(b), Nov. 21, 1997, 111 Stat. 2330, provided that: ''Section 503A of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 353a], added by subsection (a), shall take effect upon the expiration of the 1-year period beginning on the date of the enactment of this Act [Nov. 21, 1997].''

§ 353a–1. Enhanced communication

(a) Submissions from State boards of pharmacy

In a manner specified by the Secretary of Health and Human Services (referred to in this section as the ''Secretary''), the Secretary shall receive submissions from State boards of pharmacy—

(1) describing actions taken against compounding pharmacies, as described in subsection (b); or

(2) expressing concerns that a compounding pharmacy may be acting contrary to section 353a of this title.

(b) Content of submissions from State boards of pharmacy

An action referred to in subsection (a)(1) is, with respect to a pharmacy that compounds drugs, any of the following:

(1) The issuance of a warning letter, or the imposition of sanctions or penalties, by a State for violations of a State's pharmacy regulations pertaining to compounding.

(2) The suspension or revocation of a State-issued pharmacy license or registration for violations of a State's pharmacy regulations pertaining to compounding.

(3) The recall of a compounded drug due to concerns relating to the quality or purity of such drug.

(c) Consultation

The Secretary shall implement subsection (a) in consultation with the National Association of Boards of Pharmacy.

(d) Notifying State boards of pharmacy

The Secretary shall immediately notify State boards of pharmacy when—

(1) the Secretary receives a submission under subsection (a)(1); or

(2) the Secretary makes a determination that a pharmacy is acting contrary to section 353a of this title.

(Pub. L. 113–54, title I, § 105, Nov. 27, 2013, 127 Stat. 597.)

Editorial Notes

CODIFICATION

Section was enacted as part of the Compounding Quality Act and also as part of the Drug Quality and Security Act, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

§ 353b. Outsourcing facilities

(a) In general

Sections 352(f)(1), 355, and 360eee–1 of this title shall not apply to a drug compounded by or under the direct supervision of a licensed pharmacist in a facility that elects to register as an outsourcing facility if each of the following conditions is met:

(1) Registration and reporting

The drug is compounded in an outsourcing facility that is in compliance with the requirements of subsection (b).

(2) Bulk drug substances

The drug is compounded in an outsourcing facility that does not compound using bulk drug substances (as defined in section 207.3(a)(4) of title 21, Code of Federal Regulations (or any successor regulation)), unless—

(A)(i) the bulk drug substance appears on a list established by the Secretary identifying bulk drug substances for which there is a clinical need, by—

(I) publishing a notice in the Federal Register proposing bulk drug substances to be included on the list, including the rationale for such proposal;

(II) providing a period of not less than 60 calendar days for comment on the notice; and

(III) publishing a notice in the Federal Register designating bulk drug substances for inclusion on the list; or

(ii) the drug compounded from such bulk drug substance appears on the drug shortage list in effect under section 356e of this title at the time of compounding, distribution, and dispensing;

(B) if an applicable monograph exists under the United States Pharmacopeia, the National Formulary, or another compendium or pharmacopeia recognized by the Secretary for purposes of this paragraph, the bulk drug substances each comply with the monograph;

(C) the bulk drug substances are each manufactured by an establishment that is registered under section 360 of this title (including a foreign establishment that is registered under section 360(i) of this title); and

(D) the bulk drug substances are each accompanied by a valid certificate of analysis.

(3) Ingredients (other than bulk drug substances)

If any ingredients (other than bulk drug substances) are used in compounding the drug, such ingredients comply with the standards of the applicable United States Pharmacopeia or National Formulary monograph, if such monograph exists, or of another compendium or pharmacopeia recognized by the Secretary for purposes of this paragraph if any.

(4) Drugs withdrawn or removed because unsafe or not effective

The drug does not appear on a list published by the Secretary of drugs that have been withdrawn or removed from the market because such drugs or components of such drugs have been found to be unsafe or not effective.

(5) Essentially a copy of an approved drug

The drug is not essentially a copy of one or more approved drugs.

(6) Drugs presenting demonstrable difficulties for compounding

The drug—

(A) is not identified (directly or as part of a category of drugs) on a list published by the Secretary, through the process described in subsection (c), of drugs or categories of drugs that present demonstrable difficulties for compounding that are reasonably likely to lead to an adverse effect on the safety or effectiveness of the drug or category of drugs, taking into account the risks and benefits to patients; or

(B) is compounded in accordance with all applicable conditions identified on the list described in subparagraph (A) as conditions that are necessary to prevent the drug or category of drugs from presenting the demonstrable difficulties described in subparagraph (A).

(7) Elements to assure safe use

In the case of a drug that is compounded from a drug that is the subject of a risk evaluation and mitigation strategy approved with elements to assure safe use pursuant to section 355–1 of this title, or from a bulk drug substance that is a component of such drug, the outsourcing facility demonstrates to the Secretary prior to beginning compounding that such facility will utilize controls comparable to the controls applicable under the relevant risk evaluation and mitigation strategy.

(8) Prohibition on wholesaling

The drug will not be sold or transferred by an entity other than the outsourcing facility that compounded such drug. This paragraph does not prohibit administration of a drug in a health care setting or dispensing a drug pursuant to a prescription executed in accordance with section 353(b)(1) of this title.

(9) Fees

The drug is compounded in an outsourcing facility that has paid all fees owed by such facility pursuant to section 379j–62 of this title.

(10) Labeling of drugs

(A) Label

The label of the drug includes—

(i) the statement ''This is a compounded drug.'' or a reasonable comparable alternative statement (as specified by the Secretary) that prominently identifies the drug as a compounded drug;

(ii) the name, address, and phone number of the applicable outsourcing facility; and

(iii) with respect to the drug—

(I) the lot or batch number;

(II) the established name of the drug;

(III) the dosage form and strength;

(IV) the statement of quantity or volume, as appropriate;

(V) the date that the drug was compounded;

(VI) the expiration date;

(VII) storage and handling instructions;

(VIII) the National Drug Code number, if available;

(IX) the statement ''Not for resale'', and, if the drug is dispensed or distributed other than pursuant to a prescription for an individual identified patient, the statement ''Office Use Only''; and

(X) subject to subparagraph (B)(i), a list of active and inactive ingredients, identified by established name and the quantity or proportion of each ingredient.

(B) Container

The container from which the individual units of the drug are removed for dispensing or for administration (such as a plastic bag containing individual product syringes) shall include—

(i) the information described under subparagraph (A)(iii)(X), if there is not space on the label for such information;

(ii) the following information to facilitate adverse event reporting: www.fda.gov/medwatch and 1–800–FDA–1088 (or any successor Internet Web site or phone number); and

(iii) directions for use, including, as appropriate, dosage and administration.

(C) Additional information

The label and labeling of the drug shall include any other information as determined necessary and specified in regulations promulgated by the Secretary.

(11) Outsourcing facility requirement

The drug is compounded in an outsourcing facility in which the compounding of drugs occurs only in accordance with this section.

(b) Registration of outsourcing facilities and reporting of drugs

(1) Registration of outsourcing facilities

(A) Annual registration

Upon electing and in order to become an outsourcing facility, and during the period beginning on October 1 and ending on December 31 of each year thereafter, a facility—

(i) shall register with the Secretary its name, place of business, and unique facility identifier (which shall conform to the requirements for the unique facility identifier established under section 360 of this title), and a point of contact email address; and

(ii) shall indicate whether the outsourcing facility intends to compound a drug that appears on the list in effect under section 356e of this title during the subsequent calendar year.

(B) Availability of registration for inspection; list

(i) Registrations

The Secretary shall make available for inspection, to any person so requesting, any registration filed pursuant to this paragraph.

(ii) List

The Secretary shall make available on the public Internet Web site of the Food and Drug Administration a list of the name of each facility registered under this subsection as an outsourcing facility, the State in which each such facility is located, whether the facility compounds from bulk drug substances, and whether any such compounding from bulk drug substances is for sterile or nonsterile drugs.

(2) Drug reporting by outsourcing facilities

(A) In general

Upon initially registering as an outsourcing facility, once during the month of June of each year, and once during the month of December of each year, each outsourcing facility that registers with the Secretary under paragraph (1) shall submit to the Secretary a report—

(i) identifying the drugs compounded by such outsourcing facility during the previous 6-month period; and

(ii) with respect to each drug identified under clause (i), providing the active ingredient, the source of such active ingredient, the National Drug Code number of the source drug or bulk active ingredient, if available, the strength of the active ingredient per unit, the dosage form and route of administration, the package description, the number of individual units produced, and the National Drug Code number of the final product, if assigned.

(B) Form

Each report under subparagraph (A) shall be prepared in such form and manner as the Secretary may prescribe by regulation or guidance.

(C) Confidentiality

Reports submitted under this paragraph shall be exempt from inspection under paragraph (1)(B)(i), unless the Secretary finds that such an exemption would be inconsistent with the protection of the public health.

(3) Electronic registration and reporting

Registrations and drug reporting under this subsection (including the submission of updated information) shall be submitted to the Secretary by electronic means unless the Secretary grants a request for waiver of such requirement because use of electronic means is not reasonable for the person requesting waiver.

(4) Risk-based inspection frequency

(A) In general

Outsourcing facilities—

(i) shall be subject to inspection pursuant to section 374 of this title; and

(ii) shall not be eligible for the exemption under section 374(a)(2)(A) of this title.

(B) Risk-based schedule

The Secretary, acting through one or more officers or employees duly designated by the Secretary, shall inspect outsourcing facilities in accordance with a risk-based schedule established by the Secretary.

(C) Risk factors

In establishing the risk-based schedule, the Secretary shall inspect outsourcing facilities according to the known safety risks of such outsourcing facilities, which shall be based on the following factors:

(i) The compliance history of the outsourcing facility.

(ii) The record, history, and nature of recalls linked to the outsourcing facility.

(iii) The inherent risk of the drugs compounded at the outsourcing facility.

(iv) The inspection frequency and history of the outsourcing facility, including whether the outsourcing facility has been inspected pursuant to section 374 of this title within the last 4 years.

(v) Whether the outsourcing facility has registered under this paragraph as an entity that intends to compound a drug that appears on the list in effect under section 356e of this title.

(vi) Any other criteria deemed necessary and appropriate by the Secretary for purposes of allocating inspection resources.

(5) Adverse event reporting

Outsourcing facilities shall submit adverse event reports to the Secretary in accordance with the content and format requirements established through guidance or regulation under section 310.305 of title 21, Code of Federal Regulations (or any successor regulations).

(c) Regulations

(1) In general

The Secretary shall implement the list described in subsection (a)(6) through regulations.

(2) Advisory committee on compounding

Before issuing regulations to implement subsection (a)(6), the Secretary shall convene and consult an advisory committee on compounding. The advisory committee shall include representatives from the National Association of Boards of Pharmacy, the United States Pharmacopeia, pharmacists with current experience and expertise in compounding,

physicians with background and knowledge in compounding, and patient and public health advocacy organizations.

(3) Interim list

(A) In general

Before the effective date of the regulations finalized to implement subsection (a)(6), the Secretary may designate drugs, categories of drugs, or conditions as described such[1] subsection by—

(i) publishing a notice of such substances, drugs, categories of drugs, or conditions proposed for designation, including the rationale for such designation, in the Federal Register;

(ii) providing a period of not less than 60 calendar days for comment on the notice; and

(iii) publishing a notice in the Federal Register designating such drugs, categories of drugs, or conditions.

(B) Sunset of notice

Any notice provided under subparagraph (A) shall not be effective after the earlier of—

(i) the date that is 5 years after November 27, 2013; or

(ii) the effective date of the final regulations issued to implement subsection (a)(6).

(4) Updates

The Secretary shall review, and update as necessary, the regulations containing the lists of drugs, categories of drugs, or conditions described in subsection (a)(6) regularly, but not less than once every 4 years. Nothing in the previous sentence prohibits submissions to the Secretary, before or during any 4-year period described in such sentence, requesting updates to such lists.

(d)[2] Definitions

In this section:

(1) The term ''compounding'' includes the combining, admixing, mixing, diluting, pooling, reconstituting, or otherwise altering of a drug or bulk drug substance to create a drug.

(2) The term ''essentially a copy of an approved drug'' means—

(A) a drug that is identical or nearly identical to an approved drug, or a marketed drug not subject to section 353(b) of this title and not subject to approval in an application submitted under section 355 of this title, unless, in the case of an approved drug, the drug appears on the drug shortage list in effect under section 356e of this title at the time of compounding, distribution, and dispensing; or

(B) a drug, a component of which is a bulk drug substance that is a component of an approved drug or a marketed drug that is not subject to section 353(b) of this title and not subject to approval in an application submitted under section 355 of this title, unless there is a change that produces for an individual patient a clinical difference, as determined by the prescribing practitioner, between the compounded drug and the comparable approved drug.

(3) The term ''approved drug'' means a drug that is approved under section 355 of this title and does not appear on the list described in subsection (a)(4) of drugs that have been withdrawn or removed from the market because such drugs or components of such drugs have been found to be unsafe or not effective.

(4)(A) The term ''outsourcing facility'' means a facility at one geographic location or address that—

(i) is engaged in the compounding of sterile drugs;

(ii) has elected to register as an outsourcing facility; and

(iii) complies with all of the requirements of this section.

(B) An outsourcing facility is not required to be a licensed pharmacy.

(C) An outsourcing facility may or may not obtain prescriptions for identified individual patients.

(5) The term ''sterile drug'' means a drug that is intended for parenteral administration, an ophthalmic or oral inhalation drug in aqueous format, or a drug that is required to be sterile under Federal or State law.

(d)[2] Obligation to pay fees

Payment of the fee under section 379j–62 of this title, as described in subsection (a)(9), shall not relieve an outsourcing facility that is licensed as a pharmacy in any State that requires pharmacy licensing fees of its obligation to pay such State fees.

(June 25, 1938, ch. 675, § 503B, as added Pub. L. 113–54, title I, § 102(a)(2), Nov. 27, 2013, 127 Stat. 588.)

Editorial Notes

PRIOR PROVISIONS

A prior section 503B of act June 25, 1938, ch. 675, was renumbered section 503C by Pub. L. 113–54, § 102(a)(1), Nov. 27, 2013, 127 Stat. 587, and transferred to section 353c of this title.

§ 353c. Prereview of television advertisements

(a) In general

The Secretary may require the submission of any television advertisement for a drug (including any script, story board, rough, or a completed video production of the television advertisement) to the Secretary for review under this section not later than 45 days before dissemination of the television advertisement.

(b) Review

In conducting a review of a television advertisement under this section, the Secretary may make recommendations with respect to information included in the label of the drug—

(1) on changes that are—

(A) necessary to protect the consumer good and well-being; or

(B) consistent with prescribing information for the product under review; and

[1] So in original.

[2] So in original. Two subsecs. (d) have been enacted.

(2) if appropriate and if information exists, on statements for inclusion in the advertisement to address the specific efficacy of the drug as it relates to specific population groups, including elderly populations, children, and racial and ethnic minorities.

(c) No authority to require changes

Except as provided by subsection (e), this section does not authorize the Secretary to make or direct changes in any material submitted pursuant to subsection (a).

(d) Elderly populations, children, racially and ethnically diverse communities

In formulating recommendations under subsection (b), the Secretary shall take into consideration the impact of the advertised drug on elderly populations, children, and racially and ethnically diverse communities.

(e) Specific disclosures

(1) Serious risk; safety protocol

In conducting a review of a television advertisement under this section, if the Secretary determines that the advertisement would be false or misleading without a specific disclosure about a serious risk listed in the labeling of the drug involved, the Secretary may require inclusion of such disclosure in the advertisement.

(2) Date of approval

In conducting a review of a television advertisement under this section, the Secretary may require the advertisement to include, for a period not to exceed 2 years from the date of the approval of the drug under section 355 of this title or section 262 of title 42, a specific disclosure of such date of approval if the Secretary determines that the advertisement would otherwise be false or misleading.

(f) Rule of construction

Nothing in this section may be construed as having any effect on requirements under section 352(n) of this title or on the authority of the Secretary under section 314.550, 314.640, 601.45, or 601.94 of title 21, Code of Federal Regulations (or successor regulations).

(June 25, 1938, ch. 675, § 503C, formerly § 503B, as added Pub. L. 110–85, title IX, § 901(d)(2), Sept. 27, 2007, 121 Stat. 939, renumbered § 503C, Pub. L. 113–54, title I, § 102(a)(1), Nov. 27, 2013, 127 Stat. 587.)

Editorial Notes

CODIFICATION

Section was formerly classified to section 353b of this title prior to renumbering by Pub. L. 113–54.

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE

Section effective 180 days after Sept. 27, 2007, see section 909 of Pub. L. 110–85, set out as an Effective Date of 2007 Amendment note under section 331 of this title.

§ 353d. Process to update labeling for certain generic drugs

(a) Definitions

For purposes of this section:

(1) The term ''covered drug'' means a drug approved under section 355(c) of this title—

(A) for which there are no unexpired patents included in the list under section 355(j)(7) of this title and no unexpired period of exclusivity;

(B) for which the approval of the application has been withdrawn for reasons other than safety or effectiveness; and

(C) for which—

(i)(I) there is new scientific evidence available pertaining to new or existing conditions of use that is not reflected in the approved labeling;

(II) the approved labeling does not reflect current legal and regulatory requirements for content or format; or

(III) there is a relevant accepted use in clinical practice that is not reflected in the approved labeling; and

(ii) updating the approved labeling would benefit the public health.

(2) The term ''period of exclusivity'', with respect to a drug approved under section 355(c) of this title, means any period of exclusivity under clause (ii), (iii), or (iv) of section 355(c)(3)(E) of this title, clause (ii), (iii), or (iv) of section 355(j)(5)(F) of this title, or section 355a, 355f, or 360cc of this title.

(3) The term ''generic version'' means a drug approved under section 355(j) of this title whose reference listed drug is a covered drug.

(4) The term ''relevant accepted use'' means a use for a drug in clinical practice that is supported by scientific evidence that appears to the Secretary to meet the standards for approval under section 355 of this title.

(5) The term ''selected drug'' means a covered drug for which the Secretary has determined through the process under subsection (c) that the labeling should be changed.

(b) Identification of covered drugs

The Secretary may identify covered drugs for which labeling updates would provide a public health benefit. To assist in identifying covered drugs, the Secretary may do one or both of the following:

(1) Enter into cooperative agreements or contracts with public or private entities to review the available scientific evidence concerning such drugs.

(2) Seek public input concerning such drugs, including input on whether there is a relevant accepted use in clinical practice that is not reflected in the approved labeling of such drugs or whether new scientific evidence is available regarding the conditions of use for such drug, by—

(A) holding one or more public meetings;

(B) opening a public docket for the submission of public comments; or

(C) other means, as the Secretary determines appropriate.

(c) Selection of drugs for updating

If the Secretary determines, with respect to a covered drug, that the available scientific evidence meets the standards under section 355 of this title for adding or modifying information to the labeling or providing supplemental informa-

tion to the labeling regarding the use of the covered drug, the Secretary may initiate the process under subsection (d).

(d) Initiation of the process of updating

If the Secretary determines that labeling changes are appropriate for a selected drug pursuant to subsection (c), the Secretary shall provide notice to the holders of approved applications for a generic version of such drug that—

(1) summarizes the findings supporting the determination of the Secretary that the available scientific evidence meets the standards under section 355 of this title for adding or modifying information or providing supplemental information to the labeling of the covered drug pursuant to subsection (c);

(2) provides a clear statement regarding the additional, modified, or supplemental information for such labeling, according to the determination by the Secretary (including, as applicable, modifications to add the relevant accepted use to the labeling of the drug as an additional indication for the drug); and

(3) states whether the statement under paragraph (2) applies to the selected drug as a class of covered drugs or only to a specific drug product.

(e) Response to notification

Within 30 days of receipt of notification provided by the Secretary pursuant to subsection (d), the holder of an approved application for a generic version of the selected drug shall—

(1) agree to change the approved labeling to reflect the additional, modified, or supplemental information the Secretary has determined to be appropriate; or

(2) notify the Secretary that the holder of the approved application does not believe that the requested labeling changes are warranted and submit a statement detailing the reasons why such changes are not warranted.

(f) Review of application holder's response

(1) In general

Upon receipt of the application holder's response, the Secretary shall promptly review each statement received under subsection (e)(2) and determine which labeling changes pursuant to the Secretary's notice under subsection (d) are appropriate, if any. If the Secretary disagrees with the reasons why such labeling changes are not warranted, the Secretary shall provide opportunity for discussions with the application holders to reach agreement on whether the labeling for the covered drug should be updated to reflect available scientific evidence, and if so, the content of such labeling changes.

(2) Changes to labeling

After considering all responses from the holder of an approved application under paragraph (1) or (2) of subsection (e), and any discussion under paragraph (1), the Secretary may order such holder to make the labeling changes the Secretary determines are appropriate. Such holder of an approved application shall—

(A) update its paper labeling for the drug at the next printing of that labeling;

(B) update any electronic labeling for the drug within 30 days of such order; and

(C) submit the revised labeling through the form, ''Supplement—Changes Being Effected''.

(g) Violation

If the holder of an approved application for the generic version of the selected drug does not comply with the requirements of subsection (f)(2), such generic version of the selected drug shall be deemed to be misbranded under section 352 of this title.

(h) Limitations; generic drugs

(1) In general

With respect to any labeling change required under this section, the generic version shall be deemed to have the same conditions of use and the same labeling as its reference listed drug for purposes of clauses (i) and (v) of section 355(j)(2)(A) of this title. Any labeling change so required shall not have any legal effect for the applicant that is different than the legal effect that would have resulted if a supplemental application had been submitted and approved to conform the labeling of the generic version to a change in the labeling of the reference drug.

(2) Supplemental applications

Changes to labeling made in accordance with this section shall not be eligible for an exclusivity period under this chapter.

(3) Selection of drugs

The Secretary shall not identify a drug as a covered drug or select a drug label for updating under subsection (b) or (c) solely based on the availability of new safety information. Upon identification of a drug as a covered drug under subsection (b), the Secretary may then consider the availability of new safety information (as defined in section 355–1(b) of this title) in determining whether the drug is a selected drug and in determining what labeling changes are appropriate.

(i) Rules of construction

(1) Approval standards

This section shall not be construed as altering the applicability of the standards for approval of an application under section 355 of this title. No order shall be issued under this subsection unless the scientific evidence supporting the changed labeling meets the standards for approval applicable to any change to labeling under section 355 of this title.

(2) Removal of information

Nothing in this section shall be construed to give the Secretary additional authority to remove approved indications for drugs, other than the authority described in this section.

(3) Secretary authority

Nothing in this section shall be construed to limit the authority of the Secretary to require labeling changes under section 355(*o*) of this title.

(4) Maintenance of labeling

Nothing in this section shall be construed to affect the responsibility of the holder of an ap-

proved application under section 355(j) of this title to maintain its labeling in accordance with existing requirements, including subpart B of part 201 and sections 314.70 and 314.97 of title 21, Code of Federal Regulations (or any successor regulations).

(j) Reports

Not later than 4 years after December 27, 2020, and every 4 years thereafter, the Secretary shall prepare and submit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate, a report that—

(1) describes the actions of the Secretary under this section, including—

(A) the number of covered drugs and description of the types of drugs the Secretary has selected for labeling changes and the rationale for such recommended changes; and

(B) the number of times the Secretary entered into discussions concerning a disagreement with an application holder or holders and a summary of the decision regarding a labeling change, if any; and

(2) includes any recommendations of the Secretary for modifying the program under this section.

(June 25, 1938, ch. 675, § 503D, as added Pub. L. 116–260, div. BB, title III, § 324, Dec. 27, 2020, 134 Stat. 2933.)

§ 354. Veterinary feed directive drugs

(a) Lawful veterinary feed directive requirement

(1) A drug intended for use in or on animal feed which is limited by an approved application filed pursuant to section 360b(b) of this title, a conditionally-approved application filed pursuant to section 360ccc of this title, or an index listing pursuant to section 360ccc–1 of this title to use under the professional supervision of a licensed veterinarian is a veterinary feed directive drug. Any animal feed bearing or containing a veterinary feed directive drug shall be fed to animals only by or upon a lawful veterinary feed directive issued by a licensed veterinarian in the course of the veterinarian's professional practice. When labeled, distributed, held, and used in accordance with this section, a veterinary feed directive drug and any animal feed bearing or containing a veterinary feed directive drug shall be exempt from section 352(f) of this title.

(2) A veterinary feed directive is lawful if it—

(A) contains such information as the Secretary may by general regulation or by order require; and

(B) is in compliance with the conditions and indications for use of the drug set forth in the notice published pursuant to section 360b(i) of this title, or the index listing pursuant to section 360ccc–1(e) of this title.

(3)(A) Any persons involved in the distribution or use of animal feed bearing or containing a veterinary feed directive drug and the licensed veterinarian issuing the veterinary feed directive shall maintain a copy of the veterinary feed directive applicable to each such feed, except in the case of a person distributing such feed to another person for further distribution. Such person distributing the feed shall maintain a written acknowledgment from the person to whom the feed is shipped stating that that person shall not ship or move such feed to an animal production facility without a veterinary feed directive or ship such feed to another person for further distribution unless that person has provided the same written acknowledgment to its immediate supplier.

(B) Every person required under subparagraph (A) to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

(C) Any person who distributes animal feed bearing or containing a veterinary feed directive drug shall upon first engaging in such distribution notify the Secretary of that person's name and place of business. The failure to provide such notification shall be deemed to be an act which results in the drug being misbranded.

(b) Labeling and advertising

A veterinary feed directive drug and any feed bearing or containing a veterinary feed directive drug shall be deemed to be misbranded if their labeling fails to bear such cautionary statement and such other information as the Secretary may by general regulation or by order prescribe, or their advertising fails to conform to the conditions and indications for use published pursuant to section 360b(i) of this title, or the index listing pursuant to section 360ccc–1(e) of this title or fails to contain the general cautionary statement prescribed by the Secretary.

(c) Nonprescription status

Neither a drug subject to this section, nor animal feed bearing or containing such a drug, shall be deemed to be a prescription article under any Federal or State law.

(June 25, 1938, ch. 675, § 504, as added Pub. L. 104–250, § 5(b), Oct. 9, 1996, 110 Stat. 3155; amended Pub. L. 108–282, title I, § 102(b)(5)(G), (H), Aug. 2, 2004, 118 Stat. 903.)

Editorial Notes

PRIOR PROVISIONS

A prior section 354, act June 25, 1938, ch. 675, § 504, 52 Stat. 1052, which directed Secretary to promulgate regulations for listing of coal-tar colors, was repealed effective July 12, 1960, subject to provisions of section 203 of Pub. L. 86–618, by Pub. L. 86–618, title I, § 103(a)(2), title II, § 202, July 12, 1960, 74 Stat. 398, 404.

AMENDMENTS

2004—Subsec. (a)(1). Pub. L. 108–282, § 102(b)(5)(G), substituted ''360b(b) of this title, a conditionally-approved application filed pursuant to section 360ccc of this title, or an index listing pursuant to section 360ccc–1 of this title'' for ''360b(b) of this title''.

Subsecs. (a)(2)(B), (b). Pub. L. 108–282, § 102(b)(5)(H), substituted ''360b(i) of this title, or the index listing pursuant to section 360ccc–1(e) of this title'' for ''360b(i) of this title''.

§ 355. New drugs

(a) Necessity of effective approval of application

No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) is effective with respect to such drug.

(b) Filing application; contents

(1)(A) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a). Such persons shall submit to the Secretary as part of the application—

(i) full reports of investigations which have been made to show whether such drug is safe for use and whether such drug is effective in use;

(ii) a full list of the articles used as components of such drug;

(iii) a full statement of the composition of such drug;

(iv) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug;

(v) such samples of such drug and of the articles used as components thereof as the Secretary may require;

(vi) specimens of the labeling proposed to be used for such drug;

(vii) any assessments required under section 355c of this title; and

(viii) the patent number and expiration date of each patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug, and that—

(I) claims the drug for which the applicant submitted the application and is a drug substance (active ingredient) patent or a drug product (formulation or composition) patent; or

(II) claims a method of using such drug for which approval is sought or has been granted in the application.

(B) If an application is filed under this subsection for a drug, and a patent of the type described in subparagraph (A)(viii) is issued after the filing date but before approval of the application, the applicant shall amend the application to include the patent number and expiration date.

(2) An application submitted under paragraph (1) for a drug for which the investigations described in clause (A) of such paragraph and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted shall also include—

(A) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the drug for which such investigations were conducted or which claims a use for such drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under paragraph (1) or subsection (c)—

(i) that such patent information has not been filed,

(ii) that such patent has expired,

(iii) of the date on which such patent will expire, or

(iv) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

(B) if with respect to the drug for which investigations described in paragraph (1)(A) were conducted information was filed under paragraph (1) or subsection (c) for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

(3) NOTICE OF OPINION THAT PATENT IS INVALID OR WILL NOT BE INFRINGED.—

(A) AGREEMENT TO GIVE NOTICE.—An applicant that makes a certification described in paragraph (2)(A)(iv) shall include in the application a statement that the applicant will give notice as required by this paragraph.

(B) TIMING OF NOTICE.—An applicant that makes a certification described in paragraph (2)(A)(iv) shall give notice as required under this paragraph—

(i) if the certification is in the application, not later than 20 days after the date of the postmark on the notice with which the Secretary informs the applicant that the application has been filed; or

(ii) if the certification is in an amendment or supplement to the application, at the time at which the applicant submits the amendment or supplement, regardless of whether the applicant has already given notice with respect to another such certification contained in the application or in an amendment or supplement to the application.

(C) RECIPIENTS OF NOTICE.—An applicant required under this paragraph to give notice shall give notice to—

(i) each owner of the patent that is the subject of the certification (or a representative of the owner designated to receive such a notice); and

(ii) the holder of the approved application under this subsection for the drug that is claimed by the patent or a use of which is claimed by the patent (or a representative of the holder designated to receive such a notice).

(D) CONTENTS OF NOTICE.—A notice required under this paragraph shall—

(i) state that an application that contains data from bioavailability or bioequivalence studies has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification; and

(ii) include a detailed statement of the factual and legal basis of the opinion of the ap-

plicant that the patent is invalid or will not be infringed.

(4)(A) An applicant may not amend or supplement an application referred to in paragraph (2) to seek approval of a drug that is a different drug than the drug identified in the application as submitted to the Secretary.

(B) With respect to the drug for which such an application is submitted, nothing in this subsection or subsection (c)(3) prohibits an applicant from amending or supplementing the application to seek approval of a different strength.

(5)(A) The Secretary shall issue guidance for the individuals who review applications submitted under paragraph (1) or under section 262 of title 42, which shall relate to promptness in conducting the review, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards, and which shall apply equally to all individuals who review such applications.

(B) The Secretary shall meet with a sponsor of an investigation or an applicant for approval for a drug under this subsection or section 262 of title 42 if the sponsor or applicant makes a reasonable written request for a meeting for the purpose of reaching agreement on the design and size—

(i)(I) of clinical trials intended to form the primary basis of an effectiveness claim; or

(II) in the case where human efficacy studies are not ethical or feasible, of animal and any associated clinical trials which, in combination, are intended to form the primary basis of an effectiveness claim; or

(ii) with respect to an application for approval of a biological product under section 262(k) of title 42, of any necessary clinical study or studies.

The sponsor or applicant shall provide information necessary for discussion and agreement on the design and size of the clinical trials. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant upon request.

(C) Any agreement regarding the parameters of the design and size of clinical trials of a new drug under this paragraph that is reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Such agreement shall not be changed after the testing begins, except—

(i) with the written agreement of the sponsor or applicant; or

(ii) pursuant to a decision, made in accordance with subparagraph (D) by the director of the reviewing division, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.

(D) A decision under subparagraph (C)(ii) by the director shall be in writing and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant will be present and at which the director will document the scientific issue involved.

(E) The written decisions of the reviewing division shall be binding upon, and may not directly or indirectly be changed by, the field or compliance division personnel unless such field or compliance division personnel demonstrate to the reviewing division why such decision should be modified.

(F) No action by the reviewing division may be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.

(G) For purposes of this paragraph, the reviewing division is the division responsible for the review of an application for approval of a drug under this subsection or section 262 of title 42 (including all scientific and medical matters, chemistry, manufacturing, and controls).

(6) An application submitted under this subsection shall be accompanied by the certification required under section 282(j)(5)(B) of title 42. Such certification shall not be considered an element of such application.

(c) Period for approval of application; period for, notice, and expedition of hearing; period for issuance of order

(1) Within one hundred and eighty days after the filing of an application under subsection (b), or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either—

(A) approve the application if he then finds that none of the grounds for denying approval specified in subsection (d) applies, or

(B) give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) on the question whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(2) Not later than 30 days after the date of approval of an application submitted under subsection (b), the holder of the approved application shall file with the Secretary the patent number and the expiration date of any patent described in subsection (b)(1)(A)(viii), except that a patent that is identified as claiming a method of using such drug shall be filed only if the patent claims a method of use approved in the application. If a patent described in subsection (b)(1)(A)(viii) is issued after the date of approval of an application submitted under subsection (b), the holder of the approved application shall, not later than 30 days after the date of issuance of the patent, file the patent number and the expiration date of the patent, except that a patent that claims a method of using such drug shall be filed only if approval for such use has been granted in the application. If the patent information described in subsection (b) could not be filed with the submission of an application under subsection (b) because the application was filed before the patent information

was required under subsection (b) or a patent was issued after the application was approved under such subsection, the holder of an approved application shall file with the Secretary the patent number and the expiration date of any patent described in subsection (b)(1)(A)(viii). If the holder of an approved application could not file patent information under subsection (b) because it was not required at the time the application was approved, the holder shall file such information under this subsection not later than thirty days after September 24, 1984, and if the holder of an approved application could not file patent information under subsection (b) because no patent of the type for which information is required to be submitted in subsection (b)(1)(A)(viii) had been issued when an application was filed or approved, the holder shall file such information under this subsection not later than thirty days after the date the patent involved is issued. Upon the submission of patent information under this subsection, the Secretary shall publish it. Patent information that is not the type of patent information required by subsection (b)(1)(A)(viii) shall not be submitted under this paragraph.

(3) The approval of an application filed under subsection (b) which contains a certification required by paragraph (2) of such subsection shall be made effective on the last applicable date determined by applying the following to each certification made under subsection (b)(2)(A):

(A) If the applicant only made a certification described in clause (i) or (ii) of subsection (b)(2)(A) or in both such clauses, the approval may be made effective immediately.

(B) If the applicant made a certification described in clause (iii) of subsection (b)(2)(A), the approval may be made effective on the date certified under clause (iii).

(C) If the applicant made a certification described in clause (iv) of subsection (b)(2)(A), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in subsection (b)(3) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under paragraph (2) or subsection (b)(1) before the date on which the application (excluding an amendment or supplement to the application) was submitted. If such an action is brought before the expiration of such days, the approval may be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under subsection (b)(3) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—

(i) if before the expiration of such period the district court decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the approval shall be made effective on—

(I) the date on which the court enters judgment reflecting the decision; or

(II) the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed;

(ii) if before the expiration of such period the district court decides that the patent has been infringed—

(I) if the judgment of the district court is appealed, the approval shall be made effective on—

(aa) the date on which the court of appeals decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity); or

(bb) the date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent that is the subject of the certification is invalid or not infringed; or

(II) if the judgment of the district court is not appealed or is affirmed, the approval shall be made effective on the date specified by the district court in a court order under section 271(e)(4)(A) of title 35;

(iii) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective as provided in clause (i); or

(iv) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent has been infringed, the approval shall be made effective as provided in clause (ii).

In such an action, each of the parties shall reasonably cooperate in expediting the action.

(D) CIVIL ACTION TO OBTAIN PATENT CERTAINTY.—

(i) DECLARATORY JUDGMENT ABSENT INFRINGEMENT ACTION.—

(I) IN GENERAL.—No action may be brought under section 2201 of title 28 by an applicant referred to in subsection (b)(2) for a declaratory judgment with respect to a patent which is the subject of the certification referred to in subparagraph (C) unless—

(aa) the 45-day period referred to in such subparagraph has expired;

(bb) neither the owner of such patent nor the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent brought a civil action against the applicant for infringement of the patent before the expiration of such period; and

(cc) in any case in which the notice provided under paragraph (2)(B) relates

to noninfringement, the notice was accompanied by a document described in subclause (III).

(II) FILING OF CIVIL ACTION.—If the conditions described in items (aa), (bb), and as applicable, (cc) of subclause (I) have been met, the applicant referred to in such subclause may, in accordance with section 2201 of title 28, bring a civil action under such section against the owner or holder referred to in such subclause (but not against any owner or holder that has brought such a civil action against the applicant, unless that civil action was dismissed without prejudice) for a declaratory judgment that the patent is invalid or will not be infringed by the drug for which the applicant seeks approval, except that such civil action may be brought for a declaratory judgment that the patent will not be infringed only in a case in which the condition described in subclause (I)(cc) is applicable. A civil action referred to in this subclause shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(III) OFFER OF CONFIDENTIAL ACCESS TO APPLICATION.—For purposes of subclause (I)(cc), the document described in this subclause is a document providing an offer of confidential access to the application that is in the custody of the applicant referred to in subsection (b)(2) for the purpose of determining whether an action referred to in subparagraph (C) should be brought. The document providing the offer of confidential access shall contain such restrictions as to persons entitled to access, and on the use and disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade secrets and other confidential business information. A request for access to an application under an offer of confidential access shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access, and on the use and disposition of any information accessed, contained in the offer of confidential access, and those restrictions and other terms of the offer of confidential access shall be considered terms of an enforceable contract. Any person provided an offer of confidential access shall review the application for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the certification under subsection (b)(2)(A)(iv) and for no other purpose, and may not disclose information of no relevance to any issue of patent infringement to any person other than a person provided an offer of confidential access. Further, the application may be redacted by the applicant to remove any information of no relevance to any issue of patent infringement.

(ii) COUNTERCLAIM TO INFRINGEMENT ACTION.—

(I) IN GENERAL.—If an owner of the patent or the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) or this subsection on the ground that the patent does not claim either—

(aa) the drug for which the application was approved; or

(bb) an approved method of using the drug.

(II) NO INDEPENDENT CAUSE OF ACTION.—Subclause (I) does not authorize the assertion of a claim described in subclause (I) in any civil action or proceeding other than a counterclaim described in subclause (I).

(iii) NO DAMAGES.—An applicant shall not be entitled to damages in a civil action under clause (i) or a counterclaim under clause (ii).

(E)(i) Repealed. Pub. L. 117–9, §1(b)(1)(A), Apr. 23, 2021, 135 Stat. 258.

(ii) If an application submitted under subsection (b) for a drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under subsection (b), is approved after September 24, 1984, no application which refers to the drug for which the subsection (b) application was submitted and for which the investigations described in subsection (b)(1)(A)(i) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted may be submitted under subsection (b) before the expiration of five years from the date of the approval of the application under subsection (b), except that such an application may be submitted under subsection (b) after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in clause (iv) of subsection (b)(2)(A). The approval of such an application shall be made effective in accordance with this paragraph except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (C) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) for a drug, which includes an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) that has been approved in another application approved

under subsection (b), is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b) for the conditions of approval of such drug in the approved subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) if the investigations described in subsection (b)(1)(A)(i) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(iv) If a supplement to an application approved under subsection (b) is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailabilty[1] studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under subsection (b) for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) if the investigations described in subsection (b)(1)(A)(i) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(v) If an application (or supplement to an application) submitted under subsection (b) for a drug, which includes an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) that has been approved in another application under subsection (b), was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection and for which the investigations described in subsection (b)(1)(A)(i) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted and which refers to the drug for which the subsection (b) application was submitted effective before the expiration of two years from September 24, 1984.

(4) A drug manufactured in a pilot or other small facility may be used to demonstrate the safety and effectiveness of the drug and to obtain approval for the drug prior to manufacture of the drug in a larger facility, unless the Secretary makes a determination that a full scale production facility is necessary to ensure the safety or effectiveness of the drug.

(5)(A) The Secretary may rely upon qualified data summaries to support the approval of a supplemental application, with respect to a qualified indication for a drug, submitted under subsection (b), if such supplemental application complies with subparagraph (B).

(B) A supplemental application is eligible for review as described in subparagraph (A) only if—

(i) there is existing data available and acceptable to the Secretary demonstrating the safety of the drug; and

(ii) all data used to develop the qualified data summaries are submitted to the Secretary as part of the supplemental application.

(C) The Secretary shall post on the Internet website of the Food and Drug Administration and update annually—

(i) the number of applications reviewed solely under subparagraph (A) or section 262(a)(2)(E) of title 42;

(ii) the average time for completion of review under subparagraph (A) or section 262(a)(2)(E) of title 42;

(iii) the average time for review of supplemental applications where the Secretary did not use review flexibility under subparagraph (A) or section 262(a)(2)(E) of title 42; and

(iv) the number of applications reviewed under subparagraph (A) or section 262(a)(2)(E) of title 42 for which the Secretary made use of full data sets in addition to the qualified data summary.

(D) In this paragraph—

(i) the term ''qualified indication'' means an indication for a drug that the Secretary determines to be appropriate for summary level review under this paragraph; and

(ii) the term ''qualified data summary'' means a summary of clinical data that demonstrates the safety and effectiveness of a drug with respect to a qualified indication.

(d) Grounds for refusing application; approval of application; "substantial evidence" defined

If the Secretary finds, after due notice to the applicant in accordance with subsection (c) and giving him an opportunity for a hearing, in accordance with said subsection, that (1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b), do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; (4) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions; or (5) evaluated on the basis of the information submitted to him as part of the application and any other information before

[1] So in original. Probably should be ''bioavailability''.

him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or (6) the application failed to contain the patent information prescribed by subsection (b); or (7) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that clauses (1) through (6) do not apply, he shall issue an order approving the application. As used in this subsection and subsection (e), the term ''substantial evidence'' means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof. If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence. The Secretary shall implement a structured risk-benefit assessment framework in the new drug approval process to facilitate the balanced consideration of benefits and risks, a consistent and systematic approach to the discussion and regulatory decision-making, and the communication of the benefits and risks of new drugs. Nothing in the preceding sentence shall alter the criteria for evaluating an application for marketing approval of a drug.

(e) Withdrawal of approval; grounds; immediate suspension upon finding imminent hazard to public health

The Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds (1) that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved; (2) that new evidence of clinical experience, not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved; or (3) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof; or (4) the patent information prescribed by subsection (c) was not filed within thirty days after the receipt of written notice from the Secretary specifying the failure to file such information; or (5) that the application contains any untrue statement of a material fact: *Provided*, That if the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the public health, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this proviso to suspend the approval of an application shall not be delegated. The Secretary may also, after due notice and opportunity for hearing to the applicant, withdraw the approval of an application submitted under subsection (b) or (j) with respect to any drug under this section if the Secretary finds (1) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports, in accordance with a regulation or order under subsection (k) or to comply with the notice requirements of section 360(k)(2) of this title, or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection; or (2) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or (3) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of. Any order under this subsection shall state the findings upon which it is based. The Secretary may withdraw the approval of an application submitted under this section, or suspend the approval of such an application, as provided under this subsection, without first ordering the applicant to submit an assessment of the approved risk evaluation and mitigation strategy for the drug under section 355–1(g)(2)(D) of this title.

(f) Revocation of order refusing, withdrawing or suspending approval of application

Whenever the Secretary finds that the facts so require, he shall revoke any previous order under subsection (d) or (e) refusing, withdrawing, or suspending approval of an application and shall approve such application or reinstate such approval, as may be appropriate.

(g) Service of orders

Orders of the Secretary issued under this section shall be served (1) in person by any officer or employee of the department designated by the Secretary or (2) by mailing the order by registered mail or by certified mail addressed to the applicant or respondent at his last-known address in the records of the Secretary.

(h) Appeal from order

An appeal may be taken by the applicant from an order of the Secretary refusing or withdrawing approval of an application under this section. Such appeal shall be taken by filing in the United States court of appeals for the circuit wherein such applicant resides or has his principal place of business, or in the United States Court of Appeals for the District of Columbia Circuit, within sixty days after the entry of such order, a written petition praying that the order of the Secretary be set aside. A copy of such petition shall be forthwith transmitted by the clerk of the court to the Secretary, or any officer designated by him for that purpose, and thereupon the Secretary shall certify and file in the court the record upon which the order complained of was entered, as provided in section 2112 of title 28. Upon the filing of such petition such court shall have exclusive jurisdiction to affirm or set aside such order, except that until the filing of the record the Secretary may modify or set aside his order. No objection to the order of the Secretary shall be considered by the court unless such objection shall have been urged before the Secretary or unless there were reasonable grounds for failure so to do. The finding of the Secretary as to the facts, if supported by substantial evidence, shall be conclusive. If any person shall apply to the court for leave to adduce additional evidence, and shall show to the satisfaction of the court that such additional evidence is material and that there were reasonable grounds for failure to adduce such evidence in the proceeding before the Secretary, the court may order such additional evidence to be taken before the Secretary and to be adduced upon the hearing in such manner and upon such terms and conditions as to the court may seem proper. The Secretary may modify his findings as to the facts by reason of the additional evidence so taken, and he shall file with the court such modified findings which, if supported by substantial evidence, shall be conclusive, and his recommendation, if any, for the setting aside of the original order. The judgment of the court affirming or setting aside any such order of the Secretary shall be final, subject to review by the Supreme Court of the United States upon certiorari or certification as provided in section 1254 of title 28. The commencement of proceedings under this subsection shall not, unless specifically ordered by the court to the contrary, operate as a stay of the Secretary's order.

(i) Exemptions of drugs for research; discretionary and mandatory conditions; direct reports to Secretary

(1) The Secretary shall promulgate regulations for exempting from the operation of the foregoing subsections of this section drugs intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of drugs. Such regulations may, within the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon—

(A) the submission to the Secretary, before any clinical testing of a new drug is undertaken, of reports, by the manufacturer or the sponsor of the investigation of such drug, of nonclinical tests of such drug adequate to justify the proposed clinical testing;

(B) the manufacturer or the sponsor of the investigation of a new drug proposed to be distributed to investigators for clinical testing obtaining a signed agreement from each of such investigators that patients to whom the drug is administered will be under his personal supervision, or under the supervision of investigators responsible to him, and that he will not supply such drug to any other investigator, or to clinics, for administration to human beings;

(C) the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such drug, of data (including but not limited to analytical reports by investigators) obtained as the result of such investigational use of such drug, as the Secretary finds will enable him to evaluate the safety and effectiveness of such drug in the event of the filing of an application pursuant to subsection (b); and

(D) the submission to the Secretary by the manufacturer or the sponsor of the investigation of a new drug of a statement of intent regarding whether the manufacturer or sponsor has plans for assessing pediatric safety and efficacy.

(2) Subject to paragraph (3), a clinical investigation of a new drug may begin 30 days after the Secretary has received from the manufacturer or sponsor of the investigation a submission containing such information about the drug and the clinical investigation, including—

(A) information on design of the investigation and adequate reports of basic information, certified by the applicant to be accurate reports, necessary to assess the safety of the drug for use in clinical investigation; and

(B) adequate information on the chemistry and manufacturing of the drug, controls available for the drug, and primary data tabulations from nonclinical tests or human studies.

(3)(A) At any time, the Secretary may prohibit the sponsor of an investigation from conducting the investigation (referred to in this paragraph as a ''clinical hold'') if the Secretary makes a determination described in subparagraph (B). The Secretary shall specify the basis for the clinical hold, including the specific information available to the Secretary which served as the basis for such clinical hold, and confirm such determination in writing.

(B) For purposes of subparagraph (A), a determination described in this subparagraph with respect to a clinical hold is that—

(i) the drug involved represents an unreasonable risk to the safety of the persons who are

the subjects of the clinical investigation, taking into account the qualifications of the clinical investigators, information about the drug, the design of the clinical investigation, the condition for which the drug is to be investigated, and the health status of the subjects involved; or

(ii) the clinical hold should be issued for such other reasons as the Secretary may by regulation establish (including reasons established by regulation before November 21, 1997).

(C) Any written request to the Secretary from the sponsor of an investigation that a clinical hold be removed shall receive a decision, in writing and specifying the reasons therefor, within 30 days after receipt of such request. Any such request shall include sufficient information to support the removal of such clinical hold.

(4) Regulations under paragraph (1) shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational purposes certify to such manufacturer or sponsor that they will inform any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where it is not feasible, it is contrary to the best interests of such human beings, or the proposed clinical testing poses no more than minimal risk to such human beings and includes appropriate safeguards as prescribed to protect the rights, safety, and welfare of such human beings. Nothing in this subsection shall be construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs. The Secretary shall update such regulations to require inclusion in the informed consent documents and process a statement that clinical trial information for such clinical investigation has been or will be submitted for inclusion in the registry data bank pursuant to subsection (j) of section 282 of title 42.

(j) Abbreviated new drug applications

(1) Any person may file with the Secretary an abbreviated application for the approval of a new drug.

(2)(A) An abbreviated application for a new drug shall contain—

(i) information to show that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the new drug have been previously approved for a drug listed under paragraph (7) (hereinafter in this subsection referred to as a ''listed drug'');

(ii)(I) if the listed drug referred to in clause (i) has only one active ingredient, information to show that the active ingredient of the new drug is the same as that of the listed drug;

(II) if the listed drug referred to in clause (i) has more than one active ingredient, information to show that the active ingredients of the new drug are the same as those of the listed drug, or

(III) if the listed drug referred to in clause (i) has more than one active ingredient and if one of the active ingredients of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the other active ingredients of the new drug are the same as the active ingredients of the listed drug, information to show that the different active ingredient is an active ingredient of a listed drug or of a drug which does not meet the requirements of section 321(p) of this title, and such other information respecting the different active ingredient with respect to which the petition was filed as the Secretary may require;

(iii) information to show that the route of administration, the dosage form, and the strength of the new drug are the same as those of the listed drug referred to in clause (i) or, if the route of administration, the dosage form, or the strength of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), such information respecting the route of administration, dosage form, or strength with respect to which the petition was filed as the Secretary may require;

(iv) information to show that the new drug is bioequivalent to the listed drug referred to in clause (i), except that if the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in clause (i) and the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in clause (i);

(v) information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug referred to in clause (i) except for changes required because of differences approved under a petition filed under subparagraph (C) or because the new drug and the listed drug are produced or distributed by different manufacturers;

(vi) the items specified in clauses (ii) through (vi) of subsection (b)(1)(A);

(vii) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b) or (c)—

(I) that such patent information has not been filed,

(II) that such patent has expired,

(III) of the date on which such patent will expire, or

(IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

(viii) if with respect to the listed drug referred to in clause (i) information was filed under subsection (b) or (c) for a method of use patent which does not claim a use for which the applicant is seeking approval under this

subsection, a statement that the method of use patent does not claim such a use.

The Secretary may not require that an abbreviated application contain information in addition to that required by clauses (i) through (viii).

(B) NOTICE OF OPINION THAT PATENT IS INVALID OR WILL NOT BE INFRINGED.—

(i) AGREEMENT TO GIVE NOTICE.—An applicant that makes a certification described in subparagraph (A)(vii)(IV) shall include in the application a statement that the applicant will give notice as required by this subparagraph.

(ii) TIMING OF NOTICE.—An applicant that makes a certification described in subparagraph (A)(vii)(IV) shall give notice as required under this subparagraph—

(I) if the certification is in the application, not later than 20 days after the date of the postmark on the notice with which the Secretary informs the applicant that the application has been filed; or

(II) if the certification is in an amendment or supplement to the application, at the time at which the applicant submits the amendment or supplement, regardless of whether the applicant has already given notice with respect to another such certification contained in the application or in an amendment or supplement to the application.

(iii) RECIPIENTS OF NOTICE.—An applicant required under this subparagraph to give notice shall give notice to—

(I) each owner of the patent that is the subject of the certification (or a representative of the owner designated to receive such a notice); and

(II) the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent (or a representative of the holder designated to receive such a notice).

(iv) CONTENTS OF NOTICE.—A notice required under this subparagraph shall—

(I) state that an application that contains data from bioavailability or bioequivalence studies has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification; and

(II) include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed.

(C) If a person wants to submit an abbreviated application for a new drug which has a different active ingredient or whose route of administration, dosage form, or strength differ from that of a listed drug, such person shall submit a petition to the Secretary seeking permission to file such an application. The Secretary shall approve or disapprove a petition submitted under this subparagraph within ninety days of the date the petition is submitted. The Secretary shall approve such a petition unless the Secretary finds—

(i) that investigations must be conducted to show the safety and effectiveness of the drug or of any of its active ingredients, the route of administration, the dosage form, or strength which differ from the listed drug; or

(ii) that any drug with a different active ingredient may not be adequately evaluated for approval as safe and effective on the basis of the information required to be submitted in an abbreviated application.

(D)(i) An applicant may not amend or supplement an application to seek approval of a drug referring to a different listed drug from the listed drug identified in the application as submitted to the Secretary.

(ii) With respect to the drug for which an application is submitted, nothing in this subsection prohibits an applicant from amending or supplementing the application to seek approval of a different strength.

(iii) Within 60 days after December 8, 2003, the Secretary shall issue guidance defining the term ''listed drug'' for purposes of this subparagraph.

(3)(A) The Secretary shall issue guidance for the individuals who review applications submitted under paragraph (1), which shall relate to promptness in conducting the review, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards, and which shall apply equally to all individuals who review such applications.

(B) The Secretary shall meet with a sponsor of an investigation or an applicant for approval for a drug under this subsection if the sponsor or applicant makes a reasonable written request for a meeting for the purpose of reaching agreement on the design and size of bioavailability and bioequivalence studies needed for approval of such application. The sponsor or applicant shall provide information necessary for discussion and agreement on the design and size of such studies. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant.

(C) Any agreement regarding the parameters of design and size of bioavailability and bioequivalence studies of a drug under this paragraph that is reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Such agreement shall not be changed after the testing begins, except—

(i) with the written agreement of the sponsor or applicant; or

(ii) pursuant to a decision, made in accordance with subparagraph (D) by the director of the reviewing division, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.

(D) A decision under subparagraph (C)(ii) by the director shall be in writing and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant will be present and at which the director will document the scientific issue involved.

(E) The written decisions of the reviewing division shall be binding upon, and may not di-

rectly or indirectly be changed by, the field or compliance office personnel unless such field or compliance office personnel demonstrate to the reviewing division why such decision should be modified.

(F) No action by the reviewing division may be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.

(G) For purposes of this paragraph, the reviewing division is the division responsible for the review of an application for approval of a drug under this subsection (including scientific matters, chemistry, manufacturing, and controls).

(4) Subject to paragraph (5), the Secretary shall approve an application for a drug unless the Secretary finds—

(A) the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are inadequate to assure and preserve its identity, strength, quality, and purity;

(B) information submitted with the application is insufficient to show that each of the proposed conditions of use have been previously approved for the listed drug referred to in the application;

(C)(i) if the listed drug has only one active ingredient, information submitted with the application is insufficient to show that the active ingredient is the same as that of the listed drug;

(ii) if the listed drug has more than one active ingredient, information submitted with the application is insufficient to show that the active ingredients are the same as the active ingredients of the listed drug, or

(iii) if the listed drug has more than one active ingredient and if the application is for a drug which has an active ingredient different from the listed drug, information submitted with the application is insufficient to show—

(I) that the other active ingredients are the same as the active ingredients of the listed drug, or

(II) that the different active ingredient is an active ingredient of a listed drug or a drug which does not meet the requirements of section 321(p) of this title,

or no petition to file an application for the drug with the different ingredient was approved under paragraph (2)(C);

(D)(i) if the application is for a drug whose route of administration, dosage form, or strength of the drug is the same as the route of administration, dosage form, or strength of the listed drug referred to in the application, information submitted in the application is insufficient to show that the route of administration, dosage form, or strength is the same as that of the listed drug, or

(ii) if the application is for a drug whose route of administration, dosage form, or strength of the drug is different from that of the listed drug referred to in the application, no petition to file an application for the drug with the different route of administration, dosage form, or strength was approved under paragraph (2)(C);

(E) if the application was filed pursuant to the approval of a petition under paragraph (2)(C), the application did not contain the information required by the Secretary respecting the active ingredient, route of administration, dosage form, or strength which is not the same;

(F) information submitted in the application is insufficient to show that the drug is bioequivalent to the listed drug referred to in the application or, if the application was filed pursuant to a petition approved under paragraph (2)(C), information submitted in the application is insufficient to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in paragraph (2)(A)(i) and that the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in such paragraph;

(G) information submitted in the application is insufficient to show that the labeling proposed for the drug is the same as the labeling approved for the listed drug referred to in the application except for changes required because of differences approved under a petition filed under paragraph (2)(C) or because the drug and the listed drug are produced or distributed by different manufacturers;

(H) information submitted in the application or any other information available to the Secretary shows that (i) the inactive ingredients of the drug are unsafe for use under the conditions prescribed, recommended, or suggested in the labeling proposed for the drug, or (ii) the composition of the drug is unsafe under such conditions because of the type or quantity of inactive ingredients included or the manner in which the inactive ingredients are included;

(I) the approval under subsection (c) of the listed drug referred to in the application under this subsection has been withdrawn or suspended for grounds described in the first sentence of subsection (e), the Secretary has published a notice of opportunity for hearing to withdraw approval of the listed drug under subsection (c) for grounds described in the first sentence of subsection (e), the approval under this subsection of the listed drug referred to in the application under this subsection has been withdrawn or suspended under paragraph (6), or the Secretary has determined that the listed drug has been withdrawn from sale for safety or effectiveness reasons;

(J) the application does not meet any other requirement of paragraph (2)(A); or

(K) the application contains an untrue statement of material fact.

(5)(A) Within one hundred and eighty days of the initial receipt of an application under paragraph (2) or within such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall approve or disapprove the application.

(B) The approval of an application submitted under paragraph (2) shall be made effective on the last applicable date determined by applying the following to each certification made under paragraph (2)(A)(vii):

(i) If the applicant only made a certification described in subclause (I) or (II) of paragraph (2)(A)(vii) or in both such subclauses, the approval may be made effective immediately.

(ii) If the applicant made a certification described in subclause (III) of paragraph (2)(A)(vii), the approval may be made effective on the date certified under subclause (III).

(iii) If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in paragraph (2)(B) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under subsection (b)(1) or (c)(2) before the date on which the application (excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, was submitted. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—

(I) if before the expiration of such period the district court decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the approval shall be made effective on—

(aa) the date on which the court enters judgment reflecting the decision; or

(bb) the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed;

(II) if before the expiration of such period the district court decides that the patent has been infringed—

(aa) if the judgment of the district court is appealed, the approval shall be made effective on—

(AA) the date on which the court of appeals decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity); or

(BB) the date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent that is the subject of the certification is invalid or not infringed; or

(bb) if the judgment of the district court is not appealed or is affirmed, the approval shall be made effective on the date specified by the district court in a court order under section 271(e)(4)(A) of title 35;

(III) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective as provided in subclause (I); or

(IV) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent has been infringed, the approval shall be made effective as provided in subclause (II).

In such an action, each of the parties shall reasonably cooperate in expediting the action.

(iv) 180-DAY EXCLUSIVITY PERIOD.—

(I) EFFECTIVENESS OF APPLICATION.—Subject to subparagraph (D), if the application contains a certification described in paragraph (2)(A)(vii)(IV) and is for a drug for which a first applicant has submitted an application containing such a certification, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant.

(II) DEFINITIONS.—In this paragraph:

(aa) 180-DAY EXCLUSIVITY PERIOD.—The term ''180-day exclusivity period'' means the 180-day period ending on the day before the date on which an application submitted by an applicant other than a first applicant could become effective under this clause.

(bb) FIRST APPLICANT.—As used in this subsection, the term ''first applicant'' means an applicant that, on the first day on which a substantially complete application containing a certification described in paragraph (2)(A)(vii)(IV) is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a certification described in paragraph (2)(A)(vii)(IV) for the drug.

(cc) SUBSTANTIALLY COMPLETE APPLICATION.—As used in this subsection, the term ''substantially complete application'' means an application under this subsection that on its face is sufficiently complete to permit a substantive review and contains all the information required by paragraph (2)(A).

(dd) TENTATIVE APPROVAL.—

(AA) IN GENERAL.—The term ''tentative approval'' means notification to an applicant by the Secretary that an application under this subsection meets the requirements of paragraph (2)(A), but cannot receive effective approval because the application does not meet the requirements of this subparagraph, there is a period of exclusivity for the listed drug under subparagraph (F) or section 355a of this title, or there is a 7-year period of exclusivity for the listed drug under section 360cc of this title.

(BB) LIMITATION.—A drug that is granted tentative approval by the Sec-

retary is not an approved drug and shall not have an effective approval until the Secretary issues an approval after any necessary additional review of the application.

(v) 180-DAY EXCLUSIVITY PERIOD FOR COMPETITIVE GENERIC THERAPIES.—

(I) EFFECTIVENESS OF APPLICATION.—Subject to subparagraph (D)(iv), if the application is for a drug that is the same as a competitive generic therapy for which any first approved applicant has commenced commercial marketing, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the competitive generic therapy (including the commercial marketing of the listed drug) by any first approved applicant.

(II) LIMITATION.—The exclusivity period under subclause (I) shall not apply with respect to a competitive generic therapy that has previously received an exclusivity period under subclause (I).

(III) DEFINITIONS.—In this clause and subparagraph (D)(iv):

(aa) The term ''competitive generic therapy'' means a drug—

(AA) that is designated as a competitive generic therapy under section 356h of this title; and

(BB) for which there are no unexpired patents or exclusivities on the list of products described in section 355(j)(7)(A) of this title at the time of submission.

(bb) The term ''first approved applicant'' means any applicant that has submitted an application that—

(AA) is for a competitive generic therapy that is approved on the first day on which any application for such competitive generic therapy is approved;

(BB) is not eligible for a 180-day exclusivity period under clause (iv) for the drug that is the subject of the application for the competitive generic therapy; and

(CC) is not for a drug for which all drug versions have forfeited eligibility for a 180-day exclusivity period under clause (iv) pursuant to subparagraph (D).

(C) CIVIL ACTION TO OBTAIN PATENT CERTAINTY.—

(i) DECLARATORY JUDGMENT ABSENT INFRINGEMENT ACTION.—

(I) IN GENERAL.—No action may be brought under section 2201 of title 28 by an applicant under paragraph (2) for a declaratory judgment with respect to a patent which is the subject of the certification referred to in subparagraph (B)(iii) unless—

(aa) the 45-day period referred to in such subparagraph has expired;

(bb) neither the owner of such patent nor the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent brought a civil action against the applicant for infringement of the patent before the expiration of such period; and

(cc) in any case in which the notice provided under paragraph (2)(B) relates to noninfringement, the notice was accompanied by a document described in subclause (III).

(II) FILING OF CIVIL ACTION.—If the conditions described in items (aa), (bb), and as applicable, (cc) of subclause (I) have been met, the applicant referred to in such subclause may, in accordance with section 2201 of title 28, bring a civil action under such section against the owner or holder referred to in such subclause (but not against any owner or holder that has brought such a civil action against the applicant, unless that civil action was dismissed without prejudice) for a declaratory judgment that the patent is invalid or will not be infringed by the drug for which the applicant seeks approval, except that such civil action may be brought for a declaratory judgment that the patent will not be infringed only in a case in which the condition described in subclause (I)(cc) is applicable. A civil action referred to in this subclause shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(III) OFFER OF CONFIDENTIAL ACCESS TO APPLICATION.—For purposes of subclause (I)(cc), the document described in this subclause is a document providing an offer of confidential access to the application that is in the custody of the applicant under paragraph (2) for the purpose of determining whether an action referred to in subparagraph (B)(iii) should be brought. The document providing the offer of confidential access shall contain such restrictions as to persons entitled to access, and on the use and disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade secrets and other confidential business information. A request for access to an application under an offer of confidential access shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access, and on the use and disposition of any information accessed, contained in the offer of confidential access, and those restrictions and other terms of the offer of confidential access shall be considered terms of an enforceable contract. Any person provided an offer of confidential access shall review the application for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the certification under paragraph (2)(A)(vii)(IV) and for no other purpose, and may not disclose information of no relevance to any issue of patent infringement to any person other than a person provided an offer of confidential access. Further, the application may be redacted by the applicant to remove any information of no relevance to any issue of patent infringement.

(ii) COUNTERCLAIM TO INFRINGEMENT ACTION.—

(I) IN GENERAL.—If an owner of the patent or the holder of the approved application

under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) or (c) on the ground that the patent does not claim either—

(aa) the drug for which the application was approved; or

(bb) an approved method of using the drug.

(II) NO INDEPENDENT CAUSE OF ACTION.—Subclause (I) does not authorize the assertion of a claim described in subclause (I) in any civil action or proceeding other than a counterclaim described in subclause (I).

(iii) NO DAMAGES.—An applicant shall not be entitled to damages in a civil action under clause (i) or a counterclaim under clause (ii).

(D) FORFEITURE OF 180-DAY EXCLUSIVITY PERIOD.—

(i) DEFINITION OF FORFEITURE EVENT.—In this subparagraph, the term ''forfeiture event'', with respect to an application under this subsection, means the occurrence of any of the following:

(I) FAILURE TO MARKET.—The first applicant fails to market the drug by the later of—

(aa) the earlier of the date that is—

(AA) 75 days after the date on which the approval of the application of the first applicant is made effective under subparagraph (B)(iii); or

(BB) 30 months after the date of submission of the application of the first applicant; or

(bb) with respect to the first applicant or any other applicant (which other applicant has received tentative approval), the date that is 75 days after the date as of which, as to each of the patents with respect to which the first applicant submitted and lawfully maintained a certification qualifying the first applicant for the 180-day exclusivity period under subparagraph (B)(iv), at least 1 of the following has occurred:

(AA) In an infringement action brought against that applicant with respect to the patent or in a declaratory judgment action brought by that applicant with respect to the patent, a court enters a final decision from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the patent is invalid or not infringed.

(BB) In an infringement action or a declaratory judgment action described in subitem (AA), a court signs a settlement order or consent decree that enters a final judgment that includes a finding that the patent is invalid or not infringed.

(CC) The patent information submitted under subsection (b) or (c) is withdrawn by the holder of the application approved under subsection (b).

(II) WITHDRAWAL OF APPLICATION.—The first applicant withdraws the application or the Secretary considers the application to have been withdrawn as a result of a determination by the Secretary that the application does not meet the requirements for approval under paragraph (4).

(III) AMENDMENT OF CERTIFICATION.—The first applicant amends or withdraws the certification for all of the patents with respect to which that applicant submitted a certification qualifying the applicant for the 180-day exclusivity period.

(IV) FAILURE TO OBTAIN TENTATIVE APPROVAL.—The first applicant fails to obtain tentative approval of the application within 30 months after the date on which the application is filed, unless the failure is caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application is filed.

(V) AGREEMENT WITH ANOTHER APPLICANT, THE LISTED DRUG APPLICATION HOLDER, OR A PATENT OWNER.—The first applicant enters into an agreement with another applicant under this subsection for the drug, the holder of the application for the listed drug, or an owner of the patent that is the subject of the certification under paragraph (2)(A)(vii)(IV), the Federal Trade Commission or the Attorney General files a complaint, and there is a final decision of the Federal Trade Commission or the court with regard to the complaint from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the agreement has violated the antitrust laws (as defined in section 12 of title 15, except that the term includes section 45 of title 15 to the extent that that section applies to unfair methods of competition).

(VI) EXPIRATION OF ALL PATENTS.—All of the patents as to which the applicant submitted a certification qualifying it for the 180-day exclusivity period have expired.

(ii) FORFEITURE.—The 180-day exclusivity period described in subparagraph (B)(iv) shall be forfeited by a first applicant if a forfeiture event occurs with respect to that first applicant.

(iii) SUBSEQUENT APPLICANT.—If all first applicants forfeit the 180-day exclusivity period under clause (ii)—

(I) approval of any application containing a certification described in paragraph (2)(A)(vii)(IV) shall be made effective in accordance with subparagraph (B)(iii); and

(II) no applicant shall be eligible for a 180-day exclusivity period.

(iv) SPECIAL FORFEITURE RULE FOR COMPETITIVE GENERIC THERAPY.—The 180-day exclusivity period described in subparagraph (B)(v) shall be forfeited by a first approved applicant if the applicant fails to market the competitive generic therapy within 75 days after the date on which the approval of the first approved applicant's application for the competitive generic therapy is made effective.

(E) If the Secretary decides to disapprove an application, the Secretary shall give the applicant notice of an opportunity for a hearing before the Secretary on the question of whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(F)(i) Repealed. Pub. L. 117–9, §1(b)(1)(B), Apr. 23, 2021, 135 Stat. 258.

(ii) If an application submitted under subsection (b) for a drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under subsection (b), is approved after September 24, 1984, no application may be submitted under this subsection which refers to the drug for which the subsection (b) application was submitted before the expiration of five years from the date of the approval of the application under subsection (b), except that such an application may be submitted under this subsection after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in subclause (IV) of paragraph (2)(A)(vii). The approval of such an application shall be made effective in accordance with subparagraph (B) except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (B)(iii) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) for a drug, which includes an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) that has been approved in another application approved under subsection (b), is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under this subsection for the conditions of approval of such drug in the subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) for such drug.

(iv) If a supplement to an application approved under subsection (b) is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under this subsection for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b).

(v) If an application (or supplement to an application) submitted under subsection (b) for a drug, which includes an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) that has been approved in another application under subsection (b), was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted or which refers to a change approved in a supplement to the subsection (b) application effective before the expiration of two years from September 24, 1984.

(6) If a drug approved under this subsection refers in its approved application to a drug the approval of which was withdrawn or suspended for grounds described in the first sentence of subsection (e) or was withdrawn or suspended under this paragraph or which, as determined by the Secretary, has been withdrawn from sale for safety or effectiveness reasons, the approval of the drug under this subsection shall be withdrawn or suspended—

(A) for the same period as the withdrawal or suspension under subsection (e) or this paragraph, or

(B) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

(7)(A)(i) Within sixty days of September 24, 1984, the Secretary shall publish and make available to the public—

(I) a list in alphabetical order of the official and proprietary name of each drug which has been approved for safety and effectiveness under subsection (c) before September 24, 1984;

(II) the date of approval if the drug is approved after 1981 and the number of the application which was approved; and

(III) whether in vitro or in vivo bioequivalence studies, or both such studies, are required for applications filed under this subsection which will refer to the drug published.

(ii) Every thirty days after the publication of the first list under clause (i) the Secretary shall revise the list to include each drug which has been approved for safety and effectiveness under subsection (c) or approved under this subsection during the thirty-day period.

(iii) When patent information submitted under subsection (c) respecting a drug included on the list is to be published by the Secretary, the Secretary shall, in revisions made under clause (ii), include such information for such drug.

(iv) For each drug included on the list, the Secretary shall specify any exclusivity period that is applicable, for which the Secretary has determined the expiration date, and for which such period has not yet expired, under—

(I) clause (ii), (iii), or (iv) of subsection (c)(3)(E);
(II) clause (iv) or (v) of paragraph (5)(B);
(III) clause (ii), (iii), or (iv) of paragraph (5)(F);
(IV) section 355a of this title;
(V) section 355f of this title;
(VI) section 360cc(a) of this title; or
(VII) subsection (u).

(v)(I) With respect to an application submitted pursuant to subsection (b)(2) for a drug that is subject to section 353(b) of this title for which the sole difference from a listed drug relied upon in the application is a difference in inactive ingredients not permitted under clause (iii) or (iv) of section 314.94(a)(9) of title 21, Code of Federal Regulations (or any successor regulations), the Secretary shall make an evaluation with respect to whether such drug is a therapeutic equivalent (as defined in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) to another approved drug product in the prescription drug product section of the list under this paragraph as follows:

(aa) With respect to such an application submitted after December 29, 2022, the evaluation shall be made with respect to a listed drug relied upon in the application pursuant to subsection (b)(2) that is a pharmaceutical equivalent (as defined in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) to the drug in the application pursuant to subsection (b)(2) at the time of approval of such application or not later than 180 days after the date of such approval, provided that the request for such an evaluation is made in the original application (or in a resubmission to a complete response letter), and all necessary data and information are submitted in the original application (or in a resubmission in response to a complete response letter) for the therapeutic equivalence evaluation, including information to demonstrate bioequivalence, in a form and manner prescribed by the Secretary.

(bb) With respect to such an application approved prior to or on December 29, 2022, the evaluation shall be made not later than 180 days after receipt of a request for a therapeutic equivalence evaluation submitted as part of a supplement to such application; or with respect to an application that was submitted prior to December 29, 2022, but not approved as of December 29, 2022, the evaluation shall be made not later than 180 days after the date of approval of such application if a request for such evaluation is submitted as an amendment to the application, provided that—

(AA) such request for a therapeutic equivalence evaluation is being sought with respect to a listed drug relied upon in the application, and the relied upon listed drug is in the prescription drug product section of the list under this paragraph and is a pharmaceutical equivalent (as defined in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) to the drug for which a therapeutic equivalence evaluation is sought; and

(BB) the amendment or supplement, as applicable, containing such request, or the relevant application, includes all necessary data and information for the therapeutic equivalence evaluation, including information to demonstrate bioequivalence, in a form and manner prescribed by the Secretary.

(II) When the Secretary makes an evaluation under subclause (I), the Secretary shall, in revisions made to the list pursuant to clause (ii), include such information for such drug.

(B) A drug approved for safety and effectiveness under subsection (c) or approved under this subsection shall, for purposes of this subsection, be considered to have been published under subparagraph (A) on the date of its approval or September 24, 1984, whichever is later.

(C) If the approval of a drug was withdrawn or suspended for grounds described in the first sentence of subsection (e) or was withdrawn or suspended under paragraph (6) or if the Secretary determines that a drug has been withdrawn from sale for safety or effectiveness reasons, it may not be published in the list under subparagraph (A) or, if the withdrawal or suspension occurred after its publication in such list, it shall be immediately removed from such list—

(i) for the same period as the withdrawal or suspension under subsection (e) or paragraph (6), or

(ii) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

A notice of the removal shall be published in the Federal Register.

(D) In the case of a listed drug for which the list under subparagraph (A)(i) includes a patent for such drug, and any claim of the patent has been cancelled or invalidated pursuant to a final decision issued by the Patent Trial and Appeal Board of the United States Patent and Trademark Office or by a court, from which no appeal has been, or can be, taken, if the holder of the applicable application approved under subsection (c) determines that a patent for such drug, or any patent information for such drug, no longer meets the listing requirements under this section—

(i) the holder of such approved application shall notify the Secretary, in writing, within 14 days of such decision of such cancellation or invalidation and request that such patent or patent information, as applicable, be amended or withdrawn in accordance with the decision issued by the Patent Trial and Appeal Board or a court;

(ii) the holder of such approved application shall include in any notification under clause (i) information related to such patent cancellation or invalidation decision and submit such information, including a copy of such decision, to the Secretary; and

(iii) the Secretary shall, in response to a notification under clause (i), amend or remove patent or patent information in accordance with the relevant decision from the Patent Trial and Appeals Board or court, as applicable, except that the Secretary shall not re-

move from the list any patent or patent information before the expiration of any 180-day exclusivity period under paragraph (5)(B)(iv) that relies on a certification described in paragraph (2)(A)(vii)(IV).

(8) For purposes of this subsection:

(A)(i) The term ''bioavailability'' means the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug and becomes available at the site of drug action.

(ii) For a drug that is not intended to be absorbed into the bloodstream, the Secretary may assess bioavailability by scientifically valid measurements intended to reflect the rate and extent to which the active ingredient or therapeutic ingredient becomes available at the site of drug action.

(B) A drug shall be considered to be bioequivalent to a listed drug if—

(i) the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses; or

(ii) the extent of absorption of the drug does not show a significant difference from the extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the listed drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug.

(C) For a drug that is not intended to be absorbed into the bloodstream, the Secretary may establish alternative, scientifically valid methods to show bioequivalence if the alternative methods are expected to detect a significant difference between the drug and the listed drug in safety and therapeutic effect.

(9) The Secretary shall, with respect to each application submitted under this subsection, maintain a record of—

(A) the name of the applicant,

(B) the name of the drug covered by the application,

(C) the name of each person to whom the review of the chemistry of the application was assigned and the date of such assignment, and

(D) the name of each person to whom the bioequivalence review for such application was assigned and the date of such assignment.

The information the Secretary is required to maintain under this paragraph with respect to an application submitted under this subsection shall be made available to the public after the approval of such application.

(10)(A) If the proposed labeling of a drug that is the subject of an application under this subsection differs from the listed drug due to a labeling revision described under clause (i), the drug that is the subject of such application shall, notwithstanding any other provision of this chapter, be eligible for approval and shall not be considered misbranded under section 352 of this title if—

(i) a revision to the labeling of the listed drug has been approved by the Secretary within 90 days of when the application is otherwise eligible for approval under this subsection;

(ii) the sponsor of the application agrees to submit revised labeling for the drug that is the subject of the application not later than 60 days after approval under this subsection of the application;

(iii) the labeling revision described under clause (i) does not include a change to the ''Warnings'' section of the labeling; and

(iv) such application otherwise meets the applicable requirements for approval under this subsection.

(B) If, after a labeling revision described in subparagraph (A)(i), the Secretary determines that the continued presence in interstate commerce of the labeling of the listed drug (as in effect before the revision described in subparagraph (A)(i)) adversely impacts the safe use of the drug, no application under this subsection shall be eligible for approval with such labeling.

(11)(A) Subject to subparagraph (B), the Secretary shall prioritize the review of, and act within 8 months of the date of the submission of, an original abbreviated new drug application submitted for review under this subsection that is for a drug—

(i) for which there are not more than 3 approved drug products listed under paragraph (7) and for which there are no blocking patents and exclusivities; or

(ii) that has been included on the list under section 356e of this title.

(B) To qualify for priority review under this paragraph, not later than 60 days prior to the submission of an application described in subparagraph (A) or that the Secretary may prioritize pursuant to subparagraph (D), the applicant shall provide complete, accurate information regarding facilities involved in manufacturing processes and testing of the drug that is the subject of the application, including facilities in corresponding Type II active pharmaceutical ingredients drug master files referenced in an application and sites or organizations involved in bioequivalence and clinical studies used to support the application, to enable the Secretary to make a determination regarding whether an inspection of a facility is necessary. Such information shall include the relevant (as determined by the Secretary) sections of such application, which shall be unchanged relative to the date of the submission of such application, except to the extent that a change is made to such information to exclude a facility that was not used to generate data to meet any application requirements for such submission and that is not the only facility intended to conduct one or more unit operations in commercial production. Information provided by an applicant under this subparagraph shall not be considered the submission of an application under this subsection.

(C) The Secretary may expedite an inspection or reinspection under section 374 of this title of

an establishment that proposes to manufacture a drug described in subparagraph (A).

(D) Nothing in this paragraph shall prevent the Secretary from prioritizing the review of other applications as the Secretary determines appropriate.

(12) The Secretary shall publish on the internet website of the Food and Drug Administration, and update at least once every 6 months, a list of all drugs approved under subsection (c) for which all patents and periods of exclusivity under this chapter have expired and for which no application has been approved under this subsection.

(13) Upon the request of an applicant regarding one or more specified pending applications under this subsection, the Secretary shall, as appropriate, provide review status updates indicating the categorical status of the applications by each relevant review discipline.

(k) Records and reports; required information; regulations and orders; access to records

(1) In the case of any drug for which an approval of an application filed under subsection (b) or (j) is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to clinical experience and other data or information, received or otherwise obtained by such applicant with respect to such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e). Regulations and orders issued under this subsection and under subsection (i) shall have due regard for the professional ethics of the medical profession and the interests of patients and shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulations or orders are applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this section to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

(3) ACTIVE POSTMARKET RISK IDENTIFICATION.—

(A) DEFINITION.—In this paragraph, the term ''data'' refers to information with respect to a drug approved under this section or under section 262 of title 42, including claims data, patient survey data, standardized analytic files that allow for the pooling and analysis of data from disparate data environments, and any other data deemed appropriate by the Secretary.

(B) DEVELOPMENT OF POSTMARKET RISK IDENTIFICATION AND ANALYSIS METHODS.—The Secretary shall, not later than 2 years after September 27, 2007, in collaboration with public, academic, and private entities—

(i) develop methods to obtain access to disparate data sources including the data sources specified in subparagraph (C);

(ii) develop validated methods for the establishment of a postmarket risk identification and analysis system to link and analyze safety data from multiple sources, with the goals of including, in aggregate—

(I) at least 25,000,000 patients by July 1, 2010; and

(II) at least 100,000,000 patients by July 1, 2012; and

(iii) convene a committee of experts, including individuals who are recognized in the field of protecting data privacy and security, to make recommendations to the Secretary on the development of tools and methods for the ethical and scientific uses for, and communication of, postmarketing data specified under subparagraph (C), including recommendations on the development of effective research methods for the study of drug safety questions.

(C) ESTABLISHMENT OF THE POSTMARKET RISK IDENTIFICATION AND ANALYSIS SYSTEM.—

(i) IN GENERAL.—The Secretary shall, not later than 1 year after the development of the risk identification and analysis methods under subparagraph (B), establish and maintain procedures—

(I) for risk identification and analysis based on electronic health data, in compliance with the regulations promulgated under section 264(c) of the Health Insurance Portability and Accountability Act of 1996, and in a manner that does not disclose individually identifiable health information in violation of paragraph (4)(B);

(II) for the reporting (in a standardized form) of data on all serious adverse drug experiences (as defined in section 355–1(b) of this title) submitted to the Secretary under paragraph (1), and those adverse events submitted by patients, providers, and drug sponsors, when appropriate;

(III) to provide for active adverse event surveillance using the following data sources, as available:

(aa) Federal health-related electronic data (such as data from the Medicare program and the health systems of the Department of Veterans Affairs);

(bb) private sector health-related electronic data (such as pharmaceutical purchase data and health insurance claims data); and

(cc) other data as the Secretary deems necessary to create a robust system to identify adverse events and potential drug safety signals;

(IV) to identify certain trends and patterns with respect to data accessed by the system;

(V) to provide regular reports to the Secretary concerning adverse event trends, adverse event patterns, incidence and prevalence of adverse events, and other information the Secretary determines appropriate, which may include data on comparative national adverse event trends; and

(VI) to enable the program to export data in a form appropriate for further ag-

gregation, statistical analysis, and reporting.

(ii) TIMELINESS OF REPORTING.—The procedures established under clause (i) shall ensure that such data are accessed, analyzed, and reported in a timely, routine, and systematic manner, taking into consideration the need for data completeness, coding, cleansing, and standardized analysis and transmission.

(iii) PRIVATE SECTOR RESOURCES.—To ensure the establishment of the active postmarket risk identification and analysis system under this subsection not later than 1 year after the development of the risk identification and analysis methods under subparagraph (B), as required under clause (i), the Secretary may, on a temporary or permanent basis, implement systems or products developed by private entities.

(iv) COMPLEMENTARY APPROACHES.—To the extent the active postmarket risk identification and analysis system under this subsection is not sufficient to gather data and information relevant to a priority drug safety question, the Secretary shall develop, support, and participate in complementary approaches to gather and analyze such data and information, including—

(I) approaches that are complementary with respect to assessing the safety of use of a drug in domestic populations not included, or underrepresented, in the trials used to approve the drug (such as older people, people with comorbidities, pregnant women, or children); and

(II) existing approaches such as the Vaccine Adverse Event Reporting System and the Vaccine Safety Datalink or successor databases.

(v) AUTHORITY FOR CONTRACTS.—The Secretary may enter into contracts with public and private entities to fulfill the requirements of this subparagraph.

(4) ADVANCED ANALYSIS OF DRUG SAFETY DATA.—

(A) PURPOSE.—The Secretary shall establish collaborations with public, academic, and private entities, which may include the Centers for Education and Research on Therapeutics under section 299b–1 of title 42, to provide for advanced analysis of drug safety data described in paragraph (3)(C) and other information that is publicly available or is provided by the Secretary, in order to—

(i) improve the quality and efficiency of postmarket drug safety risk-benefit analysis;

(ii) provide the Secretary with routine access to outside expertise to study advanced drug safety questions; and

(iii) enhance the ability of the Secretary to make timely assessments based on drug safety data.

(B) PRIVACY.—Such analysis shall not disclose individually identifiable health information when presenting such drug safety signals and trends or when responding to inquiries regarding such drug safety signals and trends.

(C) PUBLIC PROCESS FOR PRIORITY QUESTIONS.—At least biannually, the Secretary shall seek recommendations from the Drug Safety and Risk Management Advisory Committee (or any successor committee) and from other advisory committees, as appropriate, to the Food and Drug Administration on—

(i) priority drug safety questions; and

(ii) mechanisms for answering such questions, including through—

(I) active risk identification under paragraph (3); and

(II) when such risk identification is not sufficient, postapproval studies and clinical trials under subsection (*o*)(3).

(D) PROCEDURES FOR THE DEVELOPMENT OF DRUG SAFETY COLLABORATIONS.—

(i) IN GENERAL.—Not later than 180 days after the date of the establishment of the active postmarket risk identification and analysis system under this subsection, the Secretary shall establish and implement procedures under which the Secretary may routinely contract with one or more qualified entities to—

(I) classify, analyze, or aggregate data described in paragraph (3)(C) and information that is publicly available or is provided by the Secretary;

(II) allow for prompt investigation of priority drug safety questions, including—

(aa) unresolved safety questions for drugs or classes of drugs; and

(bb) for a newly-approved drugs,[2] safety signals from clinical trials used to approve the drug and other preapproval trials; rare, serious drug side effects; and the safety of use in domestic populations not included, or underrepresented, in the trials used to approve the drug (such as older people, people with comorbidities, pregnant women, or children);

(III) perform advanced research and analysis on identified drug safety risks;

(IV) focus postapproval studies and clinical trials under subsection (*o*)(3) more effectively on cases for which reports under paragraph (1) and other safety signal detection is not sufficient to resolve whether there is an elevated risk of a serious adverse event associated with the use of a drug; and

(V) carry out other activities as the Secretary deems necessary to carry out the purposes of this paragraph.

(ii) REQUEST FOR SPECIFIC METHODOLOGY.—The procedures described in clause (i) shall permit the Secretary to request that a specific methodology be used by the qualified entity. The qualified entity shall work with the Secretary to finalize the methodology to be used.

(E) USE OF ANALYSES.—The Secretary shall provide the analyses described in this paragraph, including the methods and results of such analyses, about a drug to the sponsor or sponsors of such drug.

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[2] So in original. Probably should be ''drug,''.

(F) QUALIFIED ENTITIES.—

(i) IN GENERAL.—The Secretary shall enter into contracts with a sufficient number of qualified entities to develop and provide information to the Secretary in a timely manner.

(ii) QUALIFICATION.—The Secretary shall enter into a contract with an entity under clause (i) only if the Secretary determines that the entity has a significant presence in the United States and has one or more of the following qualifications:

(I) The research, statistical, epidemiologic, or clinical capability and expertise to conduct and complete the activities under this paragraph, including the capability and expertise to provide the Secretary de-identified data consistent with the requirements of this subsection.

(II) An information technology infrastructure in place to support electronic data and operational standards to provide security for such data.

(III) Experience with, and expertise on, the development of drug safety and effectiveness research using electronic population data.

(IV) An understanding of drug development or risk/benefit balancing in a clinical setting.

(V) Other expertise which the Secretary deems necessary to fulfill the activities under this paragraph.

(G) CONTRACT REQUIREMENTS.—Each contract with a qualified entity under subparagraph (F)(i) shall contain the following requirements:

(i) ENSURING PRIVACY.—The qualified entity shall ensure that the entity will not use data under this subsection in a manner that—

(I) violates the regulations promulgated under section 264(c) of the Health Insurance Portability and Accountability Act of 1996;

(II) violates sections 552 or 552a of title 5 with regard to the privacy of individually-identifiable beneficiary health information; or

(III) discloses individually identifiable health information when presenting drug safety signals and trends or when responding to inquiries regarding drug safety signals and trends.

Nothing in this clause prohibits lawful disclosure for other purposes.

(ii) COMPONENT OF ANOTHER ORGANIZATION.—If a qualified entity is a component of another organization—

(I) the qualified entity shall establish appropriate security measures to maintain the confidentiality and privacy of such data; and

(II) the entity shall not make an unauthorized disclosure of such data to the other components of the organization in breach of such confidentiality and privacy requirement.

(iii) TERMINATION OR NONRENEWAL.—If a contract with a qualified entity under this subparagraph is terminated or not renewed, the following requirements shall apply:

(I) CONFIDENTIALITY AND PRIVACY PROTECTIONS.—The entity shall continue to comply with the confidentiality and privacy requirements under this paragraph with respect to all data disclosed to the entity.

(II) DISPOSITION OF DATA.—The entity shall return any data disclosed to such entity under this subsection to which it would not otherwise have access or, if returning the data is not practicable, destroy the data.

(H) COMPETITIVE PROCEDURES.—The Secretary shall use competitive procedures (as defined in section 132 of title 41) to enter into contracts under subparagraph (G).

(I) REVIEW OF CONTRACT IN THE EVENT OF A MERGER OR ACQUISITION.—The Secretary shall review the contract with a qualified entity under this paragraph in the event of a merger or acquisition of the entity in order to ensure that the requirements under this paragraph will continue to be met.

(J) COORDINATION.—In carrying out this paragraph, the Secretary shall provide for appropriate communications to the public, scientific, public health, and medical communities, and other key stakeholders, and to the extent practicable shall coordinate with the activities of private entities, professional associations, or other entities that may have sources of drug safety data.

(5) The Secretary shall—

(A) conduct regular screenings of the Adverse Event Reporting System database and post a quarterly report on the Adverse Event Reporting System Web site of any new safety information or potential signal of a serious risk identified by Adverse[3] Event Reporting System within the last quarter; and[4]

(B) on an annual basis, review the entire backlog of postmarket safety commitments to determine which commitments require revision or should be eliminated, report to the Congress on these determinations, and assign start dates and estimated completion dates for such commitments; and

(C) make available on the Internet website of the Food and Drug Administration—

(i) guidelines, developed with input from experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, that detail best practices for drug safety surveillance using the Adverse Event Reporting System; and

(ii) criteria for public posting of adverse event signals.

(*l*) Public disclosure of safety and effectiveness data and action package

(1) Safety and effectiveness data and information which has been submitted in an application under subsection (b) for a drug and which has not previously been disclosed to the public shall be made available to the public, upon request, unless extraordinary circumstances are shown—

[3] So in original. Probably should be preceded by ''the''.

[4] So in original. The word ''and'' probably should not appear.

(A) if no work is being or will be undertaken to have the application approved,

(B) if the Secretary has determined that the application is not approvable and all legal appeals have been exhausted,

(C) if approval of the application under subsection (c) is withdrawn and all legal appeals have been exhausted,

(D) if the Secretary has determined that such drug is not a new drug, or

(E) upon the effective date of the approval of the first application under subsection (j) which refers to such drug or upon the date upon which the approval of an application under subsection (j) which refers to such drug could be made effective if such an application had been submitted.

(2) ACTION PACKAGE FOR APPROVAL.—

(A) ACTION PACKAGE.—The Secretary shall publish the action package for approval of an application under subsection (b) or section 262 of title 42 on the Internet Web site of the Food and Drug Administration—

(i) not later than 30 days after the date of approval of such applications—

(I) for a drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under this section; or

(II) for a biological product, no active ingredient of which has been approved in any other application under section 262 of title 42; and

(ii) not later than 30 days after the third request for such action package for approval received under section 552 of title 5 for any other drug or biological product.

(B) IMMEDIATE PUBLICATION OF SUMMARY REVIEW.—Notwithstanding subparagraph (A), the Secretary shall publish, on the Internet Web site of the Food and Drug Administration, the materials described in subparagraph (C)(iv) not later than 48 hours after the date of approval of the drug, except where such materials require redaction by the Secretary.

(C) CONTENTS.—An action package for approval of an application under subparagraph (A) shall be dated and shall include the following:

(i) Documents generated by the Food and Drug Administration related to review of the application.

(ii) Documents pertaining to the format and content of the application generated during drug development.

(iii) Labeling submitted by the applicant.

(iv) A summary review that documents conclusions from all reviewing disciplines about the drug, noting any critical issues and disagreements with the applicant and within the review team and how they were resolved, recommendations for action, and an explanation of any nonconcurrence with review conclusions.

(v) The Division Director and Office Director's decision document which includes—

(I) a brief statement of concurrence with the summary review;

(II) a separate review or addendum to the review if disagreeing with the summary review; and

(III) a separate review or addendum to the review to add further analysis.

(vi) Identification by name of each officer or employee of the Food and Drug Administration who—

(I) participated in the decision to approve the application; and

(II) consents to have his or her name included in the package.

(D) REVIEW.—A scientific review of an application is considered the work of the reviewer and shall not be altered by management or the reviewer once final.

(E) CONFIDENTIAL INFORMATION.—This paragraph does not authorize the disclosure of any trade secret, confidential commercial or financial information, or other matter listed in section 552(b) of title 5.

(m) "Patent" defined

For purposes of this section, the term ''patent'' means a patent issued by the United States Patent and Trademark Office.

(n) Scientific advisory panels

(1) For the purpose of providing expert scientific advice and recommendations to the Secretary regarding a clinical investigation of a drug or the approval for marketing of a drug under this section or section 262 of title 42, the Secretary shall establish panels of experts or use panels of experts established before November 21, 1997, or both.

(2) The Secretary may delegate the appointment and oversight authority granted under section 394 of this title to a director of a center or successor entity within the Food and Drug Administration.

(3) The Secretary shall make appointments to each panel established under paragraph (1) so that each panel shall consist of—

(A) members who are qualified by training and experience to evaluate the safety and effectiveness of the drugs to be referred to the panel and who, to the extent feasible, possess skill and experience in the development, manufacture, or utilization of such drugs;

(B) members with diverse expertise in such fields as clinical and administrative medicine, pharmacy, pharmacology, pharmacoeconomics, biological and physical sciences, and other related professions;

(C) a representative of consumer interests, and a representative of interests of the drug manufacturing industry not directly affected by the matter to be brought before the panel; and

(D) two or more members who are specialists or have other expertise in the particular disease or condition for which the drug under review is proposed to be indicated.

Scientific, trade, and consumer organizations shall be afforded an opportunity to nominate individuals for appointment to the panels. No individual who is in the regular full-time employ of the United States and engaged in the administration of this chapter may be a voting member

of any panel. The Secretary shall designate one of the members of each panel to serve as chairman thereof.

(4) The Secretary shall, as appropriate, provide education and training to each new panel member before such member participates in a panel's activities, including education regarding requirements under this chapter and related regulations of the Secretary, and the administrative processes and procedures related to panel meetings.

(5) Panel members (other than officers or employees of the United States), while attending meetings or conferences of a panel or otherwise engaged in its business, shall be entitled to receive compensation for each day so engaged, including traveltime, at rates to be fixed by the Secretary, but not to exceed the daily equivalent of the rate in effect for positions classified above grade GS–15 of the General Schedule. While serving away from their homes or regular places of business, panel members may be allowed travel expenses (including per diem in lieu of subsistence) as authorized by section 5703 of title 5, for persons in the Government service employed intermittently.

(6) The Secretary shall ensure that scientific advisory panels meet regularly and at appropriate intervals so that any matter to be reviewed by such a panel can be presented to the panel not more than 60 days after the matter is ready for such review. Meetings of the panel may be held using electronic communication to convene the meetings.

(7) Within 90 days after a scientific advisory panel makes recommendations on any matter under its review, the Food and Drug Administration official responsible for the matter shall review the conclusions and recommendations of the panel, and notify the affected persons of the final decision on the matter, or of the reasons that no such decision has been reached. Each such final decision shall be documented including the rationale for the decision.

(*o*) Postmarket studies and clinical trials; labeling

(1) In general

A responsible person may not introduce or deliver for introduction into interstate commerce the new drug involved if the person is in violation of a requirement established under paragraph (3) or (4) with respect to the drug.

(2) Definitions

For purposes of this subsection:

(A) Responsible person

The term ''responsible person'' means a person who—

(i) has submitted to the Secretary a covered application that is pending; or

(ii) is the holder of an approved covered application.

(B) Covered application

The term ''covered application'' means—

(i) an application under subsection (b) for a drug that is subject to section 353(b) of this title; and

(ii) an application under section 262 of title 42.

(C) New safety information; serious risk

The terms ''new safety information'', ''serious risk'', and ''signal of a serious risk'' have the meanings given such terms in section 355–1(b) of this title.

(3) Studies and clinical trials

(A) In general

For any or all of the purposes specified in subparagraph (B), the Secretary may, subject to subparagraph (D), require a responsible person for a drug to conduct a postapproval study or studies of the drug, or a postapproval clinical trial or trials of the drug, on the basis of scientific data deemed appropriate by the Secretary, including information regarding chemically-related or pharmacologically-related drugs.

(B) Purposes of study or clinical trial

The purposes referred to in this subparagraph with respect to a postapproval study or postapproval clinical trial are the following:

(i) To assess a known serious risk related to the use of the drug involved.

(ii) To assess signals of serious risk related to the use of the drug.

(iii) To identify an unexpected serious risk when available data indicates the potential for a serious risk.

(C) Establishment of requirement after approval of covered application

The Secretary may require a postapproval study or studies or postapproval clinical trial or trials for a drug for which an approved covered application is in effect as of the date on which the Secretary seeks to establish such requirement only if the Secretary becomes aware of new safety information.

(D) Determination by Secretary

(i) Postapproval studies

The Secretary may not require the responsible person to conduct a study under this paragraph, unless the Secretary makes a determination that the reports under subsection (k)(1) and the active postmarket risk identification and analysis system as available under subsection (k)(3) will not be sufficient to meet the purposes set forth in subparagraph (B).

(ii) Postapproval clinical trials

The Secretary may not require the responsible person to conduct a clinical trial under this paragraph, unless the Secretary makes a determination that a postapproval study or studies will not be sufficient to meet the purposes set forth in subparagraph (B).

(E) Notification; timetables; periodic reports

(i) Notification

The Secretary shall notify the responsible person regarding a requirement under this paragraph to conduct a postapproval study or clinical trial by the target dates for communication of feedback from the review team to the responsible person re-

garding proposed labeling and postmarketing study commitments as set forth in the letters described in section 101(c) of the Food and Drug Administration Amendments Act of 2007.

(ii) Timetable; periodic reports

For each study or clinical trial required to be conducted under this paragraph, the Secretary shall require that the responsible person submit a timetable for completion of the study or clinical trial. With respect to each study required to be conducted under this paragraph or otherwise undertaken by the responsible person to investigate a safety issue, the Secretary shall require the responsible person to periodically report to the Secretary on the status of such study including whether any difficulties in completing the study have been encountered. With respect to each clinical trial required to be conducted under this paragraph or otherwise undertaken by the responsible person to investigate a safety issue, the Secretary shall require the responsible person to periodically report to the Secretary on the status of such clinical trial including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to the requirements under section 282(j) of title 42. If the responsible person fails to comply with such timetable or violates any other requirement of this subparagraph, the responsible person shall be considered in violation of this subsection, unless the responsible person demonstrates good cause for such noncompliance or such other violation. The Secretary shall determine what constitutes good cause under the preceding sentence.

(F) Dispute resolution

The responsible person may appeal a requirement to conduct a study or clinical trial under this paragraph using dispute resolution procedures established by the Secretary in regulation and guidance.

(4) Safety labeling changes requested by Secretary

(A) New safety or new effectiveness information

If the Secretary becomes aware of new information, including any new safety information or information related to reduced effectiveness, that the Secretary determines should be included in the labeling of the drug, the Secretary shall promptly notify the responsible person or, if the same drug approved under subsection (b) is not currently marketed, the holder of an approved application under subsection (j).

(B) Response to notification

Following notification pursuant to subparagraph (A), the responsible person or the holder of the approved application under subsection (j) shall within 30 days—

(i) submit a supplement proposing changes to the approved labeling to reflect the new safety information, including changes to boxed warnings, contraindications, warnings, precautions, or adverse reactions, or new effectiveness information; or

(ii) notify the Secretary that the responsible person or the holder of the approved application under subsection (j) does not believe a labeling change is warranted and submit a statement detailing the reasons why such a change is not warranted.

(C) Review

Upon receipt of such supplement, the Secretary shall promptly review and act upon such supplement. If the Secretary disagrees with the proposed changes in the supplement or with the statement setting forth the reasons why no labeling change is necessary, the Secretary shall initiate discussions to reach agreement on whether the labeling for the drug should be modified to reflect the new safety or new effectiveness information, and if so, the contents of such labeling changes.

(D) Discussions

Such discussions shall not extend for more than 30 days after the response to the notification under subparagraph (B), unless the Secretary determines an extension of such discussion period is warranted.

(E) Order

Within 15 days of the conclusion of the discussions under subparagraph (D), the Secretary may issue an order directing the responsible person or the holder of the approved application under subsection (j) to make such a labeling change as the Secretary deems appropriate to address the new safety or new effectiveness information. Within 15 days of such an order, the responsible person or the holder of the approved application under subsection (j) shall submit a supplement containing the labeling change.

(F) Dispute resolution

Within 5 days of receiving an order under subparagraph (E), the responsible person or the holder of the approved application under subsection (j) may appeal using dispute resolution procedures established by the Secretary in regulation and guidance.

(G) Violation

If the responsible person or the holder of the approved application under subsection (j) has not submitted a supplement within 15 days of the date of such order under subparagraph (E), and there is no appeal or dispute resolution proceeding pending, the responsible person or holder shall be considered to be in violation of this subsection. If at the conclusion of any dispute resolution procedures the Secretary determines that a supplement must be submitted and such a supplement is not submitted within 15 days of the date of that determination, the responsible person or holder shall be in violation of this subsection.

(H) Public health threat

Notwithstanding subparagraphs (A) through (F), if the Secretary concludes that such a labeling change is necessary to protect the public health, the Secretary may accelerate the timelines in such subparagraphs.

(I) Rule of construction

This paragraph shall not be construed to affect the responsibility of the responsible person or the holder of the approved application under subsection (j) to maintain its label in accordance with existing requirements, including subpart B of part 201 and sections 314.70 and 601.12 of title 21, Code of Federal Regulations (or any successor regulations).

(5) Non-delegation

Determinations by the Secretary under this subsection for a drug shall be made by individuals at or above the level of individuals empowered to approve a drug (such as division directors within the Center for Drug Evaluation and Research).

(p) Risk evaluation and mitigation strategy

(1) In general

A person may not introduce or deliver for introduction into interstate commerce a new drug if—

(A)(i) the application for such drug is approved under subsection (b) or (j) and is subject to section 353(b) of this title; or

(ii) the application for such drug is approved under section 262 of title 42; and

(B) a risk evaluation and mitigation strategy is required under section 355–1 of this title with respect to the drug and the person fails to maintain compliance with the requirements of the approved strategy or with other requirements under section 355–1 of this title, including requirements regarding assessments of approved strategies.

(2) Certain postmarket studies

The failure to conduct a postmarket study under section 356 of this title, subpart H of part 314, or subpart E of part 601 of title 21, Code of Federal Regulations (or any successor regulations), is deemed to be a violation of paragraph (1).

(q) Petitions and civil actions regarding approval of certain applications

(1) In general

(A) Determination

The Secretary shall not delay approval of a pending application submitted under subsection (b)(2) or (j) of this section or section 262(k) of title 42 because of any request to take any form of action relating to the application, either before or during consideration of the request, unless—

(i) the request is in writing and is a petition submitted to the Secretary pursuant to section 10.30 or 10.35 of title 21, Code of Federal Regulations (or any successor regulations); and

(ii) the Secretary determines, upon reviewing the petition, that a delay is necessary to protect the public health.

Consideration of the petition shall be separate and apart from review and approval of any application.

(B) Notification

If the Secretary determines under subparagraph (A) that a delay is necessary with respect to an application, the Secretary shall provide to the applicant, not later than 30 days after making such determination, the following information:

(i) Notification of the fact that a determination under subparagraph (A) has been made.

(ii) If applicable, any clarification or additional data that the applicant should submit to the docket on the petition to allow the Secretary to review the petition promptly.

(iii) A brief summary of the specific substantive issues raised in the petition which form the basis of the determination.

(C) Format

The information described in subparagraph (B) shall be conveyed via either, at the discretion of the Secretary—

(i) a document; or

(ii) a meeting with the applicant involved.

(D) Public disclosure

Any information conveyed by the Secretary under subparagraph (C) shall be considered part of the application and shall be subject to the disclosure requirements applicable to information in such application.

(E) Denial based on intent to delay

If the Secretary determines that a petition or a supplement to the petition was submitted with the primary purpose of delaying the approval of an application and the petition does not on its face raise valid scientific or regulatory issues, the Secretary may deny the petition at any point based on such determination. The Secretary may issue guidance to describe the factors that will be used to determine under this subparagraph whether a petition is submitted with the primary purpose of delaying the approval of an application.

(F) Final agency action

The Secretary shall take final agency action on a petition not later than 150 days after the date on which the petition is submitted. The Secretary shall not extend such period for any reason, including—

(i) any determination made under subparagraph (A);

(ii) the submission of comments relating to the petition or supplemental information supplied by the petitioner; or

(iii) the consent of the petitioner.

(G) Extension of 30-month period

If the filing of an application resulted in first-applicant status under subsection (j)(5)(D)(i)(IV) and approval of the application was delayed because of a petition, the 30-month period under such subsection is deemed to be extended by a period of time

equal to the period beginning on the date on which the Secretary received the petition and ending on the date of final agency action on the petition (inclusive of such beginning and ending dates), without regard to whether the Secretary grants, in whole or in part, or denies, in whole or in part, the petition.

(H) Certification

The Secretary shall not consider a petition for review unless the party submitting such petition does so in written form and the subject document is signed and contains the following certification: ''I certify that, to my best knowledge and belief: (a) this petition includes all information and views upon which the petition relies; (b) this petition includes representative data and/or information known to the petitioner which are unfavorable to the petition; and (c) I have taken reasonable steps to ensure that any representative data and/or information which are unfavorable to the petition were disclosed to me. I further certify that the information upon which I have based the action requested herein first became known to the party on whose behalf this petition is submitted on or about the following date: _____. If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from the following persons or organizations: _____. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.'', with the date on which such information first became known to such party and the names of such persons or organizations inserted in the first and second blank space, respectively.

(I) Verification

The Secretary shall not accept for review any supplemental information or comments on a petition unless the party submitting such information or comments does so in written form and the subject document is signed and contains the following verification: ''I certify that, to my best knowledge and belief: (a) I have not intentionally delayed submission of this document or its contents; and (b) the information upon which I have based the action requested herein first became known to me on or about _____. If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from the following persons or organizations: _____. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.'', with the date on which such information first became known to the party and the names of such persons or organizations inserted in the first and second blank space, respectively.

(2) Exhaustion of administrative remedies

(A) Final agency action within 150 days

The Secretary shall be considered to have taken final agency action on a petition if—

(i) during the 150-day period referred to in paragraph (1)(F), the Secretary makes a final decision within the meaning of section 10.45(d) of title 21, Code of Federal Regulations (or any successor regulation); or

(ii) such period expires without the Secretary having made such a final decision.

(B) Dismissal of certain civil actions

If a civil action is filed against the Secretary with respect to any issue raised in the petition before the Secretary has taken final agency action on the petition within the meaning of subparagraph (A), the court shall dismiss without prejudice the action for failure to exhaust administrative remedies.

(C) Administrative record

For purposes of judicial review related to the approval of an application for which a petition under paragraph (1) was submitted, the administrative record regarding any issue raised by the petition shall include—

(i) the petition filed under paragraph (1) and any supplements and comments thereto;

(ii) the Secretary's response to such petition, if issued; and

(iii) other information, as designated by the Secretary, related to the Secretary's determinations regarding the issues raised in such petition, as long as the information was considered by the agency no later than the date of final agency action as defined under subparagraph (2)(A), and regardless of whether the Secretary responded to the petition at or before the approval of the application at issue in the petition.

(3) Annual report on delays in approvals per petitions

The Secretary shall annually submit to the Congress a report that specifies—

(A) the number of applications that were approved during the preceding 12-month period;

(B) the number of such applications whose effective dates were delayed by petitions referred to in paragraph (1) during such period;

(C) the number of days by which such applications were so delayed; and

(D) the number of such petitions that were submitted during such period.

(4) Exceptions

(A) This subsection does not apply to—

(i) a petition that relates solely to the timing of the approval of an application pursuant to subsection (j)(5)(B)(iv); or

(ii) a petition that is made by the sponsor of an application and that seeks only to have the Secretary take or refrain from taking any form of action with respect to that application.

(B) Paragraph (2) does not apply to a petition addressing issues concerning an applica-

tion submitted pursuant to section 262(k) of title 42.

(5) Definitions

(A) Application

For purposes of this subsection, the term ''application'' means an application submitted under subsection (b)(2) or (j) of this section or section 262(k) of title 42.

(B) Petition

For purposes of this subsection, other than paragraph (1)(A)(i), the term ''petition'' means a request described in paragraph (1)(A)(i).

(r) Postmarket drug safety information for patients and providers

(1) Establishment

Not later than 1 year after September 27, 2007, the Secretary shall improve the transparency of information about drugs and allow patients and health care providers better access to information about drugs by developing and maintaining an Internet Web site that—

(A) provides links to drug safety information listed in paragraph (2) for prescription drugs that are approved under this section or licensed under section 262 of title 42; and

(B) improves communication of drug safety information to patients and providers.

(2) Internet Web site

The Secretary shall carry out paragraph (1) by—

(A) developing and maintaining an accessible, consolidated Internet Web site with easily searchable drug safety information, including the information found on United States Government Internet Web sites, such as the United States National Library of Medicine's Daily Med and Medline Plus Web sites, in addition to other such Web sites maintained by the Secretary;

(B) ensuring that the information provided on the Internet Web site is comprehensive and includes, when available and appropriate—

(i) patient labeling and patient packaging inserts;

(ii) a link to a list of each drug, whether approved under this section or licensed under such section 262, for which a Medication Guide, as provided for under part 208 of title 21, Code of Federal Regulations (or any successor regulations), is required;

(iii) a link to the registry and results data bank provided for under subsections (i) and (j) of section 282 of title 42;

(iv) the most recent safety information and alerts issued by the Food and Drug Administration for drugs approved by the Secretary under this section, such as product recalls, warning letters, and import alerts;

(v) publicly available information about implemented RiskMAPs and risk evaluation and mitigation strategies under subsection (*o*);

(vi) guidance documents and regulations related to drug safety; and

(vii) other material determined appropriate by the Secretary;

(C) providing access to summaries of the assessed and aggregated data collected from the active surveillance infrastructure under subsection (k)(3) to provide information of known and serious side-effects for drugs approved under this section or licensed under such section 262;

(D) preparing and making publicly available on the Internet website established under paragraph (1) best practices for drug safety surveillance activities for drugs approved under this section or section 262 of title 42;

(E) enabling patients, providers, and drug sponsors to submit adverse event reports through the Internet Web site;

(F) providing educational materials for patients and providers about the appropriate means of disposing of expired, damaged, or unusable medications; and

(G) supporting initiatives that the Secretary determines to be useful to fulfill the purposes of the Internet Web site.

(3) Posting of drug labeling

The Secretary shall post on the Internet Web site established under paragraph (1) the approved professional labeling and any required patient labeling of a drug approved under this section or licensed under such section 262 not later than 21 days after the date the drug is approved or licensed, including in a supplemental application with respect to a labeling change.

(4) Private sector resources

To ensure development of the Internet Web site by the date described in paragraph (1), the Secretary may, on a temporary or permanent basis, implement systems or products developed by private entities.

(5) Authority for contracts

The Secretary may enter into contracts with public and private entities to fulfill the requirements of this subsection.

(6) Review

The Advisory Committee on Risk Communication under section 360bbb–6 of this title shall, on a regular basis, perform a comprehensive review and evaluation of the types of risk communication information provided on the Internet Web site established under paragraph (1) and, through other means, shall identify, clarify, and define the purposes and types of information available to facilitate the efficient flow of information to patients and providers, and shall recommend ways for the Food and Drug Administration to work with outside entities to help facilitate the dispensing of risk communication information to patients and providers.

(s) Referral to advisory committee

The Secretary shall—

(1) refer a drug or biological product to a Food and Drug Administration advisory committee for review at a meeting of such advisory committee prior to the approval of such drug or biological if it is—

(A) a drug, no active moiety (as defined by the Secretary in section 314.3 of title 21,

Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under this section; or

(B) a biological product, no active ingredient of which has been approved in any other application under section 262 of title 42; or

(2) if the Secretary does not refer a drug or biological product described in paragraph (1) to a Food and Drug Administration advisory committee prior to such approval, provide in the action letter on the application for the drug or biological product a summary of the reasons why the Secretary did not refer the drug or biological product to an advisory committee prior to approval.

(t) Database for authorized generic drugs

(1) In general

(A) Publication

The Commissioner shall—

(i) not later than 9 months after September 27, 2007, publish a complete list on the Internet Web site of the Food and Drug Administration of all authorized generic drugs (including drug trade name, brand company manufacturer, and the date the authorized generic drug entered the market); and

(ii) update the list quarterly to include each authorized generic drug included in an annual report submitted to the Secretary by the sponsor of a listed drug during the preceding 3-month period.

(B) Notification

The Commissioner shall notify relevant Federal agencies, including the Centers for Medicare & Medicaid Services and the Federal Trade Commission, when the Commissioner first publishes the information described in subparagraph (A) that the information has been published and that the information will be updated quarterly.

(2) Inclusion

The Commissioner shall include in the list described in paragraph (1) each authorized generic drug included in an annual report submitted to the Secretary by the sponsor of a listed drug after January 1, 1999.

(3) Authorized generic drug

In this section, the term ''authorized generic drug'' means a listed drug (as that term is used in subsection (j)) that—

(A) has been approved under subsection (c); and

(B) is marketed, sold, or distributed directly or indirectly to retail class of trade under a different labeling, packaging (other than repackaging as the listed drug in blister packs, unit doses, or similar packaging for use in institutions), product code, labeler code, trade name, or trade mark than the listed drug.

(u) Certain drugs containing single enantiomers

(1) In general

For purposes of subsections (c)(3)(E)(ii) and (j)(5)(F)(ii), if an application is submitted under subsection (b) for a non-racemic drug containing as an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) a single enantiomer that is contained in a racemic drug approved in another application under subsection (b), the applicant may, in the application for such non-racemic drug, elect to have the single enantiomer not be considered the same active moiety as that contained in the approved racemic drug, if—

(A)(i) the single enantiomer has not been previously approved except in the approved racemic drug; and

(ii) the application submitted under subsection (b) for such non-racemic drug—

(I) includes full reports of new clinical investigations (other than bioavailability studies)—

(aa) necessary for the approval of the application under subsections (c) and (d); and

(bb) conducted or sponsored by the applicant; and

(II) does not rely on any clinical investigations (other than bioavailability studies) that are part of an application submitted under subsection (b) for approval of the approved racemic drug; and

(B) the application submitted under subsection (b) for such non-racemic drug is not submitted for approval of a condition of use—

(i) in a therapeutic category in which the approved racemic drug has been approved; or

(ii) for which any other enantiomer of the racemic drug has been approved.

(2) Limitation

(A) No approval in certain therapeutic categories

Until the date that is 10 years after the date of approval of a non-racemic drug described in paragraph (1) and with respect to which the applicant has made the election provided for by such paragraph, the Secretary shall not approve such non-racemic drug for any condition of use in the therapeutic category in which the racemic drug has been approved.

(B) Labeling

If applicable, the labeling of a non-racemic drug described in paragraph (1) and with respect to which the applicant has made the election provided for by such paragraph shall include a statement that the non-racemic drug is not approved, and has not been shown to be safe and effective, for any condition of use of the racemic drug.

(3) Definition

(A) In general

For purposes of this subsection, the term ''therapeutic category'' means a therapeutic category identified in the list developed by the United States Pharmacopeia pursuant to section 1395w–104(b)(3)(C)(ii) of title 42 and as in effect on September 27, 2007.

(B) Publication by Secretary

The Secretary shall publish the list described in subparagraph (A) and may amend such list by regulation.

(4) Availability

The election referred to in paragraph (1) may be made only in an application that is submitted to the Secretary after September 27, 2007, and before October 1, 2027.

(v) Antibiotic drugs submitted before November 21, 1997

(1) Antibiotic drugs approved before November 21, 1997

(A) In general

Notwithstanding any provision of the Food and Drug Administration Modernization Act of 1997 or any other provision of law, a sponsor of a drug that is the subject of an application described in subparagraph (B)(i) shall be eligible for, with respect to the drug, the 3-year exclusivity period referred to under clauses (iii) and (iv) of subsection (c)(3)(E) and under clauses (iii) and (iv) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable.

(B) Application; antibiotic drug described

(i) Application

An application described in this clause is an application for marketing submitted under this section after October 8, 2008, in which the drug that is the subject of the application contains an antibiotic drug described in clause (ii).

(ii) Antibiotic drug

An antibiotic drug described in this clause is an antibiotic drug that was the subject of an application approved by the Secretary under section 357 of this title (as in effect before November 21, 1997).

(2) Antibiotic drugs submitted before November 21, 1997, but not approved

(A) In general

Notwithstanding any provision of the Food and Drug Administration Modernization Act of 1997 or any other provision of law, a sponsor of a drug that is the subject of an application described in subparagraph (B)(i) may elect to be eligible for, with respect to the drug—

(i)(I) the 3-year exclusivity period referred to under clauses (iii) and (iv) of subsection (c)(3)(E) and under clauses (iii) and (iv) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable; and

(II) the 5-year exclusivity period referred to under clause (ii) of subsection (c)(3)(E) and under clause (ii) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable; or

(ii) a patent term extension under section 156 of title 35, subject to the requirements of such section.

(B) Application; antibiotic drug described

(i) Application

An application described in this clause is an application for marketing submitted under this section after October 8, 2008, in which the drug that is the subject of the application contains an antibiotic drug described in clause (ii).

(ii) Antibiotic drug

An antibiotic drug described in this clause is an antibiotic drug that was the subject of 1 or more applications received by the Secretary under section 357 of this title (as in effect before November 21, 1997), none of which was approved by the Secretary under such section.

(3) Limitations

(A) Exclusivities and extensions

Paragraphs (1)(A) and (2)(A) shall not be construed to entitle a drug that is the subject of an approved application described in subparagraphs[5] (1)(B)(i) or (2)(B)(i), as applicable, to any market exclusivities or patent extensions other than those exclusivities or extensions described in paragraph (1)(A) or (2)(A).

(B) Conditions of use

Paragraphs (1)(A) and (2)(A)(i) shall not apply to any condition of use for which the drug referred to in subparagraph (1)(B)(i) or (2)(B)(i), as applicable, was approved before October 8, 2008.

(4) Application of certain provisions

Notwithstanding section 125, or any other provision, of the Food and Drug Administration Modernization Act of 1997, or any other provision of law, and subject to the limitations in paragraphs (1), (2), and (3), the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984 shall apply to any drug subject to paragraph (1) or any drug with respect to which an election is made under paragraph (2)(A).

(w) Deadline for determination on certain petitions

The Secretary shall issue a final, substantive determination on a petition submitted pursuant to subsection (b) of section 314.161 of title 21, Code of Federal Regulations (or any successor regulations), no later than 270 days after the date the petition is submitted.

(x) Date of approval in the case of recommended controls under the CSA

(1) In general

In the case of an application under subsection (b) with respect to a drug for which the Secretary provides notice to the sponsor that the Secretary intends to issue a scientific and medical evaluation and recommend controls under the Controlled Substances Act [21 U.S.C. 801 et seq.], approval of such application shall not take effect until the interim final rule controlling the drug is issued in accordance with section 201(j) of the Controlled Substances Act [21 U.S.C. 811(j)].

(2) Date of approval

For purposes of this section, with respect to an application described in paragraph (1), the

[5] So in original. Probably should be ''subparagraph''.

term ''date of approval'' shall mean the later of—

(A) the date an application under subsection (b) is approved under subsection (c); or

(B) the date of issuance of the interim final rule controlling the drug.

(y) Contrast agents intended for use with applicable medical imaging devices

(1) In general

The sponsor of a contrast agent for which an application has been approved under this section may submit a supplement to the application seeking approval for a new use following the authorization of a premarket submission for an applicable medical imaging device for that use with the contrast agent pursuant to section 360j(p)(1) of this title.

(2) Review of supplement

In reviewing a supplement submitted under this subsection, the agency center charged with the premarket review of drugs may—

(A) consult with the center charged with the premarket review of devices; and

(B) review information and data submitted to the Secretary by the sponsor of an applicable medical imaging device pursuant to section 360e, 360(k), or 360c(f)(2) of this title so long as the sponsor of such applicable medical imaging device has provided to the sponsor of the contrast agent a right of reference.

(3) Definitions

For purposes of this subsection—

(A) the term ''new use'' means a use of a contrast agent that is described in the approved labeling of an applicable medical imaging device described in section 360j(p) of this title, but that is not described in the approved labeling of the contrast agent; and

(B) the terms ''applicable medical imaging device'' and ''contrast agent'' have the meanings given such terms in section 360j(p) of this title.

(z)[6] Nonclinical test defined

For purposes of this section, the term ''nonclinical test'' means a test conducted in vitro, in silico, or in chemico, or a nonhuman in vivo test, that occurs before or during the clinical trial phase of the investigation of the safety and effectiveness of a drug. Such test may include the following:

(1) Cell-based assays.

(2) Organ chips and microphysiological systems.

(3) Computer modeling.

(4) Other nonhuman or human biology-based test methods, such as bioprinting.

(5) Animal tests.

(z)[6] Diversity action plan for clinical studies[7]

(1) With respect to a clinical investigation of a new drug that is a phase 3 study, as defined in section 312.21(c) of title 21, Code of Federal Regulations (or successor regulations), or, as appropriate, another pivotal study of a new drug (other than bioavailability or bioequivalence studies), the sponsor of such drug shall submit to the Secretary a diversity action plan.

(2) Such diversity action plan shall include—

(A) the sponsor's goals for enrollment in such clinical study;

(B) the sponsor's rationale for such goals; and

(C) an explanation of how the sponsor intends to meet such goals.

(3) The sponsor shall submit to the Secretary such diversity action plan, in the form and manner specified by the Secretary in guidance, as soon as practicable but not later than the date on which the sponsor submits the protocol to the Secretary for such a phase 3 study or other pivotal study of the drug. The sponsor may submit modifications to the diversity action plan. Any such modifications shall be in the form and manner specified by the Secretary in guidance.

(4)(A) On the initiative of the Secretary or at the request of a sponsor, the Secretary may waive any requirement in paragraph (1), (2), or (3) if the Secretary determines that a waiver is necessary based on what is known or what can be determined about the prevalence or incidence of the disease or condition for which the new drug is under investigation (including in terms of the patient population that may use the drug), if conducting a clinical investigation in accordance with a diversity action plan would otherwise be impracticable, or if such waiver is necessary to protect public health during a public health emergency.

(B) The Secretary shall issue a written response granting or denying a request from a sponsor for a waiver within 60 days of receiving such request.

(5) No diversity action plan shall be required for a submission described in section 360bbb of this title.

(June 25, 1938, ch. 675, § 505, 52 Stat. 1052; Pub. L. 86–507, § 1(18), June 11, 1960, 74 Stat. 201; Pub. L. 87–781, title I, §§ 102(b)–(d), 103(a), (b), 104(a)–(d)(2), Oct. 10, 1962, 76 Stat. 781–783, 784, 785; Pub. L. 92–387, § 4(d), Aug. 16, 1972, 86 Stat. 562; Pub. L. 98–417, title I, §§ 101, 102(a)–(b)(5), 103, 104, Sept. 24, 1984, 98 Stat. 1585, 1592, 1593, 1597; Pub. L. 102–282, § 5, May 13, 1992, 106 Stat. 161; Pub. L. 103–80, § 3(n), Aug. 13, 1993, 107 Stat. 777; Pub. L. 105–115, title I, §§ 115, 117, 119, 120, 124(a), Nov. 21, 1997, 111 Stat. 2313, 2315, 2316, 2318, 2324; Pub. L. 106–113, div. B, § 1000(a)(9) [title IV, § 4732(b)(11)], Nov. 29, 1999, 113 Stat. 1536, 1501A–584; Pub. L. 107–109, § 15(c)(1), Jan. 4, 2002, 115 Stat. 1420; Pub. L. 108–155, § 2(b)(1), Dec. 3, 2003, 117 Stat. 1941; Pub. L. 108–173, title XI, §§ 1101(a), (b), 1102(a), 1103(a), Dec. 8, 2003, 117 Stat. 2448, 2452, 2457, 2460; Pub. L. 110–85, title VII, § 701(b), title VIII, § 801(b)(3)(A), (B), title IX, §§ 901(a), 903, 905(a), 914(a), 915, 916, 918, 920, 921, title XI, § 1113, Sept. 27, 2007, 121 Stat. 903, 921, 922, 943, 944, 953, 957, 958, 960–962, 976; Pub. L. 110–316, title III, § 301, Aug. 14, 2008, 122 Stat. 3524; Pub. L. 110–379, § 4(a), Oct. 8, 2008, 122 Stat. 4076; Pub. L. 111–31, div. A, title I, § 103(e), June 22, 2009, 123 Stat. 1837; Pub. L. 111–148, title VII, § 7002(d)(1), title X, § 10609, Mar. 23, 2010, 124 Stat. 816, 1014; Pub. L. 112–144, title IX, § 905, title XI,

[6] So in original. Two subsecs. (z) have been enacted.

[7] See Delayed Applicability of Amendment note below.

§§ 1101, 1134(a), 1135, July 9, 2012, 126 Stat. 1092, 1108, 1123; Pub. L. 113–5, title III, § 301, Mar. 13, 2013, 127 Stat. 179; Pub. L. 114–89, § 2(a)(1), Nov. 25, 2015, 129 Stat. 698; Pub. L. 114–255, div. A, title III, §§ 3024(b), 3031(a), 3075(a), (b), 3101(a)(2)(B), 3102(1), Dec. 13, 2016, 130 Stat. 1099, 1138, 1152, 1156; Pub. L. 115–52, title VI, § 601, title VII, § 706(b), title VIII, §§ 801, 802, 808, title IX, § 901(a), Aug. 18, 2017, 131 Stat. 1048, 1059, 1068, 1069, 1074, 1076; Pub. L. 115–271, title III, § 3041(b), Oct. 24, 2018, 132 Stat. 3942; Pub. L. 116–290, § 2(a)–(d)(1), (g), Jan. 5, 2021, 134 Stat. 4889–4892; Pub. L. 117–9, § 1(a)(1), (b)(1), Apr. 23, 2021, 135 Stat. 256, 258; Pub. L. 117–180, div. F, title V, § 5004, Sept. 30, 2022, 136 Stat. 2167; Pub. L. 117–229, div. C, title III, § 305, Dec. 16, 2022, 136 Stat. 2312; Pub. L. 117–328, div. FF, title III, §§ 3105, 3209(a), 3222, 3224, 3601(a), Dec. 29, 2022, 136 Stat. 5807, 5821, 5829, 5831, 5860.)

DELAYED APPLICABILITY OF AMENDMENT

For delayed applicability of subsection (z) of this section as added by section 3601(a) of Pub. L. 117–328, see Effective Date of 2022 Amendment note below.

Editorial Notes

REFERENCES IN TEXT

Section 264(c) of the Health Insurance Portability and Accountability Act of 1996, referred to in subsec. (k)(3)(C)(i)(I), (4)(G)(i)(I), is section 264(c) of Pub. L. 104–191, which is set out as a note under section 1320d–2 of Title 42, The Public Health and Welfare.

The General Schedule, referred to in subsec. (n)(5), is set out under section 5332 of Title 5, Government Organization and Employees.

Section 101(c) of the Food and Drug Administration Amendments Act of 2007, referred to in subsec. (*o*)(3)(E)(i), is section 101(c) of Pub. L. 110–85, which is set out as a note under section 379g of this title.

The Food and Drug Administration Modernization Act of 1997, referred to in subsec. (v)(1)(A), (2)(A), (4), is Pub. L. 105–115, Nov. 21, 1997, 111 Stat. 2296. Section 125 of the Act amended sections 321, 331, 335a, 352, 360, 360j, 360aa to 360cc, 360ee, 374, 379g, 381, and 382 of this title, section 45C of Title 26, Internal Revenue Code, section 156 of Title 35, Patents, and section 8126 of Title 38, Veterans' Benefits, repealed sections 356 and 357 of this title, and enacted provisions set out as a note under this section. For complete classification of this Act to the Code, see Short Title of 1997 Amendment note set out under section 301 of this title and Tables.

The Drug Price Competition and Patent Term Restoration Act of 1984, referred to in subsec. (v)(4), is Pub. L. 98–417, Sept. 24, 1984, 98 Stat. 1585. For complete classification of this Act to the Code, see Short Title of 1984 Amendment note set out under section 301 of this title and Tables.

The Controlled Substances Act, referred to in subsec. (x)(1), is title II of Pub. L. 91–513, Oct. 27, 1970, 84 Stat. 1242, which is classified principally to subchapter I (§ 801 et seq.) of chapter 13 of this title. For complete classification of this Act to the Code, see Short Title note set out under section 801 of this title and Tables.

CODIFICATION

In subsec. (k)(4)(H), ''section 132 of title 41'' substituted for ''section 4(5) of the Federal Procurement Policy Act'' on authority of Pub. L. 111–350, § 6(c), Jan. 4, 2011, 124 Stat. 3854, which Act enacted Title 41, Public Contracts.

AMENDMENTS

2022—Subsec. (i)(1)(A). Pub. L. 117–328, § 3209(a)(1)(A), substituted ''nonclinical tests'' for ''preclinical tests (including tests on animals)''.

Subsec. (i)(2)(B). Pub. L. 117–328, § 3209(a)(1)(B), substituted ''nonclinical tests'' for ''animal''.

Subsec. (j)(7)(A)(v). Pub. L. 117–328, § 3222, added cl. (v).

Subsec. (j)(10)(A)(i) to (iii). Pub. L. 117–328, § 3224, added cls. (i) to (iii) and struck out former cls. (i) to (iii) which read as follows:

''(i) the application is otherwise eligible for approval under this subsection but for expiration of patent, an exclusivity period, or of a delay in approval described in paragraph (5)(B)(iii), and a revision to the labeling of the listed drug has been approved by the Secretary within 60 days of such expiration;

''(ii) the labeling revision described under clause (i) does not include a change to the 'Warnings' section of the labeling;

''(iii) the sponsor of the application under this subsection agrees to submit revised labeling of the drug that is the subject of such application not later than 60 days after the notification of any changes to such labeling required by the Secretary; and''.

Subsec. (u)(1)(A)(ii)(II). Pub. L. 117–328, § 3105(1), inserted ''(other than bioavailability studies)'' after ''any clinical investigations''.

Subsec. (u)(4). Pub. L. 117–328, § 3105(2), substituted ''October 1, 2027'' for ''December 24, 2022''.

Pub. L. 117–229 substituted ''December 24, 2022'' for ''December 17, 2022''.

Pub. L. 117–180 substituted ''December 17'' for ''October 1''.

Subsec. (z). Pub. L. 117–328, § 3601(a), added subsec. (z) relating to diversity action plan for clinical studies.

Pub. L. 117–328, § 3209(a)(2), added subsec. (z) defining nonclinical test.

2021—Subsec. (b)(1). Pub. L. 116–290, § 2(a)(1), amended par. (1) generally. Prior to amendment, par. (1) related to requirements for filing an application with respect to any drug subject to the provisions of subsec. (a).

Subsec. (c)(2). Pub. L. 116–290, § 2(b)(1), inserted at beginning ''Not later than 30 days after the date of approval of an application submitted under subsection (b), the holder of the approved application shall file with the Secretary the patent number and the expiration date of any patent described in subsection (b)(1)(A)(viii), except that a patent that is identified as claiming a method of using such drug shall be filed only if the patent claims a method of use approved in the application. If a patent described in subsection (b)(1)(A)(viii) is issued after the date of approval of an application submitted under subsection (b), the holder of the approved application shall, not later than 30 days after the date of issuance of the patent, file the patent number and the expiration date of the patent, except that a patent that claims a method of using such drug shall be filed only if approval for such use has been granted in the application.''; substituted ''described in subsection (b)(1)(A)(viii).'' for ''which claims the drug for which the application was submitted or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.''; inserted ''of the type for which information is required to be submitted in subsection (b)(1)(A)(viii)'' after ''could not file patent information under subsection (b) because no patent''; and inserted at end ''Patent information that is not the type of patent information required by subsection (b)(1)(A)(viii) shall not be submitted under this paragraph.''

Subsec. (c)(3)(E). Pub. L. 117–9, § 1(a)(1)(A), substituted ''active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations))'' for ''active ingredient (including any ester or salt of the active ingredient)'' wherever appearing.

Pub. L. 116–290, § 2(g)(1), substituted ''subsection (b)(1)(A)(i)'' for ''clause (A) of subsection (b)(1)'' wherever appearing.

Subsec. (c)(3)(E)(i). Pub. L. 117–9, § 1(b)(1)(A), struck out cl. (i) which read as follows: ''If an application

(other than an abbreviated new drug application) submitted under subsection (b) for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b), was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of another application for a drug for which the investigations described in subsection (b)(1)(A)(i) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted effective before the expiration of ten years from the date of the approval of the application previously approved under subsection (b).''

Subsec. (j)(2)(A)(vi). Pub. L. 116–290, §2(g)(2), substituted ''clauses (ii) through (vi) of subsection (b)(1)(A)'' for ''clauses (B) through (F) of subsection (b)(1)''.

Subsec. (j)(5)(F). Pub. L. 117–9, §1(a)(1)(B), substituted ''active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations))'' for ''active ingredient (including any ester or salt of the active ingredient)'' wherever appearing.

Subsec. (j)(5)(F)(i). Pub. L. 117–9, §1(b)(1)(B), struck out cl. (i) which read as follows: ''If an application (other than an abbreviated new drug application) submitted under subsection (b) for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b), was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted effective before the expiration of ten years from the date of the approval of the application under subsection (b).''

Subsec. (j)(7)(A)(iii). Pub. L. 116–290, §2(b)(2), struck out ''(b) or'' before ''(c)''.

Subsec. (j)(7)(A)(iv). Pub. L. 116–290, §2(c), added cl. (iv).

Subsec. (j)(7)(D). Pub. L. 116–290, §2(d)(1), added subpar. (D).

Subsec. (*l*)(2)(A)(i). Pub. L. 117–9, §1(a)(1)(C)(i), amended cl. (i) generally. Prior to amendment, cl. (i) read as follows: ''not later than 30 days after the date of approval of such application for a drug no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under this section or section 262 of title 42; and''.

Subsec. (*l*)(2)(A)(ii). Pub. L. 117–9, §1(a)(1)(C)(ii), inserted ''or biological product'' before period at end.

Subsec. (s). Pub. L. 117–9, §1(a)(1)(D), amended subsec. (s) generally. Prior to amendment, text read as follows: ''Prior to the approval of a drug no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under this section or section 262 of title 42, the Secretary shall—

''(1) refer such drug to a Food and Drug Administration advisory committee for review at a meeting of such advisory committee; or

''(2) if the Secretary does not refer such a drug to a Food and Drug Administration advisory committee prior to the approval of the drug, provide in the action letter on the application for the drug a summary of the reasons why the Secretary did not refer the drug to an advisory committee prior to approval.''

Subsec. (u)(1). Pub. L. 117–9, §1(a)(1)(E), in introductory provisions, substituted ''active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations))'' for ''active ingredient (including any ester or salt of the active ingredient)'' and ''same active moiety'' for ''same active ingredient''.

2018—Subsec. (*o*)(4)(A). Pub. L. 115–271, §3041(b)(1), substituted ''safety or new effectiveness information'' for ''safety information'' in heading and ''If the Secretary becomes aware of new information, including any new safety information or information related to reduced effectiveness, that the Secretary determines should be included in the labeling of the drug'' for ''If the Secretary becomes aware of new safety information that the Secretary believes should be included in the labeling of the drug'' in text. Amendment to heading was executed to reflect the probable intent of Congress, notwithstanding error in text directed to be stricken.

Subsec. (*o*)(4)(B)(i). Pub. L. 115–271, §3041(b)(2), inserted '', or new effectiveness information'' after ''adverse reactions''.

Subsec. (*o*)(4)(C). Pub. L. 115–271, §3041(b)(3), substituted ''safety or new effectiveness information'' for ''safety information''.

Subsec. (*o*)(4)(E). Pub. L. 115–271, §3041(b)(4), substituted ''safety or new effectiveness information'' for ''safety information''.

2017—Subsec. (j)(5)(B)(v). Pub. L. 115–52, §808(1), added cl. (v).

Subsec. (j)(5)(D)(iv). Pub. L. 115–52, §808(2), added cl. (iv).

Subsec. (j)(11), (12). Pub. L. 115–52, §801, added pars. (11) and (12).

Subsec. (j)(13). Pub. L. 115–52, §802, added par. (13).

Subsec. (k)(5). Pub. L. 115–52, §901(a), made technical amendments to directory language of Pub. L. 114–255, §3075(a). See 2016 Amendment notes below.

Subsec. (u)(4). Pub. L. 115–52, §601, substituted ''2022'' for ''2017''.

Subsec. (y). Pub. L. 115–52, §706(b), added subsec. (y).

2016—Subsec. (c)(5). Pub. L. 114–255, §3031(a), added par. (5).

Subsec. (d). Pub. L. 114–255, §3101(a)(2)(B)(i), substituted ''marketing approval'' for ''premarket approval'' in last sentence.

Subsec. (i)(4). Pub. L. 114–255, §3024(b), substituted ''except where it is not feasible, it is contrary to the best interests of such human beings, or the proposed clinical testing poses no more than minimal risk to such human beings and includes appropriate safeguards as prescribed to protect the rights, safety, and welfare of such human beings'' for ''except where it is not feasible or it is contrary to the best interests of such human beings''.

Subsec. (k)(5)(A). Pub. L. 114–255, §3075(a)(1), as amended by Pub. L. 115–52, §901(a)(1), substituted ''screenings'' for '', bi-weekly screening''.

Pub. L. 114–255, §3102(1)(A), inserted ''and'' after the semicolon.

Subsec. (k)(5)(B). Pub. L. 114–255, §3075(a)(2), as amended by Pub. L. 115–52, §901(a), substituted ''; and'' for period at end.

Pub. L. 114–255, §3102(1)(B), (C), redesignated subpar. (C) as (B) and struck out former subpar. (B) which read as follows: ''report to Congress not later than 2 year after September 27, 2007, on procedures and processes of the Food and Drug Administration for addressing ongoing post market safety issues identified by the Office of Surveillance and Epidemiology and how recommendations of the Office of Surveillance and Epidemiology are handled within the agency; and''.

Subsec. (k)(5)(C). Pub. L. 114–255, §3075(a)(3), as amended by Pub. L. 115–52, §901(a)(1), added subpar. (C).

Pub. L. 114–255, §3102(1)(C), redesignated subpar. (C) as (B).

Subsec. (q)(5)(A). Pub. L. 114–255, §3101(a)(2)(B)(ii), substituted ''subsection (b)(2) or (j) of this section or section 262(k) of title 42'' for ''subsection (b)(2) or (j) of the Act or 262(k) of title 42''.

Subsec. (r)(2)(D). Pub. L. 114–255, §3075(b), substituted ''and making publicly available on the Internet website established under paragraph (1) best practices for drug safety surveillance activities for drugs approved under this section or section 262 of title 42'' for '', by 18 months after approval of a drug or after use of the drug by 10,000 individuals, whichever is later, a summary analysis of the adverse drug reaction reports received for the drug, including identification of any new risks

not previously identified, potential new risks, or known risks reported in unusual number;''.

2015—Subsec. (x). Pub. L. 114–89 added subsec. (x).

2013—Subsec. (b)(5)(B). Pub. L. 113–5 substituted ''size—'' for ''size of clinical trials intended to form the primary basis of an effectiveness claim or, with respect to an applicant for approval of a biological product under section 262(k) of title 42, any necessary clinical study or studies.'', added cls. (i) and (ii), and designated last two sentences as concluding provisions.

2012—Subsec. (d). Pub. L. 112–144, §905, inserted at end ''The Secretary shall implement a structured risk-benefit assessment framework in the new drug approval process to facilitate the balanced consideration of benefits and risks, a consistent and systematic approach to the discussion and regulatory decisionmaking, and the communication of the benefits and risks of new drugs. Nothing in the preceding sentence shall alter the criteria for evaluating an application for premarket approval of a drug.''

Subsec. (q)(1)(A). Pub. L. 112–144, §1135(1)(A), substituted ''subsection (b)(2) or (j) of this section or section 262(k) of title 42'' for ''subsection (b)(2) or (j)'' in introductory provisions.

Subsec. (q)(1)(F). Pub. L. 112–144, §1135(1)(B), substituted ''150 days'' for ''180 days'' in introductory provisions.

Subsec. (q)(2)(A). Pub. L. 112–144, §1135(2)(A), substituted ''150'' for ''180'' in heading.

Subsec. (q)(2)(A)(i). Pub. L. 112–144, §1135(2)(B), substituted ''150-day'' for ''180-day''.

Subsec. (q)(4). Pub. L. 112–144, §1135(3), designated existing provisions as subpar. (A), redesignated former subpars. (A) and (B) as cls. (i) and (ii), respectively, of subpar. (A), and added subpar. (B).

Subsec. (q)(5)(A). Pub. L. 112–144, §1135(4), substituted ''subsection (b)(2) or (j) of the Act or 262(k) of title 42'' for ''subsection (b)(2) or (j)''.

Subsec. (u)(1)(A)(ii)(II). Pub. L. 112–144, §1101(b), inserted ''clinical'' after ''any''.

Subsec. (u)(4). Pub. L. 112–144, §1101(a), substituted ''2017'' for ''2012''.

Subsec. (w). Pub. L. 112–144, §1134(a), added subsec. (w).

2010—Subsec. (b)(5)(B). Pub. L. 111–148, §7002(d)(1), inserted ''or, with respect to an applicant for approval of a biological product under section 262(k) of title 42, any necessary clinical study or studies'' before period at end of first sentence.

Subsec. (j)(10). Pub. L. 111–148, §10609, added par. (10).

2009—Subsec. (n)(2). Pub. L. 111–31 made technical amendment to reference in original act which appears in text as reference to section 394 of this title.

2008—Subsec. (q)(1)(A). Pub. L. 110–316, §301, inserted concluding provisions.

Subsec. (v). Pub. L. 110–379 added subsec. (v).

2007—Subsec. (b)(6). Pub. L. 110–85, §801(b)(3)(B), added par. (6).

Subsec. (e). Pub. L. 110–85, §903, inserted at end ''The Secretary may withdraw the approval of an application submitted under this section, or suspend the approval of such an application, as provided under this subsection, without first ordering the applicant to submit an assessment of the approved risk evaluation and mitigation strategy for the drug under section 355–1(g)(2)(D) of this title.''

Subsec. (i)(4). Pub. L. 110–85, §801(b)(3)(A), inserted at end ''The Secretary shall update such regulations to require inclusion in the informed consent documents and process a statement that clinical trial information for such clinical investigation has been or will be submitted for inclusion in the registry data bank pursuant to subsection (j) of section 282 of title 42.''

Subsec. (k)(3), (4). Pub. L. 110–85, §905(a), added pars. (3) and (4).

Subsec. (k)(5). Pub. L. 110–85, §921, added par. (5).

Subsec. (*l*). Pub. L. 110–85, §916, designated existing provisions as par. (1), redesignated former pars. (1) to (5) as subpars. (A) to (E), respectively, of par. (1), and added par. (2).

Subsec. (n)(4) to (8). Pub. L. 110–85, §701(b), redesignated pars. (5) to (8) as (4) to (7), respectively, and struck out former par. (4) which read as follows: ''Each member of a panel shall publicly disclose all conflicts of interest that member may have with the work to be undertaken by the panel. No member of a panel may vote on any matter where the member or the immediate family of such member could gain financially from the advice given to the Secretary. The Secretary may grant a waiver of any conflict of interest requirement upon public disclosure of such conflict of interest if such waiver is necessary to afford the panel essential expertise, except that the Secretary may not grant a waiver for a member of a panel when the member's own scientific work is involved.''

Subsecs. (*o*), (p). Pub. L. 110–85, §901(a), added subsecs. (*o*) and (p).

Subsec. (q). Pub. L. 110–85, §914(a), added subsec. (q).

Subsec. (r). Pub. L. 110–85, §915, added subsec. (r).

Subsec. (s). Pub. L. 110–85, §918, added subsec. (s).

Subsec. (t). Pub. L. 110–85, §920, added subsec. (t).

Subsec. (u). Pub. L. 110–85, §1113, added subsec. (u).

2003—Subsec. (b)(1). Pub. L. 108–155, in second sentence, substituted ''(F)'' for ''and (F)'' and inserted '', and (G) any assessments required under section 355c of this title'' before period at end.

Subsec. (b)(3). Pub. L. 108–173, §1101(b)(1)(A), added par. (3) and struck out former par. (3) which, in subpar. (A), required an applicant making a certification under par. (2)(A)(iv) to include statement that applicant will give notice to each owner of the patent which is the subject of the certification and to the holder of the approved application, in subpar. (B), directed that notice state that an application has been submitted and include a detailed statement of the applicant's opinion that the patent is not valid or will not be infringed, and, in subpar. (C), provided that if an application is amended, notice shall be given when the amended application is submitted.

Subsec. (b)(4), (5). Pub. L. 108–173, §1101(b)(1)(B), added par. (4) and redesignated former par. (4) as (5).

Subsec. (c)(3). Pub. L. 108–173, §1101(b)(2)(A), substituted ''by applying the following to each certification made under subsection (b)(2)(A)'' for ''under the following'' in introductory provisions.

Subsec. (c)(3)(C). Pub. L. 108–173, §1101(b)(2)(B)(iii), which directed the substitution of ''subsection (b)(3)'' for ''paragraph (3)(B)'' in third sentence, could not be executed because such words do not appear. See note below.

Pub. L. 108–173, §1101(b)(2)(B)(ii)(VI), in concluding provisions, struck out ''Until the expiration of forty-five days from the date the notice made under paragraph (3)(B) is received, no action may be brought under section 2201 of title 28 for a declaratory judgment with respect to the patent. Any action brought under such section 2201 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.'' after ''expediting the action.''

Pub. L. 108–173, §1101(b)(2)(B)(i), (ii)(I), in first sentence of introductory provisions, substituted ''unless, before the expiration of 45 days after the date on which the notice described in subsection (b)(3) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under paragraph (2) or subsection (b)(1) before the date on which the application (excluding an amendment or supplement to the application) was submitted'' for ''unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (3)(B) is received'' and, in second sentence of introductory provisions, substituted ''subsection (b)(3)'' for ''paragraph (3)(B)''.

Subsec. (c)(3)(C)(i). Pub. L. 108–173, §1101(b)(2)(B)(ii)(II), added cl. (i) and struck out former cl. (i) which read as follows: ''if before the expiration of such period the court decides that such patent is in-

valid or not infringed, the approval may be made effective on the date of the court decision,''.

Subsec. (c)(3)(C)(ii). Pub. L. 108–173, §1101(b)(2)(B)(ii)(III), added cl. (ii) and struck out former cl. (ii) which read as follows: ''if before the expiration of such period the court decides that such patent has been infringed, the approval may be made effective on such date as the court orders under section 271(e)(4)(A) of title 35, or''.

Subsec. (c)(3)(C)(iii). Pub. L. 108–173, §1101(b)(2)(B)(ii)(IV), substituted ''as provided in clause (i); or'' for ''on the date of such court decision.''

Subsec. (c)(3)(C)(iv). Pub. L. 108–173, §1101(b)(2)(B)(ii)(V), added cl. (iv).

Subsec. (c)(3)(D), (E). Pub. L. 108–173, §1101(b)(2)(C), (D), added subpar. (D) and redesignated former subpar. (D) as (E).

Subsec. (j)(2)(B). Pub. L. 108–173, §1101(a)(1)(A), added subpar. (B) and struck out former subpar. (B) which, in cl. (i), required that an applicant making a certification under subpar. (A)(vii)(IV) include in the application a statement that notice would be given to each owner of the patent and the holder of the approved application, in cl. (ii), required that notice would state that an application had been submitted and that it would include a detailed statement of the basis of the applicant's opinion, and, in cl. (iii), directed that notice of an amended application be given when the amended application had been submitted.

Subsec. (j)(2)(D). Pub. L. 108–173, §1101(a)(1)(B), added subpar. (D).

Subsec. (j)(5)(B). Pub. L. 108–173, §1101(a)(2)(A)(i), substituted ''by applying the following to each certification made under paragraph (2)(A)(vii)'' for ''under the following'' in introductory provisions.

Subsec. (j)(5)(B)(iii). Pub. L. 108–173, §1101(a)(2)(A)(ii)(II)(ee), which directed amendment of the second sentence of subsec. (j)(5)(B)(iii) by striking ''Until the expiration'' and all that follows in the matter after and below subclause (IV), was executed by striking ''Until the expiration of forty-five days from the date the notice made under paragraph (2)(B)(i) is received, no action may be brought under section 2201 of title 28, for a declaratory judgment with respect to the patent. Any action brought under section 2201 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.'' after ''expediting the action.'' in concluding provisions, to reflect the probable intent of Congress.

Pub. L. 108–173, §1101(a)(2)(A)(ii)(I), in introductory provisions, substituted ''unless, before the expiration of 45 days after the date on which the notice described in paragraph (2)(B) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under subsection (b)(1) or (c)(2) before the date on which the application (excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, was submitted'' for ''unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received''.

Subsec. (j)(5)(B)(iii)(I). Pub. L. 108–173, §1101(a)(2)(A)(ii)(II)(aa), added subcl. (I) and struck out former subcl. (I) which read as follows: ''if before the expiration of such period the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of the court decision,''.

Subsec. (j)(5)(B)(iii)(II). Pub. L. 108–173, §1101(a)(2)(A)(ii)(II)(bb), added subcl. (II) and struck out former subcl. (II) which read as follows: ''if before the expiration of such period the court decides that such patent has been infringed, the approval shall be made effective on such date as the court orders under section 271(e)(4)(A) of title 35, or''.

Subsec. (j)(5)(B)(iii)(III). Pub. L. 108–173, §1101(a)(2)(A)(ii)(II)(cc), substituted ''as provided in subclause (I); or'' for ''on the date of such court decision.''

Subsec. (j)(5)(B)(iii)(IV). Pub. L. 108–173, §1101(a)(2)(A)(ii)(II)(dd), added subcl. (IV).

Subsec. (j)(5)(B)(iv). Pub. L. 108–173, §1102(a)(1), added cl. (iv) and struck out former cl. (iv) which read as follows: ''If the application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) and is for a drug for which a previous application has been submitted under this subsection continuing such a certification, the application shall be made effective not earlier than one hundred and eighty days after—

''(I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or

''(II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed,

whichever is earlier.''

Subsec. (j)(5)(C). Pub. L. 108–173, §1101(a)(2)(B), (C), added subpar. (C). Former subpar. (C) redesignated (E).

Subsec. (j)(5)(D). Pub. L. 108–173, §1102(a)(2), added subpar. (D).

Pub. L. 108–173, §1101(a)(2)(B), redesignated subpar. (D) as (F).

Subsec. (j)(5)(E), (F). Pub. L. 108–173, §1101(a)(2)(B), redesignated subpars. (C) and (D) as (E) and (F), respectively.

Subsec. (j)(8)(A). Pub. L. 108–173, §1103(a)(1), added subpar. (A) and struck out former subpar. (A) which read as follows: ''The term 'bioavailability' means the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug and becomes available at the site of drug action.''

Subsec. (j)(8)(C). Pub. L. 108–173, §1103(a)(2), added subpar. (C).

2002—Subsec. (i)(1)(D). Pub. L. 107–109 added subpar. (D).

1999—Subsec. (m). Pub. L. 106–113 substituted ''United States Patent and Trademark Office'' for ''Patent and Trademark Office of the Department of Commerce''.

1997—Subsec. (b)(1). Pub. L. 105–115, §115(b), inserted at end ''The Secretary shall, in consultation with the Director of the National Institutes of Health and with representatives of the drug manufacturing industry, review and develop guidance, as appropriate, on the inclusion of women and minorities in clinical trials required by clause (A).''

Subsec. (b)(4). Pub. L. 105–115, §119(a), added par. (4).

Subsec. (c)(4). Pub. L. 105–115, §124(a), added par. (4).

Subsec. (d). Pub. L. 105–115, §115(a), inserted at end ''If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence.''

Subsec. (i). Pub. L. 105–115, §117, inserted ''(1)'' after ''(i)'', redesignated former pars. (1) to (3) as subpars. (A) to (C), respectively, of par. (1), added pars. (2) to (4), and struck out closing provisions which read as follows: ''Such regulations shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational purposes certify to such manufacturer or sponsor that they will inform any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where they deem it not feasible or, in their professional judgment, contrary to the best interests of such human beings. Nothing in this subsection shall be construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs.''

Subsec. (j)(2)(A)(i). Pub. L. 105–115, §119(b)(2)(A), substituted ''paragraph (7)'' for ''paragraph (6)''.

Subsec. (j)(3). Pub. L. 105–115, §119(b)(1)(B), added par. (3). Former par. (3) redesignated (4).

Subsec. (j)(4). Pub. L. 105–115, §119(b)(1)(A), (2)(B), redesignated par. (3) as (4) and in introductory provisions substituted ''paragraph (5)'' for ''paragraph (4)''. Former par. (4) redesignated (5).

Subsec. (j)(4)(I). Pub. L. 105–115, §119(b)(2)(C), substituted ''paragraph (6)'' for ''paragraph (5)''.

Subsec. (j)(5), (6). Pub. L. 105–115, §119(b)(1)(A), redesignated pars. (4) and (5) as (5) and (6), respectively. Former par. (6) redesignated (7).

Subsec. (j)(7). Pub. L. 105–115, §119(b)(1)(A), (2)(D), redesignated par. (6) as (7) and in subpar. (C) substituted ''paragraph (6)'' for ''paragraph (5)'' in two places. Former par. (7) redesignated (8).

Subsec. (j)(8), (9). Pub. L. 105–115, §119(b)(1)(A), redesignated pars. (7) and (8) as (8) and (9), respectively.

Subsec. (n). Pub. L. 105–115, §120, added subsec. (n).

1993—Subsec. (j)(6)(A)(ii). Pub. L. 103–80, §3(n)(1)(A), substituted ''Secretary'' for ''Secretry''.

Subsec. (j)(6)(A)(iii). Pub. L. 103–80, §3(n)(1)(B), inserted comma after ''published by the Secretary''.

Subsec. (k)(1). Pub. L. 103–80, §3(n)(2), substituted ''section. Regulations'' for ''section: *Provided, however*, That regulations''.

1992—Subsec. (j)(8). Pub. L. 102–282 added par. (8).

1984—Subsec. (a). Pub. L. 98–417, §102(b)(1), inserted ''or (j)'' after ''subsection (b)''.

Subsec. (b). Pub. L. 98–417, §§102(a)(1), 103(a), designated existing provisions of subsec. (b) as par. (1) thereof and redesignated existing cls. (1) through (6) of such par. (1) as cls. (A) through (F) thereof, respectively, inserted requirement that the applicant file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably by asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug, that the applicant amend the application to include such information if an application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, and that upon approval of the application, the Secretary publish the information submitted, and added pars. (2) and (3).

Subsec. (c). Pub. L. 98–417, §§102(a)(2), (b)(2), 103(b), designated existing provisions of subsec. (c) as par. (1) thereof and in par. (1) as so designated substituted ''subsection (b)'' for ''this subsection'' and redesignated former pars. (1) and (2) as subpars. (A) and (B), respectively, and added pars. (2) and (3).

Subsec. (d)(6), (7). Pub. L. 98–417, §102(a)(3)(A), added cl. (6) relating to the failure of the application to contain the patent information prescribed by subsec. (b) of this section, and redesignated former cl. (6) as (7).

Subsec. (e). Pub. L. 98–417, §102(a)(3)(B), in first sentence, added a new cl. (4) relating to the failure to file the patent information prescribed by subsec. (c) of this section within 30 days after the receipt of written notice from the Secretary specifying the failure to file such information, and redesignated former cl. (4) as (5).

Pub. L. 98–417, §102(b)(3), (4), in second sentence, inserted in provisions preceding cl. (1) ''submitted under subsection (b) or (j)'' and in cl. (1) substituted ''under subsection (k) or to comply with the notice requirements of section 360(k)(2) of this title'' for ''under subsection (j) or to comply with the notice requirements of section 360(j)(2) of this title''.

Subsecs. (j), (k). Pub. L. 98–417, §101, added subsec. (j) and redesignated former subsec. (j) as (k).

Subsec. (k)(1). Pub. L. 98–417, §102(b)(5), substituted ''under subsection (b) or (j)'' for ''pursuant to this section''.

Subsecs. (*l*), (m). Pub. L. 98–417, §104, added subsecs. (*l*) and (m).

1972—Subsec. (e). Pub. L. 92–387 inserted ''or to comply with the notice requirements of section 360(j)(2) of this title'' in cl. (1) of second sentence relating to the maintenance of records.

1962—Subsec. (a). Pub. L. 87–781, §104(a), inserted ''an approval of'' before ''an application''.

Subsec. (b). Pub. L. 87–781, §102(b), inserted ''and whether such drug is effective in use'' after ''is safe for use''.

Subsec. (c). Pub. L. 87–781, §104(b), substituted provisions requiring the Secretary, within 180 days after filing an application, or such additional period as the Secretary and the applicant agree upon, to either approve the application, if meeting the requirements of subsec. (d) of this section, or give notice of opportunity for hearing on question of whether such application is approvable, and providing that if applicant requests hearing in writing within 30 days, the hearing shall begin within 90 days after expiration of said 30 days, unless the Secretary and applicant agree otherwise, that such hearing shall be expedited, and that the Secretary's order shall be issued within 90 days after date for filing final briefs, for provisions which had an application become effective on the sixtieth day after filing thereof unless prior thereto the Secretary postponed the date by written notice to such time, but not more than 180 days after filing, as the Secretary deemed necessary to study and investigate the application.

Subsec. (d). Pub. L. 87–781, §102(c), inserted references to subsec. (c), added cls. (5) and (6), provided that if after notice and opportunity for hearing, the Secretary finds that cls. (1) to (6) do not apply, he shall approve the application, and defined ''substantial evidence'' as used in this subsection and subsec. (e) of this section.

Subsec. (e). Pub. L. 87–781, §102(d), amended subsec. (e) generally, and among other changes, directed the Secretary to withdraw approval of an application if by tests, other scientific data or experience, or new evidence of clinical experience not contained in the application or available at the time of its approval, the drug is shown to be unsafe, or on the basis of new information, there is shown a lack of substantial evidence that the drug has the effect it is represented to have, and provided that if the Secretary, or acting Secretary, finds there is an imminent hazard to the public health, he may suspend approval immediately, notify the applicant, and give him opportunity for an expedited hearing, that the Secretary may withdraw approval if the applicant fails to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain records and make reports, or has refused access to, or copying or verification of such records, or if the Secretary finds on new evidence that the methods, facilities and controls in the manufacturing, processing, and packing are inadequate to assure and preserve the drugs' identity, strength, quality and purity, and were not made adequate within a reasonable time after receipt of written notice thereof, or finds on new evidence, that the labeling is false or misleading and was not corrected within a reasonable time after receipt of written notice thereof.

Subsec. (f). Pub. L. 87–781, §104(c), substituted provisions requiring the Secretary to revoke any previous order under subsecs. (d) or (e) of this section refusing, withdrawing, or suspending approval of an application and to approve such application or reinstate such approval, for provisions which required him to revoke an order refusing effectiveness to an application.

Subsec. (h). Pub. L. 87–781, §104(d)(1), (2), inserted ''as provided in section 2112 of title 28'', and ''except that until the filing of the record the Secretary may modify or set aside his order'', substituted ''or withdrawing approval of an application under this section'' for ''to permit the application to become effective, or suspending the effectiveness of the application'', ''United States court of appeals for the circuit'' for ''district court of the United States within any district'', ''Court of Appeals for the District of Columbia Circuit'' for ''District Court for the District of Columbia'', ''transmitted by the clerk of the court to'' for ''served upon'', and ''by the Supreme Court of the United States upon certiorari or certification as provided in section 1254 of title 28''

for ''as provided in sections 225, 346, and 347 of title 28, as amended, and in section 7, as amended, of the Act entitled 'An Act to establish a Court of Appeals for the District of Columbia', approved February 9, 1893'', and eliminated ''upon'' before ''any officer designated'', ''a transcript of'' before ''the record'' and ''and decree'' before ''of the court affirming''.

Subsec. (i). Pub. L. 87–781, § 103(b), inserted ''the foregoing subsections of'' after ''operation of'', and ''and effectiveness'' after ''safety'', and provided that the regulations may condition exemptions upon the submission of reports of preclinical tests to justify the proposed clinical testing, upon the obtaining by the manufacturer or sponsor of the investigation of a new drug of a signed agreement from each of the investigators that patients to whom the drug is administered will be under his supervision or under investigators responsible to him, and that he will not supply such drug to any other investigator, or to clinics, for administration to human beings, or upon the establishment and maintenance of records and reports of data obtained by the investigational use of such drug, as the Secretary finds will enable him to evaluate the safety and effectiveness of such drug, and provided that the regulations shall condition an exemption upon the manufacturer or sponsor of the investigation requiring that experts using such drugs certify that they will inform humans to whom such drugs or any controls connected therewith are administered, or their representatives, and will obtain the consent of such people where feasible and not contrary to the best interests of such people, and that reports on the investigational use of drugs are not required to be submitted directly to the Secretary.

Subsec. (j). Pub. L. 87–781, § 103(a), added subsec. (j).

1960—Subsec. (g). Pub. L. 86–507 inserted ''or by certified mail'' after ''registered mail''.

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 2022 AMENDMENT

Pub. L. 117–328, div. FF, title III, § 3602(c), Dec. 29, 2022, 136 Stat. 5863, provided that: ''Sections 505(z) and 520(g)(9) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(z), 360j(g)(9)], as added by section 3601, shall apply only with respect to clinical investigations for which enrollment commences after the date that is 180 days after the publication of final guidance required under this section [see section 3602(a), (b) of Pub. L. 117–328, set out below].''

EFFECTIVE DATE OF 2021 AMENDMENT

Pub. L. 116–290, § 2(d)(2), Jan. 5, 2021, 134 Stat. 4891, provided that: ''Subparagraph (D) of section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)), as added by paragraph (1), applies only with respect to a decision described in such subparagraph that is issued on or after the date of enactment of this Act [Jan. 5, 2021].''

EFFECTIVE DATE OF 2012 AMENDMENT

Pub. L. 112–144, title XI, § 1134(b), July 9, 2012, 126 Stat. 1123, provided that: ''The amendment made by subsection (a) [amending this section] shall apply to any petition that is submitted pursuant to subsection (b) of section 314.161 of title 21, Code of Federal Regulations (or any successor regulations), on or after the date of enactment of this Act [July 9, 2012].''

EFFECTIVE DATE OF 2007 AMENDMENT

Pub. L. 110–85, title VII, § 701(c), Sept. 27, 2007, 121 Stat. 904, provided that: ''The amendments made by this section [enacting section 379d–1 of this title and amending this section] shall take effect on October 1, 2007.''

Amendment by sections 901(a), 903, and 905(a) of Pub. L. 110–85 effective 180 days after Sept. 27, 2007, see section 909 of Pub. L. 110–85, set out as a note under section 331 of this title.

EFFECTIVE DATE OF 2003 AMENDMENTS

Pub. L. 108–173, title XI, § 1101(c), Dec. 8, 2003, 117 Stat. 2456, provided that:

''(1) IN GENERAL.—Except as provided in paragraphs (2) and (3), the amendments made by subsections (a) and (b) [amending this section] apply to any proceeding under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) that is pending on or after the date of the enactment of this Act [Dec. 8, 2003] regardless of the date on which the proceeding was commenced or is commenced.

''(2) NOTICE OF OPINION THAT PATENT IS INVALID OR WILL NOT BE INFRINGED.—The amendments made by subsections (a)(1) and (b)(1) apply with respect to any certification under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) submitted on or after August 18, 2003, in an application filed under subsection (b) or (j) of that section or in an amendment or supplement to an application filed under subsection (b) or (j) of that section.

''(3) EFFECTIVE DATE OF APPROVAL.—The amendments made by subsections (a)(2)(A)(ii)(I) and (b)(2)(B)(i) apply with respect to any patent information submitted under subsection (b)(1) or (c)(2) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) on or after August 18, 2003.''

Pub. L. 108–173, title XI, § 1102(b), Dec. 8, 2003, 117 Stat. 2460, provided that:

''(1) IN GENERAL.—Except as provided in paragraph (2), the amendment made by subsection (a) [amending this section] shall be effective only with respect to an application filed under section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)) after the date of the enactment of this Act [Dec. 8, 2003] for a listed drug for which no certification under section 505(j)(2)(A)(vii)(IV) of that Act was made before the date of the enactment of this Act.

''(2) COLLUSIVE AGREEMENTS.—If a forfeiture event described in section 505(j)(5)(D)(i)(V) of that Act occurs in the case of an applicant, the applicant shall forfeit the 180-day period under section 505(j)(5)(B)(iv) of that Act without regard to when the first certification under section 505(j)(2)(A)(vii)(IV) of that Act for the listed drug was made.

''(3) DECISION OF A COURT WHEN THE 180-DAY EXCLUSIVITY PERIOD HAS NOT BEEN TRIGGERED.—With respect to an application filed before, on, or after the date of the enactment of this Act [Dec. 8, 2003] for a listed drug for which a certification under section 505(j)(2)(A)(vii)(IV) of that Act was made before the date of the enactment of this Act and for which neither of the events described in subclause (I) or (II) of section 505(j)(5)(B)(iv) of that Act (as in effect on the day before the date of the enactment of this Act) has occurred on or before the date of the enactment of this Act, the term 'decision of a court' as used in clause (iv) of section 505(j)(5)(B) of that Act means a final decision of a court from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken.''

Amendment by Pub. L. 108–155 effective Dec. 3, 2003, except as otherwise provided, see section 4 of Pub. L. 108–155, set out as an Effective Date note under section 355c of this title.

EFFECTIVE DATE OF 1999 AMENDMENT

Amendment by Pub. L. 106–113 effective 4 months after Nov. 29, 1999, see section 1000(a)(9) [title IV, § 4731] of Pub. L. 106–113, set out as a note under section 1 of Title 35, Patents.

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by Pub. L. 105–115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as a note under section 321 of this title.

EFFECTIVE DATE OF 1984 AMENDMENT

Pub. L. 98–417, title I, § 105, Sept. 24, 1984, 98 Stat. 1597, provided that:

''(a) The Secretary of Health and Human Services shall promulgate, in accordance with the notice and comment requirements of section 553 of title 5, United States Code, such regulations as may be necessary for the administration of section 505 of the Federal Food, Drug, and Cosmetic Act [this section], as amended by sections 101, 102, and 103 of this Act, within one year of the date of enactment of this Act [Sept. 24, 1984].

''(b) During the period beginning sixty days after the date of the enactment of this Act [Sept. 24, 1984], and ending on the date regulations promulgated under subsection (a) take effect, abbreviated new drug applications may be submitted in accordance with the provisions of section 314.2 of title 21 of the Code of Federal Regulations and shall be considered as suitable for any drug which has been approved for safety and effectiveness under section 505(c) of the Federal Food, Drug, and Cosmetic Act [subsec. (c) of this section] before the date of the enactment of this Act. If any such provision is inconsistent with the requirements of section 505(j) of the Federal Food, Drug, and Cosmetic Act, the Secretary shall consider the application under the applicable requirements of such section. The Secretary of Health and Human Services may not approve such an abbreviated new drug application which is filed for a drug which is described in sections 505(c)(3)(D) and 505(j)(4)(D) of the Federal Food, Drug, and Cosmetic Act, except in accordance with such section.''

EFFECTIVE DATE OF 1972 AMENDMENT

Amendment by Pub. L. 92–387 effective on first day of sixth month beginning after Aug. 16, 1972, see section 5 of Pub. L. 92–387, set out as a note under section 360 of this title.

EFFECTIVE DATE OF 1962 AMENDMENT

Amendment by Pub. L. 87–781 effective on first day of seventh calendar month following October 1962, see section 107 of Pub. L. 87–781, set out as a note under section 321 of this title.

CONSTRUCTION OF AMENDMENT BY PUB. L. 110–85

Pub. L. 110–85, title IX, §905(b), Sept. 27, 2007, 121 Stat. 949, provided that: ''Nothing in this section [amending this section] or the amendment made by this section shall be construed to prohibit the lawful disclosure or use of data or information by an entity other than as described in paragraph (4)(B) or (4)(G) of section 505(k) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(k)], as added by subsection (a).''

CONSTRUCTION OF AMENDMENTS BY PUB. L. 102–282

Amendment by Pub. L. 102–282 not to preclude any other civil, criminal, or administrative remedy provided under Federal or State law, including any private right of action against any person for the same action subject to any action or civil penalty under an amendment made by Pub. L. 102–282, see section 7 of Pub. L. 102–282, set out as a note under section 335a of this title.

EXTENDING EXPIRATION DATES FOR CERTAIN DRUGS

Pub. L. 117–328, div. FF, title II, §2512(a), Dec. 29, 2022, 136 Stat. 5804, provided that: ''Not later than 1 year after the date of enactment of this Act [Dec. 29, 2022], the Secretary of Health and Human Services (referred to in this section as the 'Secretary') shall issue draft guidance, or revise existing guidance, to address recommendations for sponsors of applications submitted under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) or section 351 of the Public Health Service Act (42 U.S.C. 262) regarding—

''(1) the submission of stability testing data in such applications, including considerations for data requirements that could be streamlined or reduced to facilitate faster review of longer proposed expiration dates;

''(2) establishing in the labeling of drugs the longest feasible expiration date scientifically supported by such data, taking into consideration how extended expiration dates may—

''(A) help prevent or mitigate drug shortages; and

''(B) affect product quality; and

''(3) the use of innovative approaches for drug and combination product stability modeling to support initial product expiration dates and expiration date extensions.''

ANTIFUNGAL RESEARCH AND DEVELOPMENT

Pub. L. 117–328, div. FF, title III, §3211, Dec. 29, 2022, 136 Stat. 5825, provided that:

''(a) DRAFT GUIDANCE.—Not later than 3 years after the date of enactment of this Act [Dec. 29, 2022], the Secretary [of Health and Human Services], acting through the Commissioner of Food and Drugs, shall issue draft guidance for industry for the purposes of assisting entities seeking approval under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) or licensure under section 351 of the Public Health Service Act (42 U.S.C. 262) of antifungal therapies designed to treat coccidioidomycosis (commonly known as Valley Fever).

''(b) FINAL GUIDANCE.—Not later than 18 months after the close of the public comment period on the draft guidance issued pursuant to subsection (a), the Secretary, acting through the Commissioner of Food and Drugs, shall finalize the draft guidance.

''(c) WORKSHOP.—To assist entities developing preventive vaccines for fungal infections and coccidioidomycosis, the Secretary shall hold a public workshop.''

GUIDANCE ON DIVERSITY ACTION PLANS FOR CLINICAL STUDIES

Pub. L. 117–328, div. FF, title III, §3602(a), (b), Dec. 29, 2022, 136 Stat. 5861, 5862, provided that:

''(a) IN GENERAL.—The Secretary [of Health and Human Services] shall update or issue guidance relating to—

''(1) the format and content of the diversity action plans required by sections 505(z) and 520(g)(9) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(z); 360j(g)(9)) (as amended by section 3601) pertaining to the sponsor's goals for clinical study enrollment, disaggregated by age group, sex, and racial and ethnic demographic characteristics of clinically relevant study populations, and may include characteristics such as geographic location and socioeconomic status, including with respect to—

''(A) the rationale for the sponsor's enrollment goals, which may include—

''(i) the estimated prevalence or incidence in the United States of the disease or condition for which the drug or device is being investigated in the relevant clinical trial, if such estimated prevalence or incidence is known or can be determined based on available data;

''(ii) what is known about the disease or condition for which the drug or device is being investigated;

''(iii) any relevant pharmacokinetic or pharmacogenomic data;

''(iv) what is known about the patient population for such disease or condition, including, to the extent data is available—

''(I) demographic information, which may include age group, sex, race, geographic location, socioeconomic status, and ethnicity;

''(II) non-demographic factors, including comorbidities affecting the patient population; and

''(III) potential barriers to enrolling diverse participants, such as patient population size, geographic location, and socioeconomic status; and

''(v) any other data or information relevant to selecting appropriate enrollment goals, disaggregated by demographic subgroup, such as the inclusion of pregnant and lactating women; and

''(B) an explanation for how the sponsor intends to meet such goals, including demographic-specific

outreach and enrollment strategies, study-site selection, clinical study inclusion and exclusion practices, and any diversity training for study personnel;

''(2) submission of any modifications to the diversity action plan;

''(3) considerations for the public posting by a sponsor of key information from the diversity action plan that would be useful to patients and providers on the sponsor's website, as appropriate;

''(4) criteria that the Secretary will consider in assessing whether to grant a sponsor's request to waive the requirement to submit a diversity action plan under section 505(z)(4) or 520(g)(9)(C) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(z)(4), 360j(g)(9)(C)] (as amended by section 3601); and

''(5) how sponsors may include in regular reports otherwise required by the Secretary—

''(A) the sponsor's progress in meeting the goals referred to in paragraph (1)(A); and

''(B) any updates needed to be made to a diversity action plan referred to in paragraph (1) to help meet goals referred to in paragraph (1)(A); and

''(C) if the sponsor does not expect to meet goals referred to in paragraph (1)(A), the sponsor's reasons for why the sponsor does not expect to meet such goals.

''(b) ISSUANCE.—The Secretary shall—

''(1) not later than 12 months after the date of enactment of this Act [Dec. 29, 2022], issue new draft guidance or update existing draft guidance described in subsection (a); and

''(2) not later than 9 months after closing the comment period on such draft guidance, finalize such guidance.''

ANNUAL SUMMARY REPORT ON PROGRESS TO INCREASE DIVERSITY IN CLINICAL STUDIES

Pub. L. 117–328, div. FF, title III, § 3604, Dec. 29, 2022, 136 Stat. 5864, provided that:

''(a) IN GENERAL.—Beginning not later than 2 years after the date of enactment of this Act [Dec. 29, 2022], and each year thereafter, the Secretary [of Health and Human Services] shall submit to the Congress, and publish on the public website of the Food and Drug Administration, a report that—

''(1) summarizes, in aggregate, the diversity action plans received pursuant to section 505(z) or 520(g)(9) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(z), 360j(g)(9)], as added by section 3601; and

''(2) contains information, in the aggregate, on—

''(A) for drugs, biological products, and devices approved, licensed, cleared, or classified under section 505, 515, 510(k), or 513(f)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355; 360e; 360(k); and 360(f)(2) [probably means ''360c(f)(2)'']), or section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)), whether the clinical studies conducted with respect to such applications met the demographic subgroup enrollment goals from the diversity action plan submitted for such applications; and

''(B) the reasons provided, if any, for why enrollment goals from submitted diversity action plans were not met.

''(b) CONFIDENTIALITY.—Nothing in this section shall be construed as authorizing the Secretary to disclose any information that is a trade secret or confidential information subject to section 552(b)(4) of title 5, United States Code, or section 1905 of title 18, United States Code.''

FACILITATING THE USE OF REAL WORLD EVIDENCE

Pub. L. 117–328, div. FF, title III, § 3629, Dec. 29, 2022, 136 Stat. 5891, provided that:

''(a) GUIDANCE.—Not later than 1 year after the date of enactment of this Act [Dec. 29, 2022], the Secretary [of Health and Human Services] shall issue or revise existing guidance on considerations for the use of real world data and real world evidence to support regulatory decision-making, as follows:

''(1) With respect to drugs, such guidance shall address the use of such data and evidence to support the approval of a drug application under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) or a biological product application under section 351 of the Public Health Service Act (42 U.S.C. 262), and to support an investigational use exemption submission under section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)) or section 351(a)(3) of the Public Health Service Act (42 U.S.C. 262(a)(3)). Such guidance shall include considerations for the inclusion, in such applications and submissions, of real world data and real world evidence obtained as a result of the use of drugs authorized for emergency use under section 564 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb–3), and considerations for standards and methodologies for collection and analysis of real world evidence included in such applications and submissions, as appropriate.

''(2) With respect to devices, such guidance shall address the use of such data and evidence to support the approval, clearance, or classification of a device pursuant to an application or submission submitted under section 510(k), 513(f)(2), or 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360(k), 360c(f)(2), 360e), to support an investigational use exemption submission under section 520(g) of such Act (21 U.S.C. 360j(g)), and to support a determination by the Secretary for purposes of section 353 of the Public Health Service Act (42 U.S.C. 263a) (including the category described under subsection (d)(3) of such section). Such guidance shall include considerations for the inclusion, in such applications and submissions, of real world data and real world evidence obtained as a result of the use of devices authorized for emergency use under section 564 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb–3), including considerations related to a determination under section 353(d)(3) of the Public Health Service Act (42 U.S.C. 263a(d)(3)), and considerations for standards and methodologies for collection and analysis of real world evidence included in such applications, submissions, or determinations, as appropriate.

''(b) REPORT TO CONGRESS.—Not later than 2 years after the end of the public health emergency declared by the Secretary under section 319 of the Public Health Service Act (42 U.S.C. 247d) on January 31, 2020, with respect to COVID–19, the Secretary shall submit a report to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives on—

''(1) the number of applications, submissions, or requests submitted for clearance, approval, or authorization under section 505, 510(k), 513(f)(2), or 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355, 360(k), 360c(f)(2), 360e) or section 351 of the Public Health Service Act (42 U.S.C. 262), for which an authorization under section 564 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb–3) was previously granted;

''(2) of the number of applications so submitted, the number of such applications—

''(A) for which real world evidence was submitted and used to support a regulatory decision; and

''(B) for which real world evidence was submitted and determined to be insufficient to support a regulatory decision; and

''(3) a summary explanation of why, in the case of applications described in paragraph (2)(B), real world evidence could not be used to support regulatory decisions.

''(c) INFORMATION DISCLOSURE.—Nothing in this section shall be construed to authorize the disclosure of information that is prohibited from disclosure under section 1905 of title 18, United States Code, or subject to withholding under subsection (b)(4) of section 552 of title 5, United States Code (commonly referred to as the 'Freedom of Information Act').''

CLARIFYING FDA REGULATION OF NON-ADDICTIVE PAIN PRODUCTS

Pub. L. 115–271, title III, §3001, Oct. 24, 2018, 132 Stat. 3932, provided that:

''(a) PUBLIC MEETINGS.—Not later than one year after the date of enactment of this Act [Oct. 24, 2018], the Secretary of Health and Human Services (referred to in this section as the 'Secretary'), acting through the Commissioner of Food and Drugs, shall hold not less than one public meeting to address the challenges and barriers of developing non-addictive medical products intended to treat acute or chronic pain or addiction, which may include—

''(1) the manner by which the Secretary may incorporate the risks of misuse and abuse of a controlled substance (as defined in section 102 of the Controlled Substances Act (21 U.S.C. 802)) into the risk benefit assessments under subsections (d) and (e) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355), section 510(k) of such Act (21 U.S.C. 360(k)), or section 515(c) of such Act (21 U.S.C. 360e(c)), as applicable;

''(2) the application of novel clinical trial designs (consistent with section 3021 of the 21st Century Cures Act (Public Law 114–255) [set out as a note below]), use of real world evidence (consistent with section 505F of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355g)), and use of patient experience data (consistent with section 569C of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb–8c)) for the development of non-addictive medical products intended to treat pain or addiction;

''(3) the evidentiary standards and the development of opioid-sparing data for inclusion in the labeling of medical products intended to treat acute or chronic pain; and

''(4) the application of eligibility criteria under sections 506 and 515B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356, 360e–3) for non-addictive medical products intended to treat pain or addiction.

''(b) GUIDANCE.—Not less than one year after the public meetings are conducted under subsection (a) the Secretary shall issue one or more final guidance documents, or update existing guidance documents, to help address challenges to developing non-addictive medical products to treat pain or addiction. Such guidance documents shall include information regarding—

''(1) how the Food and Drug Administration may apply sections 506 and 515B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356, 360e–3) to non-addictive medical products intended to treat pain or addiction, including the circumstances under which the Secretary—

''(A) may apply the eligibility criteria under such sections 506 and 515B to non-addictive medical products intended to treat pain or addiction;

''(B) considers the risk of addiction of controlled substances approved to treat pain when establishing unmet medical need; and

''(C) considers pain, pain control, or pain management in assessing whether a disease or condition is a serious or life-threatening disease or condition;

''(2) the methods by which sponsors may evaluate acute and chronic pain, endpoints for non-addictive medical products intended to treat pain, the manner in which endpoints and evaluations of efficacy will be applied across and within review divisions, taking into consideration the etiology of the underlying disease, and the manner in which sponsors may use surrogate endpoints, intermediate endpoints, and real world evidence;

''(3) the manner in which the Food and Drug Administration will assess evidence to support the inclusion of opioid-sparing data in the labeling of non-addictive medical products intended to treat acute or chronic pain, including—

''(A) alternative data collection methodologies, including the use of novel clinical trial designs (consistent with section 3021 of the 21st Century Cures Act (Public Law 114–255) [set out as a note below]) and real world evidence (consistent with section 505F of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355g)), including patient registries and patient reported outcomes, as appropriate, to support product labeling;

''(B) ethical considerations of exposing subjects to controlled substances in clinical trials to develop opioid-sparing data and considerations on data collection methods that reduce harm, which may include the reduction of opioid use as a clinical benefit;

''(C) endpoints, including primary, secondary, and surrogate endpoints, to evaluate the reduction of opioid use;

''(D) best practices for communication between sponsors and the agency on the development of data collection methods, including the initiation of data collection; and

''(E) the appropriate format in which to submit such data results to the Secretary; and

''(4) the circumstances under which the Food and Drug Administration considers misuse and abuse of a controlled substance (as defined in section 102 of the Controlled Substances Act (21 U.S.C. 802)) in making the risk benefit assessment under paragraphs (2) and (4) of subsection (d) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) and in finding that a drug is unsafe under paragraph (1) or (2) of subsection (e) of such section.

''(c) DEFINITIONS.—In this section—

''(1) the term 'medical product' means a drug (as defined in section 201(g)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321(g)(1))), biological product (as defined in section 351(i) of the Public Health Service Act (42 U.S.C. 262(i))), or device (as defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321(h))); and

''(2) the term 'opioid-sparing' means reducing, replacing, or avoiding the use of opioids or other controlled substances intended to treat acute or chronic pain.''

GUIDANCE REGARDING REDUCTION IN DRUG EFFECTIVENESS

Pub. L. 115–271, title III, §3041(c), Oct. 24, 2018, 132 Stat. 3943, provided that: ''Not less than one year after the date of enactment of this Act [Oct. 24, 2018], the Secretary of Health and Human Services shall issue guidance regarding the circumstances under which the Food and Drug Administration may require postmarket studies or clinical trials to assess the potential reduction in effectiveness of a drug and how such reduction in effectiveness could result in a change to the benefits of the drug and the risks to the patient. Such guidance shall also address how the Food and Drug Administration may apply this section [amending this section and section 355–1 of this title] and the amendments made thereby with respect to circumstances under which the Food and Drug Administration may require postmarket studies or clinical trials and safety labeling changes related to the use of controlled substances for acute or chronic pain.''

ANNUAL REPORT ON INSPECTIONS

Pub. L. 115–52, title IX, §902, Aug. 18, 2017, 131 Stat. 1077, as amended by Pub. L. 117–328, div. FF, title III, §3617, Dec. 29, 2022, 136 Stat. 5876, provided that: ''Not later than 120 days after the end of each fiscal year, the Secretary of Health and Human Services shall post on the website of the Food and Drug Administration information related to inspections of facilities necessary for approval of a drug under subsection (c) or (j) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) or approval of a device under section 515 of such Act (21 U.S.C. 360e) that were conducted during the previous fiscal year. Such information shall include the following:

''(1) The median time following a request from staff of the Food and Drug Administration reviewing an

application or report to the beginning of the inspection, including—

''(A) the median time for drugs described in 505(j)(11)(A)(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(11)(A)(i));

''(B) the median time for drugs for which a notification has been submitted in accordance with section 506C(a) of such Act (21 U.S.C. 356c(a)) during the previous fiscal year; and

''(C) the median time for drugs on the drug shortage list in effect under section 506E of such Act (21 U.S.C. 356e) at the time of such request.

''(2) The median time from the issuance of a report pursuant to section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 374(b)) to the sending of a warning letter, issuance of an import alert, or holding of a regulatory meeting for inspections for which the Secretary concluded that regulatory or enforcement action was indicated, including the median time for each category of drugs listed in subparagraphs (A) through (C) of paragraph (1).

''(3) The median time from the sending of a warning letter, issuance of an import alert, or holding of a regulatory meeting related to conditions observed by the Secretary during an inspection, to the time at which the Secretary concludes that corrective actions to resolve such conditions have been taken.

''(4) The number of facilities that failed to implement adequate corrective or preventive actions following a report issued pursuant to such section 704(b), resulting in a withhold recommendation for an application under review, including the number of such facilities manufacturing each category of drugs listed in subparagraphs (A) through (C) of paragraph (1).''

REPORT ON PATIENT EXPERIENCE DRUG DEVELOPMENT

Pub. L. 114–255, div. A, title III, § 3004, Dec. 13, 2016, 130 Stat. 1085, provided that: ''Not later than June 1 of 2021, 2026, and 2031, the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs, shall prepare and publish on the Internet website of the Food and Drug Administration a report assessing the use of patient experience data in regulatory decisionmaking, in particular with respect to the review of patient experience data and information on patient-focused drug development tools as part of applications approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(c)) or section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)).''

NOVEL CLINICAL TRIAL DESIGNS

Pub. L. 114–255, div. A, title III, § 3021, Dec. 13, 2016, 130 Stat. 1095, provided that:

''(a) PROPOSALS FOR USE OF NOVEL CLINICAL TRIAL DESIGNS FOR DRUGS AND BIOLOGICAL PRODUCTS.—For purposes of assisting sponsors in incorporating complex adaptive and other novel trial designs into proposed clinical protocols and applications for new drugs under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) and biological products under section 351 of the Public Health Service Act (42 U.S.C. 262), the Secretary of Health and Human Services (referred to in this section as the 'Secretary') shall conduct a public meeting and issue guidance in accordance with subsection (b).

''(b) GUIDANCE ADDRESSING USE OF NOVEL CLINICAL TRIAL DESIGNS.—

''(1) IN GENERAL.—The Secretary, acting through the Commissioner of Food and Drugs, shall update or issue guidance addressing the use of complex adaptive and other novel trial design in the development and regulatory review and approval or licensure for drugs and biological products.

''(2) CONTENTS.—The guidance under paragraph (1) shall address—

''(A) the use of complex adaptive and other novel trial designs, including how such clinical trials proposed or submitted help to satisfy the substantial evidence standard under section 505(d) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(d));

''(B) how sponsors may obtain feedback from the Secretary on technical issues related to modeling and simulations prior to—

''(i) completion of such modeling or simulations; or

''(ii) the submission of resulting information to the Secretary;

''(C) the types of quantitative and qualitative information that should be submitted for review; and

''(D) recommended analysis methodologies.

''(3) PUBLIC MEETING.—Prior to updating or issuing the guidance required by paragraph (1), the Secretary shall consult with stakeholders, including representatives of regulated industry, academia, patient advocacy organizations, consumer groups, and disease research foundations, through a public meeting to be held not later than 18 months after the date of enactment of this Act [Dec. 13, 2016].

''(4) TIMING.—The Secretary shall update or issue a draft version of the guidance required by paragraph (1) not later than 18 months after the date of the public meeting required by paragraph (3) and finalize such guidance not later than 1 year after the date on which the public comment period for the draft guidance closes.''

VARIATIONS FROM CGMP STREAMLINED APPROACH

Pub. L. 114–255, div. A, title III, § 3038(c), Dec. 13, 2016, 130 Stat. 1110, provided that: ''Not later than 18 months after the date of enactment of this Act [Dec. 13, 2016], the Secretary of Health and Human Services (referred to in this subsection as the 'Secretary') shall identify types of combination products and manufacturing processes with respect to which the Secretary proposes that good manufacturing processes may be adopted that vary from the requirements set forth in section 4.4 of title 21, Code of Federal Regulations (or any successor regulations) or that the Secretary proposes can satisfy the requirements in section 4.4 through alternative or streamlined mechanisms. The Secretary shall identify such types, variations from such requirements, and such mechanisms, in a proposed list published in the Federal Register. After a public comment period regarding the appropriate good manufacturing practices for such types, the Secretary shall publish a final list in the Federal Register, notwithstanding section 553 of title 5, United States Code. The Secretary shall evaluate such types, variations, and mechanisms using a risk-based approach. The Secretary shall periodically review such final list.''

FDA OPIOID ACTION PLAN

Pub. L. 114–198, title I, § 106(a), July 22, 2016, 130 Stat. 702, provided that:

''(1) NEW DRUG APPLICATION.—

''(A) IN GENERAL.—Subject to subparagraph (B), prior to the approval pursuant to an application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(b)) of a new drug that is an opioid, the Secretary of Health and Human Services (referred to in this section [enacting provisions set out as notes under this section and section 355–1 of this title] as the 'Secretary') shall refer the application to an advisory committee of the Food and Drug Administration to seek recommendations from such advisory committee.

''(B) PUBLIC HEALTH EXEMPTION.—A referral to an advisory committee under subparagraph (A) is not required with respect to a new opioid drug or drugs if the Secretary—

''(i) finds that such a referral is not in the interest of protecting and promoting public health;

''(ii) finds that such a referral is not necessary based on a review of the relevant scientific information; and

''(iii) submits a notice containing the rationale for such findings to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives.

''(2) PEDIATRIC OPIOID LABELING.—The Secretary shall convene the Pediatric Advisory Committee of the Food and Drug Administration to seek recommendations from such Committee regarding a framework for the inclusion of information in the labeling of drugs that are opioids relating to the use of such drugs in pediatric populations before the Secretary approves any labeling or change to labeling for any drug that is an opioid intended for use in a pediatric population.

''(3) SUNSET.—The requirements of paragraphs (1) and (2) shall cease to be effective on October 1, 2022.''

GUIDANCE ON EVALUATING THE ABUSE DETERRENCE OF GENERIC SOLID ORAL OPIOID DRUG PRODUCTS

Pub. L. 114–198, title I, §106(c), July 22, 2016, 130 Stat. 703, provided that: ''Not later than 18 months after the end of the period for public comment on the draft guidance entitled 'General Principles for Evaluating the Abuse Deterrence of Generic Solid Oral Opioid Drug Products' issued by the Center for Drug Evaluation and Research of the Food and Drug Administration in March 2016, the Commissioner of Food and Drugs shall publish in the Federal Register a final version of such guidance.''

GUIDANCE ON PATHOGEN-FOCUSED ANTIBACTERIAL DRUG DEVELOPMENT

Pub. L. 112–144, title VIII, §806, July 9, 2012, 126 Stat. 1082, provided that:

''(a) DRAFT GUIDANCE.—Not later than June 30, 2013, in order to facilitate the development of antibacterial drugs for serious or life-threatening bacterial infections, particularly in areas of unmet need, the Secretary of Health and Human Services shall publish draft guidance that—

''(1) specifies how preclinical and clinical data can be utilized to inform an efficient and streamlined pathogen-focused antibacterial drug development program that meets the approval standards of the Food and Drug Administration; and

''(2) provides advice on approaches for the development of antibacterial drugs that target a more limited spectrum of pathogens.

''(b) FINAL GUIDANCE.—Not later than December 31, 2014, after notice and opportunity for public comment on the draft guidance under subsection (a), the Secretary of Health and Human Services shall publish final guidance consistent with this section.''

GUIDANCE ON ABUSE-DETERRENT PRODUCTS

Pub. L. 112–144, title XI, §1122(c), July 9, 2012, 126 Stat. 1113, as amended by Pub. L. 114–255, div. A, title III, §3101(b)(3)(B), Dec. 13, 2016, 130 Stat. 1156, provided that: ''Not later than 6 months after the date of enactment of this Act [July 9, 2012], the Secretary [of Health and Human Services] shall issue guidance on the development of abuse-deterrent drug products.''

EXTENSION OF PERIOD FOR FIRST APPLICANT TO OBTAIN TENTATIVE APPROVAL WITHOUT FORFEITING 180-DAY-EXCLUSIVITY PERIOD

Pub. L. 112–144, title XI, §1133, July 9, 2012, 126 Stat. 1122, provided that:

''(a) EXTENSION.—

''(1) IN GENERAL.—If a first applicant files an application during the 30-month period ending on the date of enactment of this Act [July 9, 2012] and such application initially contains a certification described in paragraph (2)(A)(vii)(IV) of section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)), or if a first applicant files an application and the application is amended during such period to first contain such a certification, the phrase '30 months' in paragraph (5)(D)(i)(IV) of such section shall, with respect to such application, be read as meaning—

''(A) during the period beginning on the date of enactment of this Act, and ending on September 30, 2015, '40 months'; and

''(B) during the period beginning on October 1, 2015, and ending on September 30, 2016, '36 months'.

''(2) CONFORMING AMENDMENT.—In the case of an application to which an extended period under paragraph (1) applies, the reference to the 30-month period under section 505(q)(1)(G) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(q)(1)(G)) shall be read to be the applicable period under paragraph (1).

''(b) PERIOD FOR OBTAINING TENTATIVE APPROVAL OF CERTAIN APPLICATIONS.—If an application is filed on or before the date of enactment of this Act [July 9, 2012] and such application is amended during the period beginning on the day after the date of enactment of this Act and ending on September 30, 2017, to first contain a certification described in paragraph (2)(A)(vii)(IV) of section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)), the date of the filing of such amendment (rather than the date of the filing of such application) shall be treated as the beginning of the 30-month period described in paragraph (5)(D)(i)(IV) of such section 505(j).

''(c) DEFINITIONS.—For the purposes of this section, the terms 'application' and 'first applicant' mean application and first applicant, as such terms are used in section 505(j)(5)(D)(i)(IV) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(5)(D)(i)(IV)).''

EFFECT OF AMENDMENTS BY PUB. L. 110–85 ON VETERINARY MEDICINE

Pub. L. 110–85, title IX, §907, Sept. 27, 2007, 121 Stat. 950, provided that: ''This subtitle [subtitle A (§§901–909) of title IX of Pub. L. 110–85, enacting sections 353c and 355–1 of this title, amending this section and sections 331, 333, and 352 of this title and section 262 of Title 42, The Public Health and Welfare, and enacting provisions set out as notes under this section and sections 331, 352, and 355a of this title], and the amendments made by this subtitle, shall have no effect on the use of drugs approved under section 505 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355] by, or on the lawful written or oral order of, a licensed veterinarian within the context of a veterinarian-client-patient relationship, as provided for under section 512(a)(5) of such Act [21 U.S.C. 360b(a)(5)].''

EFFECT OF AMENDMENT BY PUB. L. 108–173 ON ABBREVIATED NEW DRUG APPLICATIONS

Pub. L. 108–173, title XI, §1103(b), Dec. 8, 2003, 117 Stat. 2461, provided that: ''The amendment made by subsection (a) [amending this section] does not alter the standards for approval of drugs under section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)).''

FEDERAL TRADE COMMISSION REVIEW

Pub. L. 108–173, title XI, subtitle B, Dec. 8, 2003, 117 Stat. 2461, as amended by Pub. L. 115–263, §3, Oct. 10, 2018, 132 Stat. 3673; Pub. L. 115–271, title IV, §4004, Oct. 24, 2018, 132 Stat. 3960, provided that:

''SEC. 1111. DEFINITIONS.

''In this subtitle:

''(1) ANDA.—The term 'ANDA' means an abbreviated drug application, as defined under section 201(aa) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 321(aa)].

''(2) ASSISTANT ATTORNEY GENERAL.—The term 'Assistant Attorney General' means the Assistant Attorney General in charge of the Antitrust Division of the Department of Justice.

''(3) BIOSIMILAR BIOLOGICAL PRODUCT.—The term 'biosimilar biological product' means a biological product for which a biosimilar biological product application under section 351(k) of the Public Health Service Act [42 U.S.C. 262(k)] is approved.

''(4) BIOSIMILAR BIOLOGICAL PRODUCT APPLICANT.—The term 'biosimilar biological product applicant'

means a person who has filed or received approval for a biosimilar biological product application under section 351(k) of the Public Health Service Act [42 U.S.C. 262(k)].

''(5) BIOSIMILAR BIOLOGICAL PRODUCT APPLICATION.—The term 'biosimilar biological product application' means an application under section 351(k) of the Public Health Service Act [42 U.S.C. 262(k)] for licensure of a biological product as biosimilar to, or interchangeable with, a reference product.

''(6) BRAND NAME DRUG.—The term 'brand name drug' means a drug for which an application is approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(c)], including an application referred to in section 505(b)(2) of such Act [21 U.S.C. 355(b)(2)], or a biological product for which an application is approved under section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)].

''(7) BRAND NAME DRUG COMPANY.—The term 'brand name drug company' means the party that holds the approved application referred to in paragraph (6) for a brand name drug that is a listed drug in an ANDA or a reference product in a biosimilar biological product application, or a party that is the owner of a patent for which information is submitted for such drug under subsection (b) or (c) of section 505 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(b), (c)] or the owner, or exclusive licensee, of a patent included in a list provided under section 351(*l*)(3) of the Public Health Service Act [42 U.S.C. 262(*l*)(3)].

''(8) COMMISSION.—The term 'Commission' means the Federal Trade Commission.

''(9) GENERIC DRUG.—The term 'generic drug' means a drug for which an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)] is approved.

''(10) GENERIC DRUG APPLICANT.—The term 'generic drug applicant' means a person who has filed or received approval for an ANDA under section 505(j) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)].

''(11) LISTED DRUG.—The term 'listed drug' means a brand name drug that is listed under section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)(7)].

''(12) REFERENCE PRODUCT.—The term 'reference product' has the meaning given such term in section 351(i) of the Public Health Service Act [42 U.S.C. 262(i)].

''SEC. 1112. NOTIFICATION OF AGREEMENTS.

''(a) AGREEMENT WITH BRAND NAME DRUG COMPANY.—

''(1) REQUIREMENT.—A generic drug applicant that has submitted an ANDA containing a certification under section 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)(2)(A)(vii)(IV)] or a biosimilar biological product applicant who has submitted a biosimilar biological product application and a brand name drug company that enter into an agreement described in paragraph (2) shall each file the agreement in accordance with subsection (c). The agreement shall be filed prior to the date of the first commercial marketing of the generic drug that is the subject of the ANDA or the biosimilar biological product that is the subject of the biosimilar biological product application, as applicable.

''(2) SUBJECT MATTER OF AGREEMENT.—An agreement described in this paragraph between a generic drug applicant or a biosimilar biological product applicant and a brand name drug company is an agreement regarding—

''(A) the manufacture, marketing, or sale of the brand name drug that is the listed drug in the ANDA or the reference product in the biosimilar biological product application involved;

''(B) the manufacture, marketing, or sale of the generic drug for which the ANDA was submitted or of the biosimilar biological product for which the biosimilar biological product application was submitted; or

''(C) as applicable—

''(i) the 180-day period referred to in section 505(j)(5)(B)(iv) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)(5)(B)(iv)] as it applies to such ANDA or to any other ANDA based on the same listed drug; or

''(ii) any of the time periods referred to in section 351(k)(6) of the Public Health Service Act [42 U.S.C. 262(k)(6)] as such period applies to such biosimilar biological product application or to any other biosimilar biological product application based on the same reference product.

''(b) AGREEMENT WITH ANOTHER GENERIC DRUG APPLICANT OR BIOSIMILAR BIOLOGICAL PRODUCT APPLICANT.—

''(1) REQUIREMENT.—

''(A) GENERIC DRUGS.—A generic drug applicant that has submitted an ANDA containing a certification under section 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)(2)(A)(vii)(IV)] with respect to a listed drug and another generic drug applicant that has submitted an ANDA containing such a certification for the same listed drug shall each file the agreement in accordance with subsection (c). The agreement shall be filed prior to the date of the first commercial marketing of either of the generic drugs for which such ANDAs were submitted.

''(B) BIOSIMILAR BIOLOGICAL PRODUCTS.—A biosimilar biological product applicant that has submitted a biosimilar biological product application that references a reference product and another biosimilar biological product applicant that has submitted a biosimilar biological product application that references the same reference product shall each file the agreement in accordance with subsection (c). The agreement shall be filed prior to the date of the first commercial marketing of either of the biosimilar biological products for which such biosimilar biological product applications were submitted.

''(2) SUBJECT MATTER OF AGREEMENT.—An agreement described in this paragraph is, as applicable, an agreement between 2 or more generic drug applicants regarding the 180-day period referred to in section 505(j)(5)(B)(iv) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)(5)(B)(iv)] as it applies to the ANDAs with which the agreement is concerned,, [sic] an agreement between 2 or more biosimilar biological product applicants regarding a time period referred to in section 351(k)(6) of the Public Health Service Act [42 U.S.C. 262(k)(6)] as it applies to the biosimilar biological product, or an agreement between 2 or more biosimilar biological product applicants regarding the manufacture, marketing, or sale of a biosimilar biological product.

''(c) FILING.—

''(1) AGREEMENT.—The parties that are required in subsection (a) or (b) to file an agreement in accordance with this subsection shall file with the Assistant Attorney General and the Commission the text of any such agreement, except that such parties are not required to file an agreement that solely concerns—

''(A) purchase orders for raw material supplies;

''(B) equipment and facility contracts;

''(C) employment or consulting contracts; or

''(D) packaging and labeling contracts.

''(2) OTHER AGREEMENTS.—The parties that are required in subsection (a) or (b) to file an agreement in accordance with this subsection shall file with the Assistant Attorney General and the Commission the text of any agreements between the parties that are not described in such subsections and are contingent upon, provide a contingent condition for, were entered into within 30 days of, or are otherwise related to an agreement that is required in subsection (a) or (b) to be filed in accordance with this subsection.

''(3) DESCRIPTION.—In the event that any agreement required in subsection (a) or (b) to be filed in accordance with this subsection has not been reduced to text, each of the parties involved shall file written

descriptions of such agreement that are sufficient to disclose all the terms and conditions of the agreement.

''SEC. 1113. FILING DEADLINES.

''Any filing required under section 1112 shall be filed with the Assistant Attorney General and the Commission not later than 10 business days after the date the agreements are executed.

''SEC. 1114. DISCLOSURE EXEMPTION.

''Any information or documentary material filed with the Assistant Attorney General or the Commission pursuant to this subtitle shall be exempt from disclosure under section 552 of title 5, United States Code, and no such information or documentary material may be made public, except as may be relevant to any administrative or judicial action or proceeding. Nothing in this section is intended to prevent disclosure to either body of the Congress or to any duly authorized committee or subcommittee of the Congress.

''SEC. 1115. ENFORCEMENT.

''(a) CIVIL PENALTY.—Any brand name drug company, generic drug applicant, or biosimilar biological product applicant which fails to comply with any provision of this subtitle shall be liable for a civil penalty of not more than $11,000, for each day during which such entity is in violation of this subtitle. Such penalty may be recovered in a civil action brought by the United States, or brought by the Commission in accordance with the procedures established in section 16(a)(1) of the Federal Trade Commission Act (15 U.S.C. 56(a) [15 U.S.C. 56(a)(1)]).

''(b) COMPLIANCE AND EQUITABLE RELIEF.—If any brand name drug company, generic drug applicant, or biosimilar biological product applicant fails to comply with any provision of this subtitle, the United States district court may order compliance, and may grant such other equitable relief as the court in its discretion determines necessary or appropriate, upon application of the Assistant Attorney General or the Commission.

''SEC. 1116. RULEMAKING.

''The Commission, with the concurrence of the Assistant Attorney General and by rule in accordance with section 553 of title 5, United States Code, consistent with the purposes of this subtitle—

''(1) may define the terms used in this subtitle;

''(2) may exempt classes of persons or agreements from the requirements of this subtitle; and

''(3) may prescribe such other rules as may be necessary and appropriate to carry out the purposes of this subtitle.

''SEC. 1117. SAVINGS CLAUSE.

''Any action taken by the Assistant Attorney General or the Commission, or any failure of the Assistant Attorney General or the Commission to take action, under this subtitle shall not at any time bar any proceeding or any action with respect to any agreement between a brand name drug company and a generic drug applicant or a biosimilar biological product applicant, any agreement between generic drug applicants, or any agreement between biosimilar biological product applicants, under any other provision of law, nor shall any filing under this subtitle constitute or create a presumption of any violation of any competition laws.

''SEC. 1118. EFFECTIVE DATE.

''This subtitle shall—

''(1) take effect 30 days after the date of the enactment of this Act [Dec. 8, 2003]; and

''(2) shall apply to agreements described in section 1112 that are entered into 30 days after the date of the enactment of this Act.''

REPORT ON PATIENT ACCESS TO NEW THERAPEUTIC AGENTS FOR PEDIATRIC CANCER

Pub. L. 107–109, §15(d), Jan. 4, 2002, 115 Stat. 1421, provided that: ''Not later than January 31, 2003, the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs and in consultation with the Director of the National Institutes of Health, shall submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives a report on patient access to new therapeutic agents for pediatric cancer, including access to single patient use of new therapeutic agents.''

DATA REQUIREMENTS FOR DRUGS AND BIOLOGICS

Pub. L. 105–115, title I, §118, Nov. 21, 1997, 111 Stat. 2316, provided that: ''Within 12 months after the date of enactment of this Act [Nov. 21, 1997], the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs, shall issue guidance that describes when abbreviated study reports may be submitted, in lieu of full reports, with a new drug application under section 505(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(b)) and with a biologics license application under section 351 of the Public Health Service Act (42 U.S.C. 262) for certain types of studies. Such guidance shall describe the kinds of studies for which abbreviated reports are appropriate and the appropriate abbreviated report formats.''

REQUIREMENTS FOR REVIEW OF APPROVAL PROCEDURES AND CURRENT GOOD MANUFACTURING PRACTICES FOR POSITRON EMISSION TECHNOLOGY

Pub. L. 105–115, title I, §121(c), Nov. 21, 1997, 111 Stat. 2321, provided that:

''(1) PROCEDURES AND REQUIREMENTS.—

''(A) IN GENERAL.—In order to take account of the special characteristics of positron emission tomography drugs and the special techniques and processes required to produce these drugs, not later than 2 years after the date of enactment of this Act [Nov. 21, 1997], the Secretary of Health and Human Services shall establish—

''(i) appropriate procedures for the approval of positron emission tomography drugs pursuant to section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355); and

''(ii) appropriate current good manufacturing practice requirements for such drugs.

''(B) CONSIDERATIONS AND CONSULTATION.—In establishing the procedures and requirements required by subparagraph (A), the Secretary of Health and Human Services shall take due account of any relevant differences between not-for-profit institutions that compound the drugs for their patients and commercial manufacturers of the drugs. Prior to establishing the procedures and requirements, the Secretary of Health and Human Services shall consult with patient advocacy groups, professional associations, manufacturers, and physicians and scientists licensed to make or use positron emission tomography drugs.

''(2) SUBMISSION OF NEW DRUG APPLICATIONS AND ABBREVIATED NEW DRUG APPLICATIONS.—

''(A) IN GENERAL.—Except as provided in subparagraph (B), the Secretary of Health and Human Services shall not require the submission of new drug applications or abbreviated new drug applications under subsection (b) or (j) of section 505 (21 U.S.C. 355), for compounded positron emission tomography drugs that are not adulterated drugs described in section 501(a)(2)(C) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351(a)(2)(C)) (as amended by subsection (b)), for a period of 4 years after the date of enactment of this Act [Nov. 21, 1997], or for 2 years after the date on which the Secretary establishes procedures and requirements under paragraph (1), whichever is longer.

''(B) EXCEPTION.—Nothing in this Act [see Short Title of 1997 Amendment note set out under section 301 of this title] shall prohibit the voluntary submission of such applications or the review of such applications by the Secretary of Health and Human Serv-

ices. Nothing in this Act shall constitute an exemption for a positron emission tomography drug from the requirements of regulations issued under section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)).''

''COMPOUNDED POSITRON EMISSION TOPOGRAPHY DRUG'' DEFINED

Pub. L. 105–115, title I, § 121(e), Nov. 21, 1997, 111 Stat. 2322, provided that: ''As used in this section [amending sections 321 and 351 of this title and enacting provisions set out as notes under this section and section 351 of this title], the term 'compounded positron emission tomography drug' has the meaning given the term in section 201 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321).''

REQUIREMENTS FOR RADIOPHARMACEUTICALS

Pub. L. 105–115, title I, § 122, Nov. 21, 1997, 111 Stat. 2322, provided that:

''(a) REQUIREMENTS.—

''(1) REGULATIONS.—

''(A) PROPOSED REGULATIONS.—Not later than 180 days after the date of enactment of this Act [Nov. 21, 1997], the Secretary of Health and Human Services, after consultation with patient advocacy groups, associations, physicians licensed to use radiopharmaceuticals, and the regulated industry, shall issue proposed regulations governing the approval of radiopharmaceuticals. The regulations shall provide that the determination of the safety and effectiveness of such a radiopharmaceutical under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) or section 351 of the Public Health Service Act (42 U.S.C. 262) shall include consideration of the proposed use of the radiopharmaceutical in the practice of medicine, the pharmacological and toxicological activity of the radiopharmaceutical (including any carrier or ligand component of the radiopharmaceutical), and the estimated absorbed radiation dose of the radiopharmaceutical.

''(B) FINAL REGULATIONS.—Not later than 18 months after the date of enactment of this Act, the Secretary shall promulgate final regulations governing the approval of the radiopharmaceuticals.

''(2) SPECIAL RULE.—In the case of a radiopharmaceutical, the indications for which such radiopharmaceutical is approved for marketing may, in appropriate cases, refer to manifestations of disease (such as biochemical, physiological, anatomic, or pathological processes) common to, or present in, one or more disease states.

''(b) DEFINITION.—In this section, the term 'radiopharmaceutical' means—

''(1) an article—

''(A) that is intended for use in the diagnosis or monitoring of a disease or a manifestation of a disease in humans; and

''(B) that exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons; or

''(2) any nonradioactive reagent kit or nuclide generator that is intended to be used in the preparation of any such article.''

SPECIAL RULE

Pub. L. 105–115, title I, § 123(f), Nov. 21, 1997, 111 Stat. 2324, provided that: ''The Secretary of Health and Human Services shall take measures to minimize differences in the review and approval of products required to have approved biologics license applications under section 351 of the Public Health Service Act (42 U.S.C. 262) and products required to have approved new drug applications under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(b)(1)).''

TRANSITION

Pub. L. 110–379, § 4(b), Oct. 8, 2008, 122 Stat. 4077, provided that:

''(1) With respect to a patent issued on or before the date of the enactment of this Act [Oct. 8, 2008], any patent information required to be filed with the Secretary of Health and Human Services under subsection (b)(1) or (c)(2) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) to be listed on a drug to which subsection (v)(1) of such section 505 (as added by this section) applies shall be filed with the Secretary not later than 60 days after the date of the enactment of this Act.

''(2) With respect to any patent information referred to in paragraph (1) of this subsection that is filed with the Secretary within the 60-day period after the date of the enactment of this Act [Oct. 8, 2008], the Secretary shall publish such information in the electronic version of the list referred to at section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)) as soon as it is received, but in no event later than the date that is 90 days after the enactment of this Act.

''(3) With respect to any patent information referred to in paragraph (1) that is filed with the Secretary within the 60-day period after the date of enactment of this Act [Oct. 8, 2008], each applicant that, not later than 120 days after the date of the enactment of this Act, amends an application that is, on or before the date of the enactment of this Act, a substantially complete application (as defined in paragraph (5)(B)(iv) of section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j))) to contain a certification described in paragraph (2)(A)(vii)(IV) of such section 505(j) with respect to that patent shall be deemed to be a first applicant (as defined in paragraph (5)(B)(iv) of such section 505(j)).''

Pub. L. 105–115, title I, § 125(d), Nov. 21, 1997, 111 Stat. 2326, provided that:

''(1) IN GENERAL.—An application that was approved by the Secretary of Health and Human Services before the date of the enactment of this Act [Nov. 21, 1997] for the marketing of an antibiotic drug under section 507 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 357), as in effect on the day before the date of the enactment of this Act, shall, on and after such date of enactment, be considered to be an application that was submitted and filed under section 505(b) of such Act (21 U.S.C. 355(b)) and approved for safety and effectiveness under section 505(c) of such Act (21 U.S.C. 355(c)), except that if such application for marketing was in the form of an abbreviated application, the application shall be considered to have been filed and approved under section 505(j) of such Act (21 U.S.C. 355(j)).

''(2) EXCEPTION.—The following subsections of section 505 (21 U.S.C. 355) shall not apply to any application for marketing in which the drug that is the subject of the application contains an antibiotic drug and the antibiotic drug was the subject of any application for marketing received by the Secretary of Health and Human Services under section 507 of such Act (21 U.S.C. 357) before the date of the enactment of this Act [Nov. 21, 1997]:

''(A)(i) Subsections (c)(2), (d)(6), (e)(4), (j)(2)(A)(vii), (j)(2)(A)(viii), (j)(2)(B), (j)(4)(B), and (j)(4)(D); and

''(ii) The third and fourth sentences of subsection (b)(1) (regarding the filing and publication of patent information); and

''(B) Subsections (b)(2)(A), (b)(2)(B), (b)(3), and (c)(3) if the investigations relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

''(3) PUBLICATION.—For purposes of this section, the Secretary is authorized to make available to the public the established name of each antibiotic drug that was the subject of any application for marketing received by the Secretary for Health and Human Services under section 507 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 357) before the date of enactment of this Act [Nov. 21, 1997].''

TERMINATION OF ADVISORY PANELS

Advisory panels established after Jan. 5, 1973, to terminate not later than the expiration of the 2-year pe-

riod beginning on the date of their establishment, unless, in the case of a panel established by the President or an officer of the Federal Government, such panel is renewed by appropriate action prior to the expiration of such 2-year period, or in the case of a panel established by Congress, its duration is otherwise provided for by law. See sections 1001(2) and 1013 of Title 5, Government Organization and Employees.

APPEALS TAKEN PRIOR TO OCTOBER 10, 1962

Pub. L. 87–781, title I, §104(d)(3), Oct. 10, 1962, 76 Stat. 785, made amendments to subsec. (h) of this section inapplicable to any appeal taken prior to Oct. 10, 1962.

Executive Documents

TRANSFER OF FUNCTIONS

For transfer of functions of Federal Security Administrator to Secretary of Health, Education, and Welfare [now Health and Human Services], and of Food and Drug Administration in the Department of Agriculture to Federal Security Agency, see notes set out under section 321 of this title.

§ 355–1. Risk evaluation and mitigation strategies

(a) Submission of proposed strategy

(1) Initial approval

If the Secretary, in consultation with the office responsible for reviewing the drug and the office responsible for postapproval safety with respect to the drug, determines that a risk evaluation and mitigation strategy is necessary to ensure that the benefits of the drug outweigh the risks of the drug, and informs the person who submits such application of such determination, then such person shall submit to the Secretary as part of such application a proposed risk evaluation and mitigation strategy. In making such a determination, the Secretary shall consider the following factors:

(A) The estimated size of the population likely to use the drug involved.

(B) The seriousness of the disease or condition that is to be treated with the drug.

(C) The expected benefit of the drug with respect to such disease or condition.

(D) The expected or actual duration of treatment with the drug.

(E) The seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug.

(F) Whether the drug is a new molecular entity.

(2) Postapproval requirement

(A) In general

If the Secretary has approved a covered application (including an application approved before the effective date of this section) and did not when approving the application require a risk evaluation and mitigation strategy under paragraph (1), the Secretary, in consultation with the offices described in paragraph (1), may subsequently require such a strategy for the drug involved (including when acting on a supplemental application seeking approval of a new indication for use of the drug) if the Secretary becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks of the drug.

(B) Submission of proposed strategy

Not later than 120 days after the Secretary notifies the holder of an approved covered application that the Secretary has made a determination under subparagraph (A) with respect to the drug involved, or within such other reasonable time as the Secretary requires to protect the public health, the holder shall submit to the Secretary a proposed risk evaluation and mitigation strategy.

(3) Abbreviated new drug applications

The applicability of this section to an application under section 355(j) of this title is subject to subsection (i).

(4) Non-delegation

Determinations by the Secretary under this subsection for a drug shall be made by individuals at or above the level of individuals empowered to approve a drug (such as division directors within the Center for Drug Evaluation and Research).

(b) Definitions

For purposes of this section:

(1) Adverse drug experience

The term ''adverse drug experience'' means any adverse event associated with the use of a drug in humans, whether or not considered drug related, including—

(A) an adverse event occurring in the course of the use of the drug in professional practice;

(B) an adverse event occurring from an overdose of the drug, whether accidental or intentional;

(C) an adverse event occurring from abuse of the drug;

(D) an adverse event occurring from withdrawal of the drug; and

(E) any failure of expected pharmacological action of the drug, which may include reduced effectiveness under the conditions of use prescribed in the labeling of such drug, but which may not include reduced effectiveness that is in accordance with such labeling.

(2) Covered application

The term ''covered application'' means an application referred to in section 355(p)(1)(A) of this title.

(3) New safety information

The term ''new safety information'', with respect to a drug, means information derived from a clinical trial, an adverse event report, a postapproval study (including a study under section 355(*o*)(3) of this title), or peer-reviewed biomedical literature; data derived from the postmarket risk identification and analysis system under section 355(k) of this title; or other scientific data deemed appropriate by the Secretary about—

(A) a serious risk or an unexpected serious risk associated with use of the drug that the

Secretary has become aware of (that may be based on a new analysis of existing information) since the drug was approved, since the risk evaluation and mitigation strategy was required, or since the last assessment of the approved risk evaluation and mitigation strategy for the drug; or

(B) the effectiveness of the approved risk evaluation and mitigation strategy for the drug obtained since the last assessment of such strategy.

(4) Serious adverse drug experience

The term ''serious adverse drug experience'' is an adverse drug experience that—

(A) results in—

(i) death;

(ii) an adverse drug experience that places the patient at immediate risk of death from the adverse drug experience as it occurred (not including an adverse drug experience that might have caused death had it occurred in a more severe form);

(iii) inpatient hospitalization or prolongation of existing hospitalization;

(iv) a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions; or

(v) a congenital anomaly or birth defect; or

(B) based on appropriate medical judgment, may jeopardize the patient and may require a medical or surgical intervention to prevent an outcome described under subparagraph (A).

(5) Serious risk

The term ''serious risk'' means a risk of a serious adverse drug experience.

(6) Signal of a serious risk

The term ''signal of a serious risk'' means information related to a serious adverse drug experience associated with use of a drug and derived from—

(A) a clinical trial;

(B) adverse event reports;

(C) a postapproval study, including a study under section 355(*o*)(3) of this title;

(D) peer-reviewed biomedical literature;

(E) data derived from the postmarket risk identification and analysis system under section 355(k)(4) of this title; or

(F) other scientific data deemed appropriate by the Secretary.

(7) Responsible person

The term ''responsible person'' means the person submitting a covered application or the holder of the approved such application.

(8) Unexpected serious risk

The term ''unexpected serious risk'' means a serious adverse drug experience that is not listed in the labeling of a drug, or that may be symptomatically and pathophysiologically related to an adverse drug experience identified in the labeling, but differs from such adverse drug experience because of greater severity, specificity, or prevalence.

(c) Contents

A proposed risk evaluation and mitigation strategy under subsection (a) shall—

(1) include the timetable required under subsection (d); and

(2) to the extent required by the Secretary, in consultation with the office responsible for reviewing the drug and the office responsible for postapproval safety with respect to the drug, include additional elements described in subsections (e) and (f).

(d) Minimal strategy

For purposes of subsection (c)(1), the risk evaluation and mitigation strategy for a drug shall require a timetable for submission of assessments of the strategy that—

(1) includes an assessment, by the date that is 18 months after the strategy is initially approved;

(2) includes an assessment by the date that is 3 years after the strategy is initially approved;

(3) includes an assessment in the seventh year after the strategy is so approved; and

(4) subject to paragraphs (1), (2), and (3)—

(A) is at a frequency specified in the strategy;

(B) is increased or reduced in frequency as necessary as provided for in subsection (g)(4)(A); and

(C) is eliminated after the 3-year period described in paragraph (1) if the Secretary determines that serious risks of the drug have been adequately identified and assessed and are being adequately managed.

(e) Additional potential elements of strategy

(1) In general

The Secretary, in consultation with the offices described in subsection (c)(2), may under such subsection require that the risk evaluation and mitigation strategy for a drug include 1 or more of the additional elements described in this subsection if the Secretary makes the determination required with respect to each element involved.

(2) Medication Guide; patient package insert

The risk evaluation and mitigation strategy for a drug may require that, as applicable, the responsible person develop for distribution to each patient when the drug is dispensed—

(A) a Medication Guide, as provided for under part 208 of title 21, Code of Federal Regulations (or any successor regulations); and

(B) a patient package insert, if the Secretary determines that such insert may help mitigate a serious risk of the drug.

(3) Communication plan

The risk evaluation and mitigation strategy for a drug may require that the responsible person conduct a communication plan to health care providers, if, with respect to such drug, the Secretary determines that such plan may support implementation of an element of the strategy (including under this paragraph). Such plan may include—

(A) sending letters to health care providers;

(B) disseminating information about the elements of the risk evaluation and mitigation strategy to encourage implementation

by health care providers of components that apply to such health care providers, or to explain certain safety protocols (such as medical monitoring by periodic laboratory tests)[1]

(C) disseminating information to health care providers through professional societies about any serious risks of the drug and any protocol to assure safe use; or

(D) disseminating information to health care providers about drug formulations or properties, including information about the limitations or patient care implications of such formulations or properties, and how such formulations or properties may be related to serious adverse drug events associated with use of the drug.

(4) Packaging and disposal

The Secretary may require a risk evaluation mitigation strategy for a drug for which there is a serious risk of an adverse drug experience described in subparagraph (B) or (C) of subsection (b)(1), taking into consideration the factors described in subparagraphs (C) and (D) of subsection (f)(2) and in consultation with other relevant Federal agencies with authorities over drug disposal packaging, which may include requiring that—

(A) the drug be made available for dispensing to certain patients in unit dose packaging, packaging that provides a set duration, or another packaging system that the Secretary determines may mitigate such serious risk; or

(B) the drug be dispensed to certain patients with a safe disposal packaging or safe disposal system if the Secretary determines that such safe disposal packaging or system may mitigate such serious risk and is sufficiently available.

(f) Providing safe access for patients to drugs with known serious risks that would otherwise be unavailable

(1) Allowing safe access to drugs with known serious risks

The Secretary, in consultation with the offices described in subsection (c)(2), may require that the risk evaluation and mitigation strategy for a drug include such elements as are necessary to assure safe use of the drug, because of its inherent toxicity or potential harmfulness, if the Secretary determines that—

(A) the drug, which has been shown to be effective, but is associated with a serious adverse drug experience, can be approved only if, or would be withdrawn unless, such elements are required as part of such strategy to mitigate a specific serious risk listed in the labeling of the drug; and

(B) for a drug initially approved without elements to assure safe use, other elements under subsections (c), (d), and (e) are not sufficient to mitigate such serious risk.

(2) Assuring access and minimizing burden

Such elements to assure safe use under paragraph (1) shall—

(A) be commensurate with the specific serious risk listed in the labeling of the drug;

(B) within 30 days of the date on which any element under paragraph (1) is imposed, be posted publicly by the Secretary with an explanation of how such elements will mitigate the observed safety risk;

(C) considering such risk, not be unduly burdensome on patient access to the drug, considering in particular—

(i) patients with serious or life-threatening diseases or conditions;

(ii) patients who have difficulty accessing health care (such as patients in rural or medically underserved areas); and

(iii) patients with functional limitations; and

(D) to the extent practicable, so as to minimize the burden on the health care delivery system—

(i) conform with elements to assure safe use for other drugs with similar, serious risks; and

(ii) be designed to be compatible with established distribution, procurement, and dispensing systems for drugs.

(3) Elements to assure safe use

The elements to assure safe use under paragraph (1) shall include 1 or more goals to mitigate a specific serious risk listed in the labeling of the drug and, to mitigate such risk, may require that—

(A) health care providers who prescribe the drug have particular training or experience, or are specially certified (the opportunity to obtain such training or certification with respect to the drug shall be available to any willing provider from a frontier area in a widely available training or certification method (including an on-line course or via mail) as approved by the Secretary at reasonable cost to the provider);

(B) pharmacies, practitioners, or health care settings that dispense the drug are specially certified (the opportunity to obtain such certification shall be available to any willing provider from a frontier area);

(C) the drug be dispensed to patients only in certain health care settings, such as hospitals;

(D) the drug be dispensed to patients with evidence or other documentation of safe-use conditions, such as laboratory test results;

(E) each patient using the drug be subject to certain monitoring; or

(F) each patient using the drug be enrolled in a registry.

(4) Implementation system

The elements to assure safe use under paragraph (1) that are described in subparagraphs (B), (C), and (D) of paragraph (3) may include a system through which the applicant is able to take reasonable steps to—

(A) monitor and evaluate implementation of such elements by health care providers, pharmacists, and other parties in the health care system who are responsible for implementing such elements; and

(B) work to improve implementation of such elements by such persons.

[1] So in original. Probably should be followed by a semicolon.

(5) Evaluation of elements to assure safe use

The Secretary, through the Drug Safety and Risk Management Advisory Committee (or successor committee) or other advisory committee of the Food and Drug Administration, shall—

(A) seek input from patients, physicians, pharmacists, and other health care providers about how elements to assure safe use under this subsection for 1 or more drugs may be standardized so as not to be—

(i) unduly burdensome on patient access to the drug; and

(ii) to the extent practicable, minimize[2] the burden on the health care delivery system;

(B) periodically evaluate, for 1 or more drugs, the elements to assure safe use of such drug to assess whether the elements—

(i) assure safe use of the drug;

(ii) are not unduly burdensome on patient access to the drug; and

(iii) to the extent practicable, minimize the burden on the health care delivery system; and

(C) considering such input and evaluations—

(i) issue or modify agency guidance about how to implement the requirements of this subsection; and

(ii) modify elements under this subsection for 1 or more drugs as appropriate.

(6) Additional mechanisms to assure access

The mechanisms under section 360bbb of this title to provide for expanded access for patients with serious or life-threatening diseases or conditions may be used to provide access for patients with a serious or life-threatening disease or condition, the treatment of which is not an approved use for the drug, to a drug that is subject to elements to assure safe use under this subsection. The Secretary shall promulgate regulations for how a physician may provide the drug under the mechanisms of section 360bbb of this title.

(7) Repealed. Pub. L. 113–5, title III, § 302(c)(1), Mar. 13, 2013, 127 Stat. 185

(8) Limitation

No holder of an approved covered application shall use any element to assure safe use required by the Secretary under this subsection to block or delay approval of an application under section 355(b)(2) or (j) of this title or to prevent application of such element under subsection (i)(1)(B) to a drug that is the subject of an abbreviated new drug application.

(g) Assessment and modification of approved strategy

(1) Voluntary assessments

After the approval of a risk evaluation and mitigation strategy under subsection (a), the responsible person involved may, subject to paragraph (2), submit to the Secretary an assessment of the approved strategy for the drug involved at any time.

[2] So in original. Does not follow from introductory provisions.

(2) Required assessments

A responsible person shall submit an assessment of the approved risk evaluation and mitigation strategy for a drug—

(A) when submitting a supplemental application for a new indication for use under section 355(b) of this title or under section 262 of title 42, unless the drug is not subject to section 353(b) of this title and the risk evaluation and mitigation strategy for the drug includes only the timetable under subsection (d);

(B) when required by the strategy, as provided for in such timetable under subsection (d);

(C) within a time period to be determined by the Secretary, if the Secretary, in consultation with the offices described in subsection (c)(2), determines that an assessment is needed to evaluate whether the approved strategy should be modified to—

(i) ensure the benefits of the drug outweigh the risks of the drug; or

(ii) minimize the burden on the health care delivery system of complying with the strategy.

(3) Requirements for assessments

An assessment under paragraph (1) or (2) of an approved risk evaluation and mitigation strategy for a drug shall include, with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether 1 or more such goals or such elements should be modified.

(4) Modification

(A) On initiative of responsible person

After the approval of a risk evaluation and mitigation strategy by the Secretary, the responsible person may, at any time, submit to the Secretary a proposal to modify the approved strategy. Such proposal may propose the addition, modification, or removal of any goal or element of the approved strategy and shall include an adequate rationale to support such proposed addition, modification, or removal of any goal or element of the strategy.

(B) On initiative of Secretary

After the approval of a risk evaluation and mitigation strategy by the Secretary, the Secretary may, at any time, require a responsible person to submit a proposed modification to the strategy within 120 days or within such reasonable time as the Secretary specifies, if the Secretary, in consultation with the offices described in subsection (c)(2), determines that 1 or more goals or elements should be added, modified, or removed from the approved strategy to—

(i) ensure the benefits of the drug outweigh the risks of the drug;

(ii) minimize the burden on the health care delivery system of complying with the strategy; or

(iii) accommodate different, comparable aspects of the elements to assure safe use

for a drug that is the subject of an application under section 355(j) of this title, and the applicable listed drug.

(h) Review of proposed strategies; review of assessments and modifications of approved strategies

(1) In general

The Secretary, in consultation with the offices described in subsection (c)(2), shall promptly review each proposed risk evaluation and mitigation strategy for a drug submitted under subsection (a) and each assessment of and proposed modification to an approved risk evaluation and mitigation strategy for a drug submitted under subsection (g), and, if necessary, promptly initiate discussions with the responsible person about such proposed strategy, assessment, or modification.

(2) Action

(A) In general

(i) Timeframe

Unless the dispute resolution process described under paragraph (3) or (4) applies, and, except as provided in clause (ii) or clause (iii) below, the Secretary, in consultation with the offices described in subsection (c)(2), shall review and act on the proposed risk evaluation and mitigation strategy for a drug or any proposed modification to any required strategy within 180 days of receipt of the proposed strategy or modification.

(ii) Minor modifications

The Secretary shall review and act on a proposed minor modification, as defined by the Secretary in guidance, within 60 days of receipt of such modification.

(iii) REMS modification due to safety labeling changes

Not later than 60 days after the Secretary receives a proposed modification to an approved risk evaluation and mitigation strategy to conform the strategy to approved safety labeling changes, including safety labeling changes initiated by the responsible person in accordance with FDA regulatory requirements, or to a safety labeling change that the Secretary has directed the holder of the application to make pursuant to section 355(*o*)(4) of this title, the Secretary shall review and act on such proposed modification to the approved strategy.

(iv) Guidance

The Secretary shall establish, through guidance, that responsible persons may implement certain modifications to an approved risk evaluation and mitigation strategy following notification to the Secretary.

(B) Inaction

An approved risk evaluation and mitigation strategy shall remain in effect until the Secretary acts, if the Secretary fails to act as provided under subparagraph (A).

(C) Public availability

Upon acting on a proposed risk evaluation and mitigation strategy or proposed modification to a risk evaluation and mitigation strategy under subparagraph (A), the Secretary shall make publicly available an action letter describing the actions taken by the Secretary under such subparagraph (A).

(3) Dispute resolution at initial approval

If a proposed risk evaluation and mitigation strategy is submitted under subsection (a)(1) in an application for initial approval of a drug and there is a dispute about the strategy, the responsible person shall use the major dispute resolution procedures as set forth in the letters described in section 101(c) of the Food and Drug Administration Amendments Act of 2007.

(4) Dispute resolution in all other cases

(A) Request for review

(i) In general

The responsible person may, after the sponsor is required to make a submission under subsection (a)(2) or (g), request in writing that a dispute about the strategy be reviewed by the Drug Safety Oversight Board under subsection (j), except that the determination of the Secretary to require a risk evaluation and mitigation strategy is not subject to review under this paragraph. The preceding sentence does not prohibit review under this paragraph of the particular elements of such a strategy.

(ii) Scheduling

Upon receipt of a request under clause (i), the Secretary shall schedule the dispute involved for review under subparagraph (B) and, not later than 5 business days of[3] scheduling the dispute for review, shall publish by posting on the Internet or otherwise a notice that the dispute will be reviewed by the Drug Safety Oversight Board.

(B) Scheduling review

If a responsible person requests review under subparagraph (A), the Secretary—

(i) shall schedule the dispute for review at 1 of the next 2 regular meetings of the Drug Safety Oversight Board, whichever meeting date is more practicable; or

(ii) may convene a special meeting of the Drug Safety Oversight Board to review the matter more promptly, including to meet an action deadline on an application (including a supplemental application).

(C) Agreement after discussion or administrative appeals

(i) Further discussion or administrative appeals

A request for review under subparagraph (A) shall not preclude further discussions to reach agreement on the risk evaluation and mitigation strategy, and such a request shall not preclude the use of administrative appeals within the Food and Drug Administration to reach agreement on the strategy, including appeals as described in the letters described in section 101(c) of the Food and Drug Administration Amend-

[3] So in original.

ments Act of 2007 for procedural or scientific matters involving the review of human drug applications and supplemental applications that cannot be resolved at the divisional level. At the time a review has been scheduled under subparagraph (B) and notice of such review has been posted, the responsible person shall either withdraw the request under subparagraph (A) or terminate the use of such administrative appeals.

(ii) Agreement terminates dispute resolution

At any time before a decision and order is issued under subparagraph (G), the Secretary (in consultation with the offices described in subsection (c)(2)) and the responsible person may reach an agreement on the risk evaluation and mitigation strategy through further discussion or administrative appeals, terminating the dispute resolution process, and the Secretary shall issue an action letter or order, as appropriate, that describes the strategy.

(D) Meeting of the Board

At a meeting of the Drug Safety Oversight Board described in subparagraph (B), the Board shall—

(i) hear from both parties via written or oral presentation; and

(ii) review the dispute.

(E) Record of proceedings

The Secretary shall ensure that the proceedings of any such meeting are recorded, transcribed, and made public within 90 days of the meeting. The Secretary shall redact the transcript to protect any trade secrets and other information that is exempted from disclosure under section 552 of title 5 or section 552a of title 5.

(F) Recommendation of the Board

Not later than 5 days after any such meeting, the Drug Safety Oversight Board shall provide a written recommendation on resolving the dispute to the Secretary. Not later than 5 days after the Board provides such written recommendation to the Secretary, the Secretary shall make the recommendation available to the public.

(G) Action by the Secretary

(i) Action letter

With respect to a proposal or assessment referred to in paragraph (1), the Secretary shall issue an action letter that resolves the dispute not later than the later of—

(I) the action deadline for the action letter on the application; or

(II) 7 days after receiving the recommendation of the Drug Safety Oversight Board.

(ii) Order

With respect to an assessment of an approved risk evaluation and mitigation strategy under subsection (g)(1) or under any of subparagraphs (B) through (D) of subsection (g)(2), the Secretary shall issue an order, which shall be made public, that resolves the dispute not later than 7 days after receiving the recommendation of the Drug Safety Oversight Board.

(H) Inaction

An approved risk evaluation and mitigation strategy shall remain in effect until the Secretary acts, if the Secretary fails to act as provided for under subparagraph (G).

(I) Effect on action deadline

With respect to a proposal or assessment referred to in paragraph (1), the Secretary shall be considered to have met the action deadline for the action letter on the application if the responsible person requests the dispute resolution process described in this paragraph and if the Secretary has complied with the timing requirements of scheduling review by the Drug Safety Oversight Board, providing a written recommendation, and issuing an action letter under subparagraphs (B), (F), and (G), respectively.

(J) Disqualification

No individual who is an employee of the Food and Drug Administration and who reviews a drug or who participated in an administrative appeal under subparagraph (C)(i) with respect to such drug may serve on the Drug Safety Oversight Board at a meeting under subparagraph (D) to review a dispute about the risk evaluation and mitigation strategy for such drug.

(K) Additional expertise

The Drug Safety Oversight Board may add members with relevant expertise from the Food and Drug Administration, including the Office of Pediatrics, the Office of Women's Health, or the Office of Rare Diseases, or from other Federal public health or health care agencies, for a meeting under subparagraph (D) of the Drug Safety Oversight Board.

(5) Use of advisory committees

The Secretary may convene a meeting of 1 or more advisory committees of the Food and Drug Administration to—

(A) review a concern about the safety of a drug or class of drugs, including before an assessment of the risk evaluation and mitigation strategy or strategies of such drug or drugs is required to be submitted under subparagraph (B) or (C) of subsection (g)(2);

(B) review the risk evaluation and mitigation strategy or strategies of a drug or group of drugs; or

(C) review a dispute under paragraph (3) or (4).

(6) Process for addressing drug class effects

(A) In general

When a concern about a serious risk of a drug may be related to the pharmacological class of the drug, the Secretary, in consultation with the offices described in subsection (c)(2), may defer assessments of the approved risk evaluation and mitigation strategies for such drugs until the Secretary has convened 1 or more public meetings to consider possible responses to such concern.

(B) Notice

If the Secretary defers an assessment under subparagraph (A), the Secretary shall—

(i) give notice of the deferral to the holder of the approved covered application not later than 5 days after the deferral;

(ii) publish the deferral in the Federal Register; and

(iii) give notice to the public of any public meetings to be convened under subparagraph (A), including a description of the deferral.

(C) Public meetings

Such public meetings may include—

(i) 1 or more meetings of the responsible person for such drugs;

(ii) 1 or more meetings of 1 or more advisory committees of the Food and Drug Administration, as provided for under paragraph (6);[4] or

(iii) 1 or more workshops of scientific experts and other stakeholders.

(D) Action

After considering the discussions from any meetings under subparagraph (A), the Secretary may—

(i) announce in the Federal Register a planned regulatory action, including a modification to each risk evaluation and mitigation strategy, for drugs in the pharmacological class;

(ii) seek public comment about such action; and

(iii) after seeking such comment, issue an order addressing such regulatory action.

(7) International coordination

The Secretary, in consultation with the offices described in subsection (c)(2), may coordinate the timetable for submission of assessments under subsection (d), or a study or clinical trial under section 355(*o*)(3) of this title, with efforts to identify and assess the serious risks of such drug by the marketing authorities of other countries whose drug approval and risk management processes the Secretary deems comparable to the drug approval and risk management processes of the United States. If the Secretary takes action to coordinate such timetable, the Secretary shall give notice to the responsible person.

(8) Effect

Use of the processes described in paragraphs (6) and (7) shall not be the sole source of delay of action on an application or a supplement to an application for a drug.

(i) Abbreviated new drug applications

(1) In general

A drug that is the subject of an abbreviated new drug application under section 355(j) of this title is subject to only the following elements of the risk evaluation and mitigation strategy required under subsection (a) for the applicable listed drug:

(A) A Medication Guide or patient package insert, if required under subsection (e) for the applicable listed drug.

(B) A packaging or disposal requirement, if required under subsection (e)(4) for the applicable listed drug.

(C)(i) Elements to assure safe use, if required under subsection (f) for the listed drug, which, subject to clause (ii), for a drug that is the subject of an application under section 355(j) of this title may use—

(I) a single, shared system with the listed drug under subsection (f); or

(II) a different, comparable aspect of the elements to assure safe use under subsection (f).

(ii) The Secretary may require a drug that is the subject of an application under section 355(j) of this title and the listed drug to use a single, shared system under subsection (f), if the Secretary determines that no different, comparable aspect of the elements to assure safe use could satisfy the requirements of subsection (f).

(2) Action by Secretary

For an applicable listed drug for which a drug is approved under section 355(j) of this title, the Secretary—

(A) shall undertake any communication plan to health care providers required under subsection (e)(3) for the applicable listed drug;

(B) shall permit packaging systems and safe disposal packaging or safe disposal systems that are different from those required for the applicable listed drug under subsection (e)(4); and

(C) shall inform the responsible person for the drug that is so approved if the risk evaluation and mitigation strategy for the applicable listed drug is modified.

(3) Shared REMS

If the Secretary approves, in accordance with paragraph (1)(C)(i)(II), a different, comparable aspect of the elements to assure safe use under subsection (f) for a drug that is the subject of an abbreviated new drug application under section 355(j) of this title, the Secretary may require that such different comparable aspect of the elements to assure safe use can be used with respect to any other drug that is the subject of an application under section 355(j) or 355(b) of this title that references the same listed drug.

(j) Drug Safety Oversight Board

(1) In general

There is established a Drug Safety Oversight Board.

(2) Composition; meetings

The Drug Safety Oversight Board shall—

(A) be composed of scientists and health care practitioners appointed by the Secretary, each of whom is an employee of the Federal Government;

(B) include representatives from offices throughout the Food and Drug Administration, including the offices responsible for postapproval safety of drugs;

[4] See References in Text note below.

(C) include at least 1 representative each from the National Institutes of Health and the Department of Health and Human Services (other than the Food and Drug Administration);

(D) include such representatives as the Secretary shall designate from other appropriate agencies that wish to provide representatives; and

(E) meet at least monthly to provide oversight and advice to the Secretary on the management of important drug safety issues.

(k) Waiver in public health emergencies

The Secretary may waive any requirement of this section with respect to a qualified countermeasure (as defined in section 247d–6a(a)(2) of title 42) to which a requirement under this section has been applied, if the Secretary determines that such waiver is required to mitigate the effects of, or reduce the severity of, the circumstances under which—

(1) a determination described in subparagraph (A), (B), or (C) of section 360bbb–3(b)(1) of this title has been made by the Secretary of Homeland Security, the Secretary of Defense, or the Secretary, respectively; or

(2) the identification of a material threat described in subparagraph (D) of section 360bbb–3(b)(1) of this title has been made pursuant to section 247d–6b of title 42.

***(l)* Provision of samples not a violation of strategy**

The provision of samples of a covered product to an eligible product developer (as those terms are defined in section 355–2(a) of this title) shall not be considered a violation of the requirements of any risk evaluation and mitigation strategy that may be in place under this section for such drug.

(m) Separate REMS

When used in this section, the term ''different, comparable aspect of the elements to assure safe use'' means a risk evaluation and mitigation strategy for a drug that is the subject of an application under section 355(j) of this title that uses different methods or operational means than the strategy required under subsection (a) for the applicable listed drug, or other application under section 355(j) of this title with the same such listed drug, but achieves the same level of safety as such strategy.

(June 25, 1938, ch. 675, § 505–1, as added Pub. L. 110–85, title IX, § 901(b), Sept. 27, 2007, 121 Stat. 926; amended Pub. L. 112–144, title XI, § 1132(a), (b), July 9, 2012, 126 Stat. 1119, 1120; Pub. L. 113–5, title III, § 302(c), Mar. 13, 2013, 127 Stat. 185; Pub. L. 114–255, div. A, title III, §§ 3075(c), 3101(a)(2)(C), Dec. 13, 2016, 130 Stat. 1139, 1153; Pub. L. 115–52, title VI, § 606, Aug. 18, 2017, 131 Stat. 1049; Pub. L. 115–271, title III, §§ 3032(a)–(c), 3041(a), Oct. 24, 2018, 132 Stat. 3940–3942; Pub. L. 116–94, div. N, title I, § 610(d), (f), Dec. 20, 2019, 133 Stat. 3135, 3136; Pub. L. 117–328, div. FF, title III, § 3221, Dec. 29, 2022, 136 Stat. 5829.)

Editorial Notes

REFERENCES IN TEXT

For the effective date of this section, referred to in subsec. (a)(2)(A), see Effective Date note below.

Section 101(c) of the Food and Drug Administration Amendments Act of 2007, referred to in subsec. (h)(3), (4)(C)(i), is section 101(c) of Pub. L. 110–85, which is set out as a note under section 379g of this title.

Paragraph (6), referred to in subsec. (h)(6)(C)(ii), was redesignated par. (5) of subsec. (h) of this section by Pub. L. 112–144, title XI, § 1132(b)(4), July 9, 2012, 126 Stat. 1120.

AMENDMENTS

2022—Subsec. (e)(4)(B). Pub. L. 117–328 struck out ''for purposes of rendering drugs nonretrievable (as defined in section 1300.05 of title 21, Code of Federal Regulations (or any successor regulation))'' before ''if the Secretary determines''.

2019—Subsec. (g)(4)(B)(iii). Pub. L. 116–94, § 610(f)(1), added cl. (iii).

Subsec. (i)(1)(C). Pub. L. 116–94, § 610(f)(2), added subpar. (C) and struck out former subpar. (C) which read as follows: ''Elements to assure safe use, if required under subsection (f) for the listed drug. A drug that is the subject of an abbreviated new drug application and the listed drug shall use a single, shared system under subsection (f). The Secretary may waive the requirement under the preceding sentence for a drug that is the subject of an abbreviated new drug application, and permit the applicant to use a different, comparable aspect of the elements to assure safe use, if the Secretary determines that—

''(i) the burden of creating a single, shared system outweighs the benefit of a single, system, taking into consideration the impact on health care providers, patients, the applicant for the abbreviated new drug application, and the holder of the reference drug product; or

''(ii) an aspect of the elements to assure safe use for the applicable listed drug is claimed by a patent that has not expired or is a method or process that, as a trade secret, is entitled to protection, and the applicant for the abbreviated new drug application certifies that it has sought a license for use of an aspect of the elements to assure safe use for the applicable listed drug and that it was unable to obtain a license.

A certification under clause (ii) shall include a description of the efforts made by the applicant for the abbreviated new drug application to obtain a license. In a case described in clause (ii), the Secretary may seek to negotiate a voluntary agreement with the owner of the patent, method, or process for a license under which the applicant for such abbreviated new drug application may use an aspect of the elements to assure safe use, if required under subsection (f) for the applicable listed drug, that is claimed by a patent that has not expired or is a method or process that as a trade secret is entitled to protection.''

Subsec. (i)(3). Pub. L. 116–94, § 610(f)(3), added par. (3).

Subsec. (*l*). Pub. L. 116–94, § 610(d), added subsec. (*l*).

Subsec. (m). Pub. L. 116–94, § 610(f)(4), added subsec. (m).

2018—Subsec. (b)(1)(E). Pub. L. 115–271, § 3041(a), substituted ''of the drug, which may include reduced effectiveness under the conditions of use prescribed in the labeling of such drug, but which may not include reduced effectiveness that is in accordance with such labeling'' for ''of the drug''.

Subsec. (e)(4). Pub. L. 115–271, § 3032(a), added par. (4).

Subsec. (f)(2)(C)(iii). Pub. L. 115–271, § 3032(b), added cl. (iii).

Subsec. (i)(1)(B), (C). Pub. L. 115–271, § 3032(c)(1), added subpar. (B) and redesignated former subpar. (B) as (C).

Subsec. (i)(2)(B), (C). Pub. L. 115–271, § 3032(c)(2), added subpar. (B) and redesignated former subpar. (B) as (C).

2017—Subsec. (e)(3)(B). Pub. L. 115–52, § 606(1), struck out ''; or'' at end.

Subsec. (e)(3)(D). Pub. L. 115–52, § 606(2), (3), added subpar. (D).

2016—Subsec. (f)(5). Pub. L. 114–255, § 3075(c)(1), inserted ''or other advisory committee'' after ''(or successor committee)'' in introductory provisions.

Subsec. (f)(5)(B). Pub. L. 114–255, § 3075(c)(2), substituted ''periodically'' for ''at least annually,'' in introductory provisions.

Subsec. (h)(2)(A)(iii). Pub. L. 114–255, §3101(a)(2)(C)(i), substituted, in heading, ''labeling'' for ''label'' and in text, ''approved safety labeling changes'' for ''approved safety label changes'', ''responsible person'' for ''sponsor'', and ''a safety labeling change'' for ''a safety label change''.

Subsec. (h)(8). Pub. L. 114–255, §3101(a)(2)(C)(ii), struck out period after ''(7)''.

2013—Subsec. (f)(7). Pub. L. 113–5, §302(c)(1), struck out par. (7) which related to waiver of subsec. (f) requirements in public health emergencies.

Subsec. (k). Pub. L. 113–5, §302(c)(2), added subsec. (k).

2012—Subsec. (g)(1). Pub. L. 112–144, §1132(a)(1), struck out '', and propose a modification to,'' after ''an assessment of''.

Subsec. (g)(2). Pub. L. 112–144, §1132(a)(2)(A), in introductory provisions, struck out '', subject to paragraph (5),'' after ''shall'' and '', and may propose a modification to,'' after ''an assessment of''.

Subsec. (g)(2)(C). Pub. L. 112–144, §1132(a)(2)(B), substituted ''an assessment is needed to evaluate whether the approved strategy should be modified to—'' and cls. (i) and (ii) for ''new safety or effectiveness information indicates that—

''(i) an element under subsection (d) or (e) should be modified or included in the strategy; or

''(ii) an element under subsection (f) should be modified or included in the strategy; or''.

Subsec. (g)(2)(D). Pub. L. 112–144, §1132(a)(2)(C), struck out subpar. (D) which read as follows: ''within 15 days when ordered by the Secretary, in consultation with the offices described in subsection (c)(2), if the Secretary determines that there may be a cause for action by the Secretary under section 355(e) of this title.''

Subsec. (g)(3). Pub. L. 112–144, §1132(a)(3), substituted ''for a drug shall include, with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether 1 or more such goals or such elements should be modified.'' for ''for a drug shall include—'' and struck out subpars. (A) to (C) which related to assessment of elements to assure safe use, postapproval studies, and postapproval clinical trials.

Subsec. (g)(4). Pub. L. 112–144, §1132(a)(4), amended par. (4) generally. Prior to amendment, text read as follows: ''A modification (whether an enhancement or a reduction) to the approved risk evaluation and mitigation strategy for a drug may include the addition or modification of any element under subsection (d) or the addition, modification, or removal of any element under subsection (e) or (f), such as—

''(A) modifying the timetable for assessments of the strategy as provided in subsection (d)(3), including to eliminate assessments; or

''(B) adding, modifying, or removing an element to assure safe use under subsection (f).''

Subsec. (h). Pub. L. 112–144, §1132(b)(1), inserted ''and modifications'' after ''review of assessments'' in heading.

Subsec. (h)(1). Pub. L. 112–144, §1132(b)(2), inserted ''and proposed modification to'' after ''under subsection (a) and each assessment of'' and '', and, if necessary, promptly initiate discussions with the responsible person about such proposed strategy, assessment, or modification'' after ''subsection (g)''.

Subsec. (h)(2). Pub. L. 112–144, §1132(b)(3), (4), redesignated par. (3) as (2) and struck out former par. (2). Prior to amendment, text of par. (2) read as follows: ''The Secretary, in consultation with the offices described in subsection (c)(2), shall initiate discussions with the responsible person for purposes of this subsection to determine a strategy not later than 60 days after any such assessment is submitted or, in the case of an assessment submitted under subsection (g)(2)(D), not later than 30 days after such assessment is submitted.''

Subsec. (h)(2)(A). Pub. L. 112–144, §1132(b)(5)(A), amended subpar. (A) generally. Prior to amendment, subpar. (A) related to Secretary's description of any required risk evaluation and mitigation strategy for a drug as part of the action letter on the application or in an order.

Subsec. (h)(2)(C). Pub. L. 112–144, §1132(b)(5)(B), amended subpar. (C) generally. Prior to amendment, text read as follows: ''Any action letter described in subparagraph (A)(i) or order described in subparagraph (A)(ii) shall be made publicly available.''

Subsec. (h)(3), (4). Pub. L. 112–144, §1132(b)(4), redesignated pars. (4) and (5) as (3) and (4), respectively. Former par. (3) redesignated (2).

Subsec. (h)(4)(A)(i). Pub. L. 112–144, §1132(b)(6)(A), substituted ''The responsible'' for ''Not earlier than 15 days, and not later than 35 days, after discussions under paragraph (2) have begun, the responsible'' and inserted '', after the sponsor is required to make a submission under subsection (a)(2) or (g),'' before ''request in writing''.

Subsec. (h)(4)(I). Pub. L. 112–144, §1132(b)(6)(B), substituted ''if the Secretary has complied with the timing requirements of scheduling review by the Drug Safety Oversight Board, providing a written recommendation, and issuing an action letter under subparagraphs (B), (F), and (G), respectively.'' for ''if the Secretary—'' and struck out cls. (i) and (ii) which read as follows:

''(i) has initiated the discussions described under paragraph (2) not less than 60 days before such action deadline; and

''(ii) has complied with the timing requirements of scheduling review by the Drug Safety Oversight Board, providing a written recommendation, and issuing an action letter under subparagraphs (B), (F), and (G), respectively.''

Subsec. (h)(5). Pub. L. 112–144, §1132(b)(4), (7), redesignated par. (6) as (5) and substituted ''subparagraph (B) or (C)'' for ''any of subparagraphs (B) through (D)'' in subpar. (A) and ''paragraph (3) or (4)'' for ''paragraph (4) or (5)'' in subpar. (C). Former par. (5) redesignated (4).

Subsec. (h)(6), (7). Pub. L. 112–144, §1132(b)(4), redesignated pars. (7) and (8) as (6) and (7), respectively. Former par. (6) redesignated (5).

Subsec. (h)(8), (9). Pub. L. 112–144, §1132(b)(4), (8), redesignated par. (9) as (8) and substituted ''paragraphs (6) and (7).'' for ''paragraphs (7) and (8)''. Former par. (8) redesignated (7).

Statutory Notes and Related Subsidiaries

Effective Date

Section effective 180 days after Sept. 27, 2007, see section 909 of Pub. L. 110–85, set out as an Effective Date of 2007 Amendment note under section 331 of this title.

Evidence-Based Opioid Analgesic Prescribing Guidelines and Report

Pub. L. 115–271, title III, §3002, Oct. 24, 2018, 132 Stat. 3934, provided that:

''(a) Guidelines.—The Commissioner of Food and Drugs shall develop evidence-based opioid analgesic prescribing guidelines for the indication-specific treatment of acute pain only for the relevant therapeutic areas where such guidelines do not exist.

''(b) Public Input.—In developing the guidelines under subsection (a), the Commissioner of Food and Drugs shall—

''(1) consult with stakeholders, which may include conducting a public meeting of medical professional societies (including any State-based societies), health care providers, State medical boards, medical specialties including pain medicine specialty societies, patient groups, pharmacists, academic or medical research entities, and other entities with experience in health care, as appropriate;

''(2) collaborate with the Director of the Centers for Disease Control and Prevention, as applicable and appropriate, and other Federal agencies with relevant expertise as appropriate; and

''(3) provide for a notice and comment period consistent with section 701(h) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 371(h)) for the submission of comments by the public.

''(c) REPORT.—Not later than 1 year after the date of enactment of this Act [Oct. 24, 2018], or, if earlier, at the time the guidelines under subsection (a) are finalized, the Commissioner of Food and Drugs shall submit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate, and post on the public website of the Food and Drug Administration, a report on how the Food and Drug Administration will utilize the guidelines under subsection (a) to protect the public health and a description of the public health need with respect to each such indication-specific treatment guideline.

''(d) UPDATES.—The Commissioner of Food and Drugs shall periodically—

''(1) update the guidelines under subsection (a), informed by public input described in subsection (b); and

''(2) submit to the committees specified in subsection (c) and post on the public website of the Food and Drug Administration an updated report under such subsection.

''(e) STATEMENT TO ACCOMPANY GUIDELINES AND RECOMMENDATIONS.—The Commissioner of Food and Drugs shall ensure that opioid analgesic prescribing guidelines and other recommendations developed under this section are accompanied by a clear statement that such guidelines or recommendations, as applicable—

''(1) are intended to help inform clinical decision-making by prescribers and patients; and

''(2) are not intended to be used for the purposes of restricting, limiting, delaying, or denying coverage for, or access to, a prescription issued for a legitimate medical purpose by an individual practitioner acting in the usual course of professional practice.''

PRESCRIBER EDUCATION

Pub. L. 114–198, title I, §106(b), July 22, 2016, 130 Stat. 703, provided that: ''Not later than 1 year after the date of the enactment of this Act [July 22, 2016], the Secretary [of Health and Human Services], acting through the Commissioner of Food and Drugs, as part of the Food and Drug Administration's evaluation of the Extended-Release/Long-Acting Opioid Analgesics Risk Evaluation and Mitigation Strategy, and in consultation with relevant stakeholders, shall develop recommendations regarding education programs for prescribers of opioids pursuant to section 505–1 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355–1), including recommendations on—

''(1) which prescribers should participate in such programs; and

''(2) how often participation in such programs is necessary.''

GUIDANCE

Pub. L. 112–144, title XI, §1132(c), July 9, 2012, 126 Stat. 1122, provided that: ''Not later than 1 year after the date of enactment of this Act [July 9, 2012], the Secretary of Health and Human Services shall issue guidance that, for purposes of section 505–1(h)(2)(A) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355–1(h)(2)(A)), describes the types of modifications to approved risk evaluation and mitigation strategies that shall be considered to be minor modifications of such strategies.''

§ 355–2. Actions for delays of generic drugs and biosimilar biological products

(a) Definitions

In this section—

(1) the term ''commercially reasonable, market-based terms'' means—

(A) a nondiscriminatory price for the sale of the covered product at or below, but not greater than, the most recent wholesale acquisition cost for the drug, as defined in section 1395w–3a(c)(6)(B) of title 42;

(B) a schedule for delivery that results in the transfer of the covered product to the eligible product developer consistent with the timing under subsection (b)(2)(A)(iv); and

(C) no additional conditions are imposed on the sale of the covered product;

(2) the term ''covered product''—

(A) means—

(i) any drug approved under subsection (c) or (j) of section 355 of this title or biological product licensed under subsection (a) or (k) of section 262 of title 42;

(ii) any combination of a drug or biological product described in clause (i); or

(iii) when reasonably necessary to support approval of an application under section 355 of this title, or section 262 of title 42, as applicable, or otherwise meet the requirements for approval under either such section, any product, including any device, that is marketed or intended for use with such a drug or biological product; and

(B) does not include any drug or biological product that appears on the drug shortage list in effect under section 356e of this title, unless—

(i) the drug or biological product has been on the drug shortage list in effect under such section 356e of this title continuously for more than 6 months; or

(ii) the Secretary determines that inclusion of the drug or biological product as a covered product is likely to contribute to alleviating or preventing a shortage.

(3) the term ''device'' has the meaning given the term in section 321 of this title;

(4) the term ''eligible product developer'' means a person that seeks to develop a product for approval pursuant to an application for approval under subsection (b)(2) or (j) of section 355 of this title or for licensing pursuant to an application under section 262(k) of title 42;

(5) the term ''license holder'' means the holder of an application approved under subsection (c) or (j) of section 355 of this title or the holder of a license under subsection (a) or (k) of section 262 of title 42 for a covered product;

(6) the term ''REMS'' means a risk evaluation and mitigation strategy under section 355–1 of this title;

(7) the term ''REMS with ETASU'' means a REMS that contains elements to assure safe use under section 355–1(f) of this title;

(8) the term ''Secretary'' means the Secretary of Health and Human Services;

(9) the term ''single, shared system of elements to assure safe use'' means a single, shared system of elements to assure safe use under section 355–1(f) of this title; and

(10) the term ''sufficient quantities'' means an amount of a covered product that the eligible product developer determines allows it to—

(A) conduct testing to support an application under—

(i) subsection (b)(2) or (j) of section 355 of this title; or

(ii) section 262(k) of title 42; and

(B) fulfill any regulatory requirements relating to approval of such an application.

(b) Civil action for failure to provide sufficient quantities of a covered product

(1) In general

An eligible product developer may bring a civil action against the license holder for a covered product seeking relief under this subsection in an appropriate district court of the United States alleging that the license holder has declined to provide sufficient quantities of the covered product to the eligible product developer on commercially reasonable, market-based terms.

(2) Elements

(A) In general

To prevail in a civil action brought under paragraph (1), an eligible product developer shall prove, by a preponderance of the evidence—

(i) that—

(I) the covered product is not subject to a REMS with ETASU; or

(II) if the covered product is subject to a REMS with ETASU—

(aa) the eligible product developer has obtained a covered product authorization from the Secretary in accordance with subparagraph (B); and

(bb) the eligible product developer has provided a copy of the covered product authorization to the license holder;

(ii) that, as of the date on which the civil action is filed, the eligible product developer has not obtained sufficient quantities of the covered product on commercially reasonable, market-based terms;

(iii) that the eligible product developer has submitted a written request to purchase sufficient quantities of the covered product to the license holder, and such request—

(I) was sent to a named corporate officer of the license holder;

(II) was made by certified or registered mail with return receipt requested;

(III) specified an individual as the point of contact for the license holder to direct communications related to the sale of the covered product to the eligible product developer and a means for electronic and written communications with that individual; and

(IV) specified an address to which the covered product was to be shipped upon reaching an agreement to transfer the covered product; and

(iv) that the license holder has not delivered to the eligible product developer sufficient quantities of the covered product on commercially reasonable, market-based terms—

(I) for a covered product that is not subject to a REMS with ETASU, by the date that is 31 days after the date on which the license holder received the request for the covered product; and

(II) for a covered product that is subject to a REMS with ETASU, by 31 days after the later of—

(aa) the date on which the license holder received the request for the covered product; or

(bb) the date on which the license holder received a copy of the covered product authorization issued by the Secretary in accordance with subparagraph (B).

(B) Authorization for covered product subject to a REMS with ETASU

(i) Request

An eligible product developer may submit to the Secretary a written request for the eligible product developer to be authorized to obtain sufficient quantities of an individual covered product subject to a REMS with ETASU.

(ii) Authorization

Not later than 120 days after the date on which a request under clause (i) is received, the Secretary shall, by written notice, authorize the eligible product developer to obtain sufficient quantities of an individual covered product subject to a REMS with ETASU for purposes of—

(I) development and testing that does not involve human clinical trials, if the eligible product developer has agreed to comply with any conditions the Secretary determines necessary; or

(II) development and testing that involves human clinical trials, if the eligible product developer has—

(aa)(AA) submitted protocols, informed consent documents, and informational materials for testing that include protections that provide safety protections comparable to those provided by the REMS for the covered product; or

(BB) otherwise satisfied the Secretary that such protections will be provided; and

(bb) met any other requirements the Secretary may establish.

(iii) Notice

A covered product authorization issued under this subparagraph shall state that the provision of the covered product by the license holder under the terms of the authorization will not be a violation of the REMS for the covered product.

(3) Affirmative defense

In a civil action brought under paragraph (1), it shall be an affirmative defense, on which the defendant has the burden of persuasion by a preponderance of the evidence—

(A) that, on the date on which the eligible product developer requested to purchase sufficient quantities of the covered product from the license holder—

(i) neither the license holder nor any of its agents, wholesalers, or distributors was engaged in the manufacturing or commercial marketing of the covered product; and

(ii) neither the license holder nor any of its agents, wholesalers, or distributors otherwise had access to inventory of the covered product to supply to the eligible product developer on commercially reasonable, market-based terms;

(B) that—

(i) the license holder sells the covered product through agents, distributors, or wholesalers;

(ii) the license holder has placed no restrictions, explicit or implicit, on its agents, distributors, or wholesalers to sell covered products to eligible product developers; and

(iii) the covered product can be purchased by the eligible product developer in sufficient quantities on commercially reasonable, market-based terms from the agents, distributors, or wholesalers of the license holder; or

(C) that the license holder made an offer to the individual specified pursuant to paragraph (2)(A)(iii)(III), by a means of communication (electronic, written, or both) specified pursuant to such paragraph, to sell sufficient quantities of the covered product to the eligible product developer at commercially reasonable market-based terms—

(i) for a covered product that is not subject to a REMS with ETASU, by the date that is 14 days after the date on which the license holder received the request for the covered product, and the eligible product developer did not accept such offer by the date that is 7 days after the date on which the eligible product developer received such offer from the license holder; or

(ii) for a covered product that is subject to a REMS with ETASU, by the date that is 20 days after the date on which the license holder received the request for the covered product, and the eligible product developer did not accept such offer by the date that is 10 days after the date on which the eligible product developer received such offer from the license holder.

(4) Remedies

(A) In general

If an eligible product developer prevails in a civil action brought under paragraph (1), the court shall—

(i) order the license holder to provide to the eligible product developer without delay sufficient quantities of the covered product on commercially reasonable, market-based terms;

(ii) award to the eligible product developer reasonable attorney's fees and costs of the civil action; and

(iii) award to the eligible product developer a monetary amount sufficient to deter the license holder from failing to provide eligible product developers with sufficient quantities of a covered product on commercially reasonable, market-based terms, if the court finds, by a preponderance of the evidence—

(I) that the license holder delayed providing sufficient quantities of the covered product to the eligible product developer without a legitimate business justification; or

(II) that the license holder failed to comply with an order issued under clause (i).

(B) Maximum monetary amount

A monetary amount awarded under subparagraph (A)(iii) shall not be greater than the revenue that the license holder earned on the covered product during the period—

(i) beginning on—

(I) for a covered product that is not subject to a REMS with ETASU, the date that is 31 days after the date on which the license holder received the request; or

(II) for a covered product that is subject to a REMS with ETASU, the date that is 31 days after the later of—

(aa) the date on which the license holder received the request; or

(bb) the date on which the license holder received a copy of the covered product authorization issued by the Secretary in accordance with paragraph (2)(B); and

(ii) ending on the date on which the eligible product developer received sufficient quantities of the covered product.

(C) Avoidance of delay

The court may issue an order under subparagraph (A)(i) before conducting further proceedings that may be necessary to determine whether the eligible product developer is entitled to an award under clause (ii) or (iii) of subparagraph (A), or the amount of any such award.

(c) Limitation of liability

A license holder for a covered product shall not be liable for any claim under Federal, State, or local law arising out of the failure of an eligible product developer to follow adequate safeguards to assure safe use of the covered product during development or testing activities described in this section, including transportation, handling, use, or disposal of the covered product by the eligible product developer.

(d) Omitted

(e) Rule of construction

(1) Definition

In this subsection, the term ''antitrust laws''—

(A) has the meaning given the term in subsection (a) of section 12 of title 15; and

(B) includes section 45 of title 15 to the extent that such section applies to unfair methods of competition.

(2) Antitrust laws

Nothing in this section shall be construed to limit the operation of any provision of the antitrust laws.

(f) Omitted

(g) Rule of construction

Nothing in this section, the amendments made by this section, or in section 355–1 of this title, shall be construed as—

(1) prohibiting a license holder from providing an eligible product developer access to a covered product in the absence of an authorization under this section; or

(2) in any way negating the applicability of a REMS with ETASU, as otherwise required under such section 355–1 of this title, with respect to such covered product.

(Pub. L. 116–94, div. N, title I, § 610, Dec. 20, 2019, 133 Stat. 3130.)

Editorial Notes

CODIFICATION

Section was enacted as part of the Further Consolidated Appropriations Act, 2020, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

Section is comprised of section 610 of Pub. L. 116–94. Subsecs. (d) and (f) of section 610 of Pub. L. 116–94 amended section 355–1 of this title.

§ 355a. Pediatric studies of drugs

(a) Definitions

As used in this section, the term ''pediatric studies'' or ''studies'' means at least one clinical investigation (that, at the Secretary's discretion, may include pharmacokinetic studies) in pediatric age groups (including neonates in appropriate cases) in which a drug is anticipated to be used, and, at the discretion of the Secretary, may include preclinical studies.

(b) Market exclusivity for new drugs

(1) In general

Except as provided in paragraph (2), if, prior to approval of an application that is submitted under section 355(b)(1) of this title, the Secretary determines that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, the Secretary makes a written request for pediatric studies (which shall include a timeframe for completing such studies), the applicant agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with subsection (d)(4)—

(A)(i)(I) the period referred to in subsection (c)(3)(E)(ii) of section 355 of this title, and in subsection (j)(5)(F)(ii) of such section, is deemed to be five years and six months rather than five years, and the references in subsections (c)(3)(E)(ii) and (j)(5)(F)(ii) of such section to four years, to forty-eight months, and to seven and one-half years are deemed to be four and one-half years, fifty-four months, and eight years, respectively; or

(II) the period referred to in clauses (iii) and (iv) of subsection (c)(3)(E) of such section, and in clauses (iii) and (iv) of subsection (j)(5)(F) of such section, is deemed to be three years and six months rather than three years; and

(ii) if the drug is designated under section 360bb of this title for a rare disease or condition, the period referred to in section 360cc(a) of this title is deemed to be seven years and six months rather than seven years; and

(B)(i) if the drug is the subject of—

(I) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 355 of this title and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

(II) a listed patent for which a certification has been submitted under subsections (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 355 of this title,

the period during which an application may not be approved under section 355(c)(3) of this title or section 355(j)(5)(B) of this title shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

(ii) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 355 of this title, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 355(c)(3) of this title or section 355(j)(5)(B) of this title shall be extended by a period of six months after the date the patent expires (including any patent extensions).

(2) Exception

The Secretary shall not extend the period referred to in paragraph (1)(A) or (1)(B) if the determination made under subsection (d)(4) is made later than 9 months prior to the expiration of such period.

(c) Market exclusivity for already-marketed drugs

(1) In general

Except as provided in paragraph (2), if the Secretary determines that information relating to the use of an approved drug in the pediatric population may produce health benefits in that population and makes a written request to the holder of an approved application under section 355(b)(1) of this title for pediatric studies (which shall include a timeframe for completing such studies), the holder agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with subsection (d)(4)—

(A)(i)(I) the period referred to in subsection (c)(3)(E)(ii) of section 355 of this title, and in subsection (j)(5)(F)(ii) of such section, is deemed to be five years and six months rather than five years, and the references in subsections (c)(3)(E)(ii) and (j)(5)(F)(ii) of such section to four years, to forty-eight months, and to seven and one-half years are deemed to be four and one-half years, fifty-four months, and eight years, respectiv ely; or

(II) the period referred to in clauses (iii) and (iv) of subsection (c)(3)(E) of such sec-

tion, and in clauses (iii) and (iv) of subsection (j)(5)(F) of such section, is deemed to be three years and six months rather than three years; and

(ii) if the drug is designated under section 360bb of this title for a rare disease or condition, the period referred to in section 360cc(a) of this title is deemed to be seven years and six months rather than seven years; and

(B)(i) if the drug is the subject of—

(I) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 355 of this title and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

(II) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 355 of this title,

the period during which an application may not be approved under section 355(c)(3) of this title or section 355(j)(5)(B)(ii) of this title shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

(ii) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 355 of this title, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 355(c)(3) of this title or section 355(j)(5)(B) of this title shall be extended by a period of six months after the date the patent expires (including any patent extensions).

(2) Exception

The Secretary shall not extend the period referred to in paragraph (1)(A) or (1)(B) if the determination made under subsection (d)(4) is made later than 9 months prior to the expiration of such period.

(d) Conduct of pediatric studies

(1) Request for studies

(A) In general

The Secretary may, after consultation with the sponsor of an application for an investigational new drug under section 355(i) of this title, the sponsor of an application for a new drug under section 355(b)(1) of this title, or the holder of an approved application for a drug under section 355(b)(1) of this title, issue to the sponsor or holder a written request for the conduct of pediatric studies for such drug. In issuing such request, the Secretary shall take into account adequate representation of children of ethnic and racial minorities. Such request to conduct pediatric studies shall be in writing and shall include a timeframe for such studies and a request to the sponsor or holder to propose pediatric labeling resulting from such studies. If a request under this subparagraph does not request studies in neonates, such request shall include a statement describing the rationale for not requesting studies in neonates.

(B) Single written request

A single written request—

(i) may relate to more than one use of a drug; and

(ii) may include uses that are both approved and unapproved.

(2) Written request for pediatric studies

(A) Request and response

(i) In general

If the Secretary makes a written request for pediatric studies (including neonates, as appropriate) under subsection (b) or (c), the applicant or holder, not later than 180 days after receiving the written request, shall respond to the Secretary as to the intention of the applicant or holder to act on the request by—

(I) indicating when the pediatric studies will be initiated, if the applicant or holder agrees to the request; or

(II) indicating that the applicant or holder does not agree to the request and stating the reasons for declining the request.

(ii) Disagree with request

If, on or after September 27, 2007, the applicant or holder does not agree to the request on the grounds that it is not possible to develop the appropriate pediatric formulation, the applicant or holder shall submit to the Secretary the reasons such pediatric formulation cannot be developed.

(B) Adverse event reports

An applicant or holder that, on or after September 27, 2007, agrees to the request for such studies shall provide the Secretary, at the same time as the submission of the reports of such studies, with all postmarket adverse event reports regarding the drug that is the subject of such studies and are available prior to submission of such reports.

(3) Action on submissions

The Secretary shall review and act upon a submission by a sponsor or holder of a proposed pediatric study request or a proposed amendment to a written request for pediatric studies within 120 calendar days of the submission.

(4) Meeting the studies requirement

Not later than 180 days after the submission of the reports of the studies, the Secretary shall accept or reject such reports and so notify the sponsor or holder. The Secretary's only responsibility in accepting or rejecting the reports shall be to determine, within the 180-day period, whether the studies fairly respond to the written request, have been conducted in accordance with commonly accepted scientific principles and protocols, and have been reported in accordance with the requirements of the Secretary for filing.

(5) Effect of subsection

Nothing in this subsection alters or amends section 331(j) of this title or section 552 of title 5 or section 1905 of title 18.

(6) Consultation

With respect to a drug that is a qualified countermeasure (as defined in section 247d–6a of title 42), a security countermeasure (as defined in section 247d–6b of title 42), or a qualified pandemic or epidemic product (as defined in section 247d–6d of title 42), the Secretary shall solicit input from the Assistant Secretary for Preparedness and Response regarding the need for and, from the Director of the Biomedical Advanced Research and Development Authority regarding the conduct of, pediatric studies under this section.

(e) Notice of determinations on studies requirement

(1) In general

The Secretary shall publish a notice of any determination, made on or after September 27, 2007, that the requirements of subsection (d) have been met and that submissions and approvals under subsection (b)(2) or (j) of section 355 of this title for a drug will be subject to the provisions of this section. Such notice shall be published not later than 30 days after the date of the Secretary's determination regarding market exclusivity and shall include a copy of the written request made under subsection (b) or (c).

(2) Identification of certain drugs

The Secretary shall publish a notice identifying any drug for which, on or after September 27, 2007, a pediatric formulation was developed, studied, and found to be safe and effective in the pediatric population (or specified subpopulation) if the pediatric formulation for such drug is not introduced onto the market within one year after the date that the Secretary publishes the notice described in paragraph (1). Such notice identifying such drug shall be published not later than 30 days after the date of the expiration of such one year period.

(f) Internal review of written requests and pediatric studies

(1) Internal review

The Secretary shall utilize the internal review committee established under section 355d of this title to review all written requests issued on or after September 27, 2007, in accordance with paragraph (2).

(2) Review of written requests

The committee referred to in paragraph (1) shall review all written requests issued pursuant to this section prior to being issued.

(3) Review of pediatric studies

The committee referred to in paragraph (1) may review studies conducted pursuant to this section to make a recommendation to the Secretary whether to accept or reject such reports under subsection (d)(4).

(4) Activity by committee

The committee referred to in paragraph (1) may operate using appropriate members of such committee and need not convene all members of the committee.

(5) Documentation of committee action

For each drug, the committee referred to in paragraph (1) shall document, for each activity described in paragraph (2) or (3), which members of the committee participated in such activity.

(6) Tracking pediatric studies and labeling changes

The Secretary, in consultation with the committee referred to in paragraph (1), shall track and make available to the public, in an easily accessible manner, including through posting on the Web site of the Food and Drug Administration—

(A) the number of studies conducted under this section and under section 284m of title 42;

(B) the specific drugs and drug uses, including labeled and off-labeled indications, studied under such sections;

(C) the types of studies conducted under such sections, including trial design, the number of pediatric patients studied, and the number of centers and countries involved;

(D) the number of pediatric formulations developed and the number of pediatric formulations not developed and the reasons such formulations were not developed;

(E) the labeling changes made as a result of studies conducted under such sections;

(F) an annual summary of labeling changes made as a result of studies conducted under such sections for distribution pursuant to subsection (k)(2); and

(G) information regarding reports submitted on or after September 27, 2007.

(7) Informing internal review committee

The Secretary shall provide to the committee referred to in paragraph (1) any response issued to an applicant or holder with respect to a proposed pediatric study request.

(g) Limitations

Notwithstanding subsection (c)(2), a drug to which the six-month period under subsection (b) or (c) has already been applied—

(1) may receive an additional six-month period under subsection (c)(1)(A)(i)(II) for a supplemental application if all other requirements under this section are satisfied, except that such drug may not receive any additional such period under subsection (c)(1)(B); and

(2) may not receive any additional such period under subsection (c)(1)(A)(ii).

(h) Relationship to pediatric research requirements

Exclusivity under this section shall only be granted for the completion of a study or studies that are the subject of a written request and for which reports are submitted and accepted in accordance with subsection (d)(4). Written requests under this section may consist of a study or studies required under section 355c of this title.

(i) Labeling changes

(1) Priority status for pediatric applications and supplements

Any application or supplement to an application under section 355 of this title proposing a labeling change as a result of any pediatric study conducted pursuant to this section—

(A) shall be considered to be a priority application or supplement; and

(B) shall be subject to the performance goals established by the Commissioner for priority drugs.

(2) Dispute resolution

(A) Request for labeling change and failure to agree

If, on or after September 27, 2007, the Commissioner determines that the sponsor and the Commissioner have been unable to reach agreement on appropriate changes to the labeling for the drug that is the subject of the application, not later than 180 days after the date of submission of the application—

(i) the Commissioner shall request that the sponsor of the application make any labeling change that the Commissioner determines to be appropriate; and

(ii) if the sponsor of the application does not agree within 30 days after the Commissioner's request to make a labeling change requested by the Commissioner, the Commissioner shall refer the matter to the Pediatric Advisory Committee.

(B) Action by the Pediatric Advisory Committee

Not later than 90 days after receiving a referral under subparagraph (A)(ii), the Pediatric Advisory Committee shall—

(i) review the pediatric study reports; and

(ii) make a recommendation to the Commissioner concerning appropriate labeling changes, if any.

(C) Consideration of recommendations

The Commissioner shall consider the recommendations of the Pediatric Advisory Committee and, if appropriate, not later than 30 days after receiving the recommendation, make a request to the sponsor of the application to make any labeling change that the Commissioner determines to be appropriate.

(D) Misbranding

If the sponsor of the application, within 30 days after receiving a request under subparagraph (C), does not agree to make a labeling change requested by the Commissioner, the Commissioner may deem the drug that is the subject of the application to be misbranded.

(E) No effect on authority

Nothing in this subsection limits the authority of the United States to bring an enforcement action under this chapter when a drug lacks appropriate pediatric labeling. Neither course of action (the Pediatric Advisory Committee process or an enforcement action referred to in the preceding sentence) shall preclude, delay, or serve as the basis to stay the other course of action.

(j) Other labeling changes

If, on or after September 27, 2007, the Secretary determines that a pediatric study conducted under this section does or does not demonstrate that the drug that is the subject of the study is safe and effective, including whether such study results are inconclusive, in pediatric populations or subpopulations, the Secretary shall order the labeling of such product to include information about the results of the study and a statement of the Secretary's determination.

(k) Dissemination of pediatric information

(1) In general

Not later than 210 days after the date of submission of a report on a pediatric study under this section, the Secretary shall make available to the public the medical, statistical, and clinical pharmacology reviews of pediatric studies conducted under subsection (b) or (c).

(2) Dissemination of information regarding labeling changes

Beginning on September 27, 2007, the Secretary shall include as a requirement of a written request that the sponsors of the studies that result in labeling changes that are reflected in the annual summary developed pursuant to subsection (f)(6)(F) distribute, at least annually (or more frequently if the Secretary determines that it would be beneficial to the public health), such information to physicians and other health care providers.

(3) Effect of subsection

Nothing in this subsection alters or amends section 331(j) of this title or section 552 of title 5 or section 1905 of title 18.

(*l*) Adverse event reporting

(1) Reporting in first 18-month period

Beginning on September 27, 2007, during the 18-month period beginning on the date a labeling change is approved pursuant to subsection (i), the Secretary shall ensure that all adverse event reports that have been received for such drug (regardless of when such report was received) are referred to the Office of Pediatric Therapeutics established under section 393a of this title. In considering the reports, the Director of such Office shall provide for the review of the reports by the Pediatric Advisory Committee, including obtaining any recommendations of such Committee regarding whether the Secretary should take action under this chapter in response to such reports.

(2) Reporting in subsequent periods

Following the 18-month period described in paragraph (1), the Secretary shall, as appropriate, refer to the Office of Pediatric Therapeutics all pediatric adverse event reports for a drug for which a pediatric study was conducted under this section. In considering such reports, the Director of such Office may provide for the review of such reports by the Pediatric Advisory Committee, including obtaining any recommendation of such Committee

regarding whether the Secretary should take action in response to such reports.

(3) Preservation of authority

Nothing in this subsection shall prohibit the Office of Pediatric Therapeutics from providing for the review of adverse event reports by the Pediatric Advisory Committee prior to the 18-month period referred to in paragraph (1), if such review is necessary to ensure safe use of a drug in a pediatric population.

(4) Effect

The requirements of this subsection shall supplement, not supplant, other review of such adverse event reports by the Secretary.

(m) Clarification of interaction of market exclusivity under this section and market exclusivity awarded to an applicant for approval of a drug under section 355(j) of this title

If a 180-day period under section 355(j)(5)(B)(iv) of this title overlaps with a 6-month exclusivity period under this section, so that the applicant for approval of a drug under section 355(j) of this title entitled to the 180-day period under that section loses a portion of the 180-day period to which the applicant is entitled for the drug, the 180-day period shall be extended from—

(1) the date on which the 180-day period would have expired by the number of days of the overlap, if the 180-day period would, but for the application of this subsection, expire after the 6-month exclusivity period; or

(2) the date on which the 6-month exclusivity period expires, by the number of days of the overlap if the 180-day period would, but for the application of this subsection, expire during the six-month exclusivity period.

(n) Referral if pediatric studies not submitted

(1) In general

Beginning on September 27, 2007, if pediatric studies of a drug have not been submitted by the date specified in the written request issued or if the applicant or holder does not agree to the request under subsection (d) and if the Secretary, through the committee established under section 355d of this title, determines that there is a continuing need for information relating to the use of the drug in the pediatric population (including neonates, as appropriate), the Secretary shall carry out the following:

(A) For a drug for which a listed patent has not expired, or for which a period of exclusivity eligible for extension under subsection (b)(1) or (c)(1) of this section or under subsection (m)(2) or (m)(3) of section 262 of title 42 has not ended, make a determination regarding whether an assessment shall be required to be submitted under section 355c(b) of this title.

(B) For a drug that has no unexpired listed patents and for which no unexpired periods of exclusivity eligible for extension under subsection (b)(1) or (c)(1) of this section or under subsection (m)(2) or (m)(3) of section 262 of title 42 apply, the Secretary shall refer the drug for inclusion on the list established under section 284m of title 42 for the conduct of studies.

(C) For a drug that is a qualified countermeasure (as defined in section 247d–6a of title 42), a security countermeasure (as defined in section 247d–6b of title 42), or a qualified pandemic or epidemic product (as defined in section 247d–6d of title 42), in addition to any action with respect to such drug under subparagraph (A) or (B), the Secretary shall notify the Assistant Secretary for Preparedness and Response and the Director of the Biomedical Advanced Research and Development Authority of all pediatric studies in the written request issued by the Commissioner of Food and Drugs.

(2) Public notice

The Secretary shall give the public notice of a decision under paragraph (1)(A) not to require an assessment under section 355c of this title and the basis for such decision.

(3) Effect of subsection

Nothing in this subsection alters or amends section 331(j) of this title or section 552 of title 5 or section 1905 of title 18.

***(o)* Prompt approval of drugs when pediatric information is added to labeling**

(1) General rule

A drug for which an application has been submitted or approved under subsection (b)(2) or (j) of section 355 of this title shall not be considered ineligible for approval under that section or misbranded under section 352 of this title on the basis that the labeling of the drug omits a pediatric indication or any other aspect of labeling pertaining to pediatric use when the omitted indication or other aspect is protected by patent, or by exclusivity under clause (iii) or (iv) of section 355(j)(5)(F) of this title, clause (iii) or (iv) of section 355(c)(3)(E) of this title, or section 360cc(a) of this title, or by an extension of such exclusivity under this section or section 355f of this title.

(2) Labeling

Notwithstanding clauses (iii) and (iv) of section 355(j)(5)(F) of this title, clauses (iii) and (iv) of section 355(c)(3)(E) of this title, or section 360cc of this title, the Secretary may require that the labeling of a drug approved pursuant to an application submitted under subsection (b)(2) or (j) of section 355 of this title that omits a pediatric indication or other aspect of labeling as described in paragraph (1) include—

(A) a statement that, because of marketing exclusivity for a manufacturer—

(i) the drug is not labeled for pediatric use; or

(ii) in the case of a drug for which there is an additional pediatric use not referred to in paragraph (1), the drug is not labeled for the pediatric use under paragraph (1); and

(B) a statement of any appropriate pediatric contraindications, warnings, precautions, or other information that the Secretary considers necessary to assure safe use.

(3) Preservation of pediatric exclusivity and extensions

This subsection does not affect—

(A) the availability or scope of exclusivity under—

(i) this section;

(ii) section 355 of this title for pediatric formulations; or

(iii) section 360cc of this title;

(B) the availability or scope of an extension to any such exclusivity, including an extension under this section or section 355f of this title;

(C) the question of the eligibility for approval under section 355 of this title of any application described in subsection (b)(2) or (j) of such section that omits any other aspect of labeling protected by exclusivity under—

(i) clause (iii) or (iv) of section 355(j)(5)(F) of this title;

(ii) clause (iii) or (iv) of section 355(c)(3)(E) of this title; or

(iii) section 360cc(a) of this title; or

(D) except as expressly provided in paragraphs (1) and (2), the operation of section 355 of this title or section 360cc of this title.

(June 25, 1938, ch. 675, § 505A, as added Pub. L. 105–115, title I, § 111, Nov. 21, 1997, 111 Stat. 2305; amended Pub. L. 107–109, §§ 2, 4, 5(b)(2), 7–11(a), 18(a), 19, Jan. 4, 2002, 115 Stat. 1408, 1411, 1413–1415, 1423, 1424; Pub. L. 108–155, §§ 2(b)(2), 3(a), (b)(1), Dec. 3, 2003, 117 Stat. 1941; Pub. L. 108–173, title XI, § 1104, Dec. 8, 2003, 117 Stat. 2461; Pub. L. 110–85, title V, § 502(a)(1), Sept. 27, 2007, 121 Stat. 876; Pub. L. 111–148, title VII, § 7002(g)(2)(B), Mar. 23, 2010, 124 Stat. 820; Pub. L. 112–144, title V, §§ 501(a), 502(a)(1), (b), 509(a), July 9, 2012, 126 Stat. 1039, 1040, 1047; Pub. L. 113–5, title III, § 307(a), Mar. 13, 2013, 127 Stat. 191; Pub. L. 114–255, div. A, title III, § 3102(2), Dec. 13, 2016, 130 Stat. 1156; Pub. L. 115–52, title V, § 505(a)–(b)(2)(A), title VI, § 608, Aug. 18, 2017, 131 Stat. 1046, 1050; Pub. L. 117–9, § 1(b)(2), Apr. 23, 2021, 135 Stat. 258.)

Editorial Notes

AMENDMENTS

2021—Subsec. (c)(1)(A)(i)(II). Pub. L. 117–9 substituted ''(c)(3)(E)'' for ''(c)(3)(D)''.

2017—Subsecs. (b), (c). Pub. L. 115–52, § 505(b)(2)(A), substituted ''subsection (d)(4)'' for ''subsection (d)(3)'' in introductory provisions of par. (1) and in par. (2).

Subsec. (d)(3) to (6). Pub. L. 115–52, § 505(b)(1), added par. (3) and redesignated former pars. (3) to (5) as (4) to (6), respectively.

Subsec. (f)(3). Pub. L. 115–52, § 505(b)(2)(A), substituted ''subsection (d)(4)'' for ''subsection (d)(3)''.

Subsec. (f)(7). Pub. L. 115–52, § 505(a), added par. (7).

Subsec. (h). Pub. L. 115–52, § 505(b)(2)(A), substituted ''subsection (d)(4)'' for ''subsection (d)(3)''.

Subsec. (*o*). Pub. L. 115–52, § 608(1), struck out ''under section 355(j)'' after ''approval of drugs'' in heading.

Subsec. (*o*)(1). Pub. L. 115–52, § 608(2), substituted ''under subsection (b)(2) or (j) of section 355 of this title'' for ''under section 355(j) of this title'' and '', or by exclusivity under clause (iii) or (iv) of section 355(j)(5)(F) of this title, clause (iii) or (iv) of section 355(c)(3)(E) of this title, or section 360cc(a) of this title, or by an extension of such exclusivity under this section or section 355f of this title'' for ''or by exclusivity under clause (iii) or (iv) of section 355(j)(5)(F) of this title''.

Subsec. (*o*)(2). Pub. L. 115–52, § 608(3), in introductory provisions, inserted ''clauses (iii) and (iv) of section 355(c)(3)(E) of this title, or section 360cc of this title,'' after ''section 355(j)(5)(F) of this title,'' and substituted ''drug approved pursuant to an application submitted under subsection (b)(2) or (j) of section 355 of this title'' for ''drug approved under section 355(j) of this title''.

Subsec. (*o*)(3). Pub. L. 115–52, § 608(4), amended par. (3) generally. Prior to amendment, text read as follows: ''This subsection does not affect—

''(A) the availability or scope of exclusivity under this section;

''(B) the availability or scope of exclusivity under section 355 of this title for pediatric formulations;

''(C) the question of the eligibility for approval of any application under section 355(j) of this title that omits any other conditions of approval entitled to exclusivity under clause (iii) or (iv) of section 355(j)(5)(F) of this title; or

''(D) except as expressly provided in paragraphs (1) and (2), the operation of section 355 of this title.''

2016—Subsec. (p). Pub. L. 114–255 struck out subsec. (p) which related to Institute of Medicine study.

2013—Subsec. (d)(5). Pub. L. 113–5, § 307(a)(1), added par. (5).

Subsec. (n)(1)(C). Pub. L. 113–5, § 307(a)(2), added subpar. (C).

2012—Subsec. (d)(1)(A). Pub. L. 112–144, § 502(b), inserted at end ''If a request under this subparagraph does not request studies in neonates, such request shall include a statement describing the rationale for not requesting studies in neonates.''

Subsec. (h). Pub. L. 112–144, § 502(a)(1), amended subsec. (h) generally. Prior to amendment, text read as follows: ''Notwithstanding any other provision of law, if any pediatric study is required by a provision of law (including a regulation) other than this section and such study meets the completeness, timeliness, and other requirements of this section, such study shall be deemed to satisfy the requirement for market exclusivity pursuant to this section.''

Subsec. (k)(2). Pub. L. 112–144, § 509(a)(1), substituted ''subsection (f)(6)(F)'' for ''subsection (f)(3)(F)''.

Subsec. (*l*)(1). Pub. L. 112–144, § 509(a)(2)(A), substituted ''first 18-month period'' for ''year one'' in heading and ''18-month'' for ''one-year'' in text.

Subsec. (*l*)(2). Pub. L. 112–144, § 509(a)(2)(B), substituted ''periods'' for ''years'' in heading and ''18-month period'' for ''one-year period'' in text.

Subsec. (*l*)(3), (4). Pub. L. 112–144, § 509(a)(2)(C), (D), added par. (3) and redesignated former par. (3) as (4).

Subsec. (n). Pub. L. 112–144, § 509(a)(3)(A), substituted ''submitted'' for ''completed'' in heading.

Subsec. (n)(1). Pub. L. 112–144, § 509(a)(3)(B)(i), substituted ''have not been submitted by the date specified in the written request issued or if the applicant or holder does not agree to the request'' for ''have not been completed'' in introductory provisions.

Subsec. (n)(1)(A). Pub. L. 112–144, § 509(a)(3)(B)(ii), inserted '', or for which a period of exclusivity eligible for extension under subsection (b)(1) or (c)(1) of this section or under subsection (m)(2) or (m)(3) of section 262 of title 42 has not ended'' after ''expired'' and struck out at end ''Prior to making such a determination, the Secretary may not take more than 30 days to certify whether the Foundation for the National Institutes of Health has sufficient funding at the time of such certification to initiate and fund all of the studies in the written request in their entirety within the timeframes specified within the written request. Only if the Secretary makes such certification in the affirmative, the Secretary shall refer all pediatric studies in the written request to the Foundation for the National Institutes of Health for the conduct of such studies, and such Foundation shall fund such studies. If no certification has been made at the end of the 30-day period, or if the Secretary certifies that funds are not sufficient to initiate and fund all the studies in their entirety, the Secretary shall consider whether assessments shall be required under section 355c(b) of this title for such drug.''

Subsec. (n)(1)(B). Pub. L. 112–144, § 509(a)(3)(B)(iii), substituted ''no unexpired listed patents and for which

no unexpired periods of exclusivity eligible for extension under subsection (b)(1) or (c)(1) of this section or under subsection (m)(2) or (m)(3) of section 262 of title 42 apply,'' for ''no listed patents or has 1 or more listed patents that have expired,''.

Subsec. (*o*)(2)(B). Pub. L. 112–144, § 509(a)(4), amended subpar. (B) generally. Prior to amendment, subpar. (B) read as follows: ''a statement of any appropriate pediatric contraindications, warnings, or precautions that the Secretary considers necessary.''

Subsec. (q). Pub. L. 112–144, § 501(a), struck out subsec. (q). Text read as follows: ''A drug may not receive any 6-month period under subsection (b) or (c) unless—

''(1) on or before October 1, 2012, the Secretary makes a written request for pediatric studies of the drug;

''(2) on or before October 1, 2012, an application for the drug is accepted for filing under section 355(b) of this title; and

''(3) all requirements of this section are met.''

2010—Subsec. (p)(4) to (6). Pub. L. 111–148 added pars. (4) to (6) and struck out former pars. (4) and (5) which read as follows:

''(4) review and assess the pediatric studies of biological products as required under subsections (a) and (b) of section 355c of this title; and

''(5) make recommendations regarding appropriate incentives for encouraging pediatric studies of biologics.''

2007—Pub. L. 110–85 amended section generally. Prior to amendment, text consisted of subsecs. (a) to (n) relating to pediatric studies of drugs, including market exclusivity, conduct of pediatric studies, delay of effective date for certain applications, notice of determinations on studies requirement, limitations, research requirements, labeling supplements, dissemination of information, prompt approval of drugs, report to Congress not later than Jan. 1, 2001, and sunset provisions.

2003—Subsec. (b)(1)(A)(i). Pub. L. 108–173, § 1104(1), substituted ''(j)(5)(F)(ii)'' for ''(j)(5)(D)(ii)'' in two places.

Subsec. (b)(1)(A)(ii). Pub. L. 108–173, § 1104(2), substituted ''(j)(5)(F)'' for ''(j)(5)(D)''.

Subsec. (b)(2). Pub. L. 108–155, § 3(a), substituted ''355(j)(5)(B)'' for ''355(j)(4)(B)'' in two places.

Subsec. (c)(1)(A)(i). Pub. L. 108–173, § 1104(1), substituted ''(j)(5)(F)(ii)'' for ''(j)(5)(D)(ii)'' in two places.

Subsec. (c)(1)(A)(ii). Pub. L. 108–173, § 1104(2), substituted ''(j)(5)(F)'' for ''(j)(5)(D)''.

Subsec. (c)(2). Pub. L. 108–155, § 3(a), substituted ''355(j)(5)(B)'' for ''355(j)(4)(B)'' in two places.

Subsec. (e). Pub. L. 108–173, § 1104(3), substituted ''355(j)(5)(F)'' for ''355(j)(5)(D)''.

Subsec. (h). Pub. L. 108–155, § 2(b)(2), substituted ''pediatric research requirements'' for ''regulations'' in heading and ''by a provision of law (including a regulation) other than this section'' for ''pursuant to regulations promulgated by the Secretary'' in text.

Subsec. (i)(2). Pub. L. 108–155, § 3(b)(1), struck out ''Advisory Subcommittee of the Anti-Infective Drugs'' before ''Advisory Committee'' wherever appearing.

Subsec. (*l*). Pub. L. 108–173, § 1104(3), substituted ''355(j)(5)(F)'' for ''355(j)(5)(D)'' wherever appearing.

2002—Subsec. (a). Pub. L. 107–109, § 19(2), (3), redesignated subsec. (g) as (a). Former subsec. (a) redesignated (b).

Subsec. (a)(1)(A). Pub. L. 107–109, § 19(1)(A), (B), substituted ''(j)(5)(D)(ii)'' for ''(j)(4)(D)(ii)'' in two places in cl. (i) and ''(j)(5)(D)'' for ''(j)(4)(D)'' in cl. (ii).

Subsec. (b). Pub. L. 107–109, § 19(2), (3), redesignated subsec. (a) as (b).

Pub. L. 107–109, § 2(1), struck out heading and text of subsec. (b). Text read as follows: ''Not later than 180 days after November 21, 1997, the Secretary, after consultation with experts in pediatric research shall develop, prioritize, and publish an initial list of approved drugs for which additional pediatric information may produce health benefits in the pediatric population. The Secretary shall annually update the list.''

Subsec. (c). Pub. L. 107–109, § 2(2), in introductory provisions, inserted ''determines that information relating to the use of an approved drug in the pediatric population may produce health benefits in that population and'' after ''the Secretary'' and struck out ''concerning a drug identified in the list described in subsection (b) of this section'' after ''such studies)''.

Subsec. (c)(1)(A). Pub. L. 107–109, § 19(1)(A), (B), substituted ''(j)(5)(D)(ii)'' for ''(j)(4)(D)(ii)'' in two places in cl. (i) and ''(j)(5)(D)'' for ''(j)(4)(D)'' in cl. (ii).

Subsec. (d)(1). Pub. L. 107–109, § 19(4), substituted ''subsection (b) or (c)'' for ''subsection (a) or (c)'' in introductory provisions.

Subsec. (d)(2). Pub. L. 107–109, §§ 18(a), 19(4), substituted ''subsection (b) or (c)'' for ''subsection (a) or (c)'' and inserted ''In reaching an agreement regarding written protocols, the Secretary shall take into account adequate representation of children of ethnic and racial minorities.'' after first sentence.

Subsec. (d)(3). Pub. L. 107–109, § 19(4), substituted ''subsection (b) or (c)'' for ''subsection (a) or (c)''.

Subsec. (d)(4). Pub. L. 107–109, § 4, added par. (4).

Subsec. (e). Pub. L. 107–109, § 19(1)(C), (4), substituted ''section 355(j)(5)(D)'' for ''section 355(j)(4)(D)'' and ''subsection (b) or (c)'' for ''subsection (a) or (c)''.

Subsec. (g). Pub. L. 107–109, § 19(2), (3), (5), redesignated subsec. (h) as (g) and substituted ''subsection (b) or (c)'' for ''subsection (a) or (b)'' in introductory provisions. Former subsec. (g) redesignated (a).

Pub. L. 107–109, § 7, inserted ''(including neonates in appropriate cases)'' after ''pediatric age groups''.

Subsec. (h). Pub. L. 107–109, § 19(2), (3), redesignated subsec. (i) as (h). Former subsec. (h) redesignated (g).

Subsec. (i). Pub. L. 107–109, § 19(2), (3), redesignated subsec. (*l*) as (i). Former subsec. (i) redesignated (h).

Subsec. (j). Pub. L. 107–109, § 19(2), (3), redesignated subsec. (m) as (j). Former subsec. (j) redesignated (n).

Pub. L. 107–109, § 8, added subsec. (j) and struck out heading and text of former subsec. (j). Text read as follows: ''A drug may not receive any six-month period under subsection (a) or (c) of this section unless the application for the drug under section 355(b)(1) of this title is submitted on or before January 1, 2002. After January 1, 2002, a drug shall receive a six-month period under subsection (c) of this section if—

''(1) the drug was in commercial distribution as of November 21, 1997;

''(2) the drug was included by the Secretary on the list under subsection (b) of this section as of January 1, 2002;

''(3) the Secretary determines that there is a continuing need for information relating to the use of the drug in the pediatric population and that the drug may provide health benefits in that population; and

''(4) all requirements of this section are met.''

Subsec. (k). Pub. L. 107–109, § 19(2), (3), redesignated subsec. (n) as (k). Former subsec. (k) redesignated (m).

Subsec. (*l*). Pub. L. 107–109, § 19(2), (3), redesignated subsec. (*o*) as (*l*). Former subsec. (*l*) redesignated (i).

Pub. L. 107–109, § 5(b)(2), added subsec. (*l*).

Subsec. (m). Pub. L. 107–109, § 19(2), (3), redesignated subsec. (k) as (m). Former subsec. (m) redesignated (j).

Pub. L. 107–109, § 9, added subsec. (m).

Subsec. (n). Pub. L. 107–109, § 19(4), which directed substitution of ''subsection (b) or (c)'' for ''subsection (a) or (c)'' in subsec. (m), was executed by making the substitution in introductory provisions of subsec. (n), to reflect the probable intent of Congress.

Pub. L. 107–109, § 19(2), (3), redesignated subsec. (j) as (n). Former subsec. (n) redesignated (k).

Pub. L. 107–109, § 10, added subsec. (n).

Subsec. (*o*). Pub. L. 107–109, § 19(2), (3), redesignated subsec. (*o*) as (*l*).

Pub. L. 107–109, § 11(a), added subsec. (*o*).

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 2012 AMENDMENT

Pub. L. 112–144, title V, § 509(g), July 9, 2012, 126 Stat. 1050, provided that:

''(1) APPLICATION.—Notwithstanding any provision of section 505A and 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a, 355c) stating that a provision applies beginning on the date of the enactment of the Best Pharmaceuticals for Children Act of 2007 [Sept. 27, 2007] or the date of the enactment of the Pediatric Research Equity Act of 2007 [Sept. 27, 2007], any amendment made by this Act to such a provision applies beginning on the date of the enactment of this Act [July 9, 2012].

''(2) TRANSITIONAL RULE FOR ADVERSE EVENT REPORTING.—With respect to a drug for which a labeling change described under section 505A(*l*)(1) or 505B(i)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a(*l*)(1); 355c(i)(1)) is approved or made, respectively, during the one-year period that ends on the day before the date of enactment of this Act [July 9, 2012], the Secretary [of Health and Human Services] shall apply section 505A(*l*) and section 505B(i), as applicable, to such drug, as such sections were in effect on such day.''

EFFECTIVE DATE OF 2007 AMENDMENT

Pub. L. 110–85, title V, § 502(a)(2), Sept. 27, 2007, 121 Stat. 885, provided that:

''(A) IN GENERAL.—The amendment made by this subsection [amending this section] shall apply to written requests under section 505A of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a) issued on or after the date of the enactment of this Act [Sept. 27, 2007].

''(B) CERTAIN WRITTEN REQUESTS.—A written request issued under section 505A of the Federal Food, Drug, and Cosmetic Act, as in effect on the day before the date of the enactment of this Act, which has been accepted and for which no determination under subsection (d)(2) of such section has been made before such date of enactment, shall be subject to such section 505A, except that such written requests shall be subject to subsections (d)(2)(A)(ii), (e)(1) and (2), (f), (i)(2)(A), (j), (k)(1), (*l*)(1), and (n) of section 505A of the Federal Food, Drug, and Cosmetic Act, as in effect on or after the date of the enactment of this Act.''

EFFECTIVE DATE OF 2003 AMENDMENT

Amendment by Pub. L. 108–155 effective Dec. 3, 2003, except as otherwise provided, see section 4 of Pub. L. 108–155, set out as an Effective Date note under section 355c of this title.

EFFECTIVE DATE OF 2002 AMENDMENT

Pub. L. 107–109, § 11(b), Jan. 4, 2002, 115 Stat. 1416, provided that: ''The amendment made by subsection (a) [amending this section] takes effect on the date of enactment of this Act [Jan. 4, 2002], including with respect to applications under section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)) that are approved or pending on that date.''

CONSTRUCTION OF 2007 AMENDMENTS ON PEDIATRIC STUDIES

Pub. L. 110–85, title IX, § 901(e), Sept. 27, 2007, 121 Stat. 942, provided that: ''This title [enacting sections 353c, 355–1, 355e, 360a, and 360bbb–6 of this title, amending sections 331, 333, 334, 352, 355, and 381 of this title and section 262 of Title 42, The Public Health and Welfare, and enacting provisions set out as notes under sections 331, 352, and 355 of this title] and the amendments made by this title may not be construed as affecting the authority of the Secretary of Health and Human Services to request pediatric studies under section 505A of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355a] or to require such studies under section 505B of such Act [21 U.S.C. 355c].''

PLAN FOR EARLIER SUBMISSION OF PEDIATRIC STUDIES

Pub. L. 115–52, title V, § 505(c), Aug. 18, 2017, 131 Stat. 1046, provided that: ''The Secretary of Health and Human Services, acting through the internal review committee established under section 505C of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355d) shall, not later than one year after the date of enactment of this Act [Aug. 18, 2017], develop and implement a plan to achieve, when appropriate, earlier submission of pediatric studies under section 505A of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a) or section 351(m) of the Public Health Service Act (42 U.S.C. 262(m)). Such plan shall include recommendations to achieve—

''(1) earlier discussion of proposed pediatric study requests and written requests with sponsors, and if appropriate, discussion of such requests at the meeting required under section 505B(e)(2)(C) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355c(e)(2)(C)), as amended by section 503(a);

''(2) earlier issuance of written requests for a pediatric study under such section 505A, including for investigational new drugs prior to the submission of an application under section 505(b)(1) of such Act (21 U.S.C. 355(b)(1)); and

''(3) shorter timelines, when appropriate, for the completion of studies pursuant to a written request under such section 505A or such section 351(m).''

DRAFT GUIDANCE FOR NEONATAL STUDIES

Pub. L. 115–52, title V, § 505(d)(2), Aug. 18, 2017, 131 Stat. 1047, provided that: ''Not later than 2 years after the date of enactment of this Act [Aug. 18, 2017], the Secretary shall issue draft guidance on clinical pharmacology considerations for neonatal studies for drugs and biological products.''

COMMUNICATION WITH PEDIATRIC REVIEW COMMITTEE

Pub. L. 112–144, title V, § 503, July 9, 2012, 126 Stat. 1040, provided that: ''Not later than 1 year after the date of enactment of this Act [July 9, 2012], the Secretary of Health and Human Services (referred to in this title [see Tables for classification] as the 'Secretary') shall issue internal standard operating procedures that provide for the review by the internal review committee established under section 505C of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355d) of any significant modifications to initial pediatric study plans, agreed initial pediatric study plans, and written requests under sections 505A and 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a, 355c). Such internal standard operating procedures shall be made publicly available on the Internet Web site of the Food and Drug Administration.''

ACCESS TO DATA

Pub. L. 112–144, title V, § 504, July 9, 2012, 126 Stat. 1040, provided that: ''Not later than 3 years after the date of enactment of this Act [July 9, 2012], the Secretary [of Health and Human Services] shall make available to the public, including through posting on the Internet Web site of the Food and Drug Administration, the medical, statistical, and clinical pharmacology reviews of, and corresponding written requests issued to an applicant, sponsor, or holder for, pediatric studies submitted between January 4, 2002, and September 27, 2007, under subsection (b) or (c) of section 505A of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a) for which 6 months of market exclusivity was granted and that resulted in a labeling change. The Secretary shall make public the information described in the preceding sentence in a manner consistent with how the Secretary releases information under section 505A(k) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a(k)).''

REPORT ON PEDIATRIC EXCLUSIVITY PROGRAM

Pub. L. 107–109, § 16, Jan. 4, 2002, 115 Stat. 1421, as amended by Pub. L. 108–155, § 3(b)(4), Dec. 3, 2003, 117 Stat. 1942, required the Comptroller General, not later than Oct. 1, 2006, and in consultation with the Secretary of Health and Human Services, to submit to Congress a report on specified issues concerning the effectiveness of the pediatric exclusivity program.

STUDY BY GENERAL ACCOUNTING OFFICE

Pub. L. 107–109, §18(b), Jan. 4, 2002, 115 Stat. 1423, required the Comptroller General, not later than Jan. 10, 2003, to conduct a study relating to the representation of children of ethnic and racial minorities in studies under section 355a of this title and to submit a report to Congress describing the findings of the study.

§ 355b. Adverse-event reporting

(a) Toll-free number in labeling

Not later than one year after January 4, 2002, the Secretary of Health and Human Services shall promulgate a final rule requiring that the labeling of each drug for which an application is approved under section 505 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355] (regardless of the date on which approved) include the toll-free number maintained by the Secretary for the purpose of receiving reports of adverse events regarding drugs and a statement that such number is to be used for reporting purposes only, not to receive medical advice. With respect to the final rule:

(1) The rule shall provide for the implementation of such labeling requirement in a manner that the Secretary considers to be most likely to reach the broadest consumer audience.

(2) In promulgating the rule, the Secretary shall seek to minimize the cost of the rule on the pharmacy profession.

(3) The rule shall take effect not later than 60 days after the date on which the rule is promulgated.

(b) Drugs with pediatric market exclusivity

(1) In general

During the one year beginning on the date on which a drug receives a period of market exclusivity under 505A[1] of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355a], any report of an adverse event regarding the drug that the Secretary of Health and Human Services receives shall be referred to the Office of Pediatric Therapeutics established under section 393a of this title. In considering the report, the Director of such Office shall provide for the review of the report by the Pediatric Advisory Committee, including obtaining any recommendations of such subcommittee[2] regarding whether the Secretary should take action under the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 301 et seq.] in response to the report.

(2) Rule of construction

Paragraph (1) may not be construed as restricting the authority of the Secretary of Health and Human Services to continue carrying out the activities described in such paragraph regarding a drug after the one-year period described in such paragraph regarding the drug has expired.

(Pub. L. 107–109, §17, Jan. 4, 2002, 115 Stat. 1422; Pub. L. 108–155, §3(b)(5), Dec. 3, 2003, 117 Stat. 1942.)

[1] So in original. Probably should be preceded by ''section''.

[2] So in original. Probably should be ''Committee''.

Editorial Notes

REFERENCES IN TEXT

The Federal Food, Drug, and Cosmetic Act, referred to in subsec. (b)(1), is act June 25, 1938, ch. 675, 52 Stat. 1040, which is classified generally to this chapter. For complete classification of this Act to the Code, see section 301 of this title and Tables.

CODIFICATION

Section was enacted as part of the Best Pharmaceuticals for Children Act, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

AMENDMENTS

2003—Subsec. (b)(1). Pub. L. 108–155 struck out ''Advisory Subcommittee of the Anti-Infective Drugs'' before ''Advisory Committee''.

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 2003 AMENDMENT

Amendment by Pub. L. 108–155 effective Dec. 3, 2003, except as otherwise provided, see section 4 of Pub. L. 108–155, set out as an Effective Date note under section 355c of this title.

§ 355c. Research into pediatric uses for drugs and biological products

(a) New drugs and biological products

(1) In general

(A) General requirements

Except with respect to an application for which subparagraph (B) applies, a person that submits, on or after September 27, 2007, an application (or supplement to an application) for a drug—

(i) under section 355 of this title for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration; or

(ii) under section 262 of title 42 for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration,

shall submit with the application the assessments described in paragraph (2).

(B) Certain molecularly targeted cancer indications

A person that submits, on or after the date that is 3 years after August 18, 2017, an original application for a new active ingredient under section 355 of this title or section 262 of title 42, shall submit with the application reports on the investigation described in paragraph (3) if the drug or biological product that is the subject of the application is—

(i) intended for the treatment of an adult cancer; and

(ii) directed at a molecular target that the Secretary determines to be substantially relevant to the growth or progression of a pediatric cancer.

(2) Assessments

(A) In general

The assessments referred to in paragraph (1)(A) shall contain data, gathered using appropriate formulations for each age group

for which the assessment is required, that are adequate—

(i) to assess the safety and effectiveness of the drug or the biological product for the claimed indications in all relevant pediatric subpopulations; and

(ii) to support dosing and administration for each pediatric subpopulation for which the drug or the biological product is safe and effective.

(B) Similar course of disease or similar effect of drug or biological product

(i) In general

If the course of the disease and the effects of the drug are sufficiently similar in adults and pediatric patients, the Secretary may conclude that pediatric effectiveness can be extrapolated from adequate and well-controlled studies in adults, usually supplemented with other information obtained in pediatric patients, such as pharmacokinetic studies.

(ii) Extrapolation between age groups

A study may not be needed in each pediatric age group if data from one age group can be extrapolated to another age group.

(iii) Information on extrapolation

A brief documentation of the scientific data supporting the conclusion under clauses (i) and (ii) shall be included in any pertinent reviews for the application under section 355 of this title or section 262 of title 42.

(3) Molecularly targeted pediatric cancer investigation

(A) In general

With respect to a drug or biological product described in paragraph (1)(B), the investigation described in this paragraph is a molecularly targeted pediatric cancer investigation, which shall be designed to yield clinically meaningful pediatric study data, gathered using appropriate formulations for each age group for which the study is required, regarding dosing, safety, and preliminary efficacy to inform potential pediatric labeling.

(B) Extrapolation of data

Paragraph (2)(B) shall apply to investigations described in this paragraph to the same extent and in the same manner as paragraph (2)(B) applies with respect to the assessments required under paragraph (1)(A).

(C) Deferrals and waivers

Deferrals and waivers under paragraphs (4) and (5) shall apply to investigations described in this paragraph to the same extent and in the same manner as such deferrals and waivers apply with respect to the assessments under paragraph (2)(B).

(4) Deferral

(A) In general

On the initiative of the Secretary or at the request of the applicant, the Secretary may defer submission of some or all assessments required under paragraph (1)(A) or reports on the investigation required under paragraph (1)(B) until a specified date after approval of the drug or issuance of the license for a biological product if—

(i) the Secretary finds that—

(I) the drug or biological product is ready for approval for use in adults before pediatric studies are complete;

(II) pediatric studies should be delayed until additional safety or effectiveness data have been collected; or

(III) there is another appropriate reason for deferral; and

(ii) the applicant submits to the Secretary—

(I) certification of the grounds for deferring the assessments or reports on the investigation;

(II) a pediatric study plan as described in subsection (e);

(III) evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time; and

(IV) a timeline for the completion of such studies.

(B) Deferral extension

(i) In general

On the initiative of the Secretary or at the request of the applicant, the Secretary may grant an extension of a deferral approved under subparagraph (A) for submission of some or all assessments required under paragraph (1)(A) or reports on the investigation required under paragraph (1)(B) if—

(I) the Secretary determines that the conditions described in subclause (II) or (III) of subparagraph (A)(i) continue to be met; and

(II) the applicant submits a new timeline under subparagraph (A)(ii)(IV) and any significant updates to the information required under subparagraph (A)(ii).

(ii) Timing and information

If the deferral extension under this subparagraph is requested by the applicant, the applicant shall submit the deferral extension request containing the information described in this subparagraph not less than 90 days prior to the date that the deferral would expire. The Secretary shall respond to such request not later than 45 days after the receipt of such letter. If the Secretary grants such an extension, the specified date shall be the extended date. The sponsor of the required assessment under paragraph (1)(A) or reports on the investigation under paragraph (1)(B) shall not be issued a letter described in subsection (d) unless the specified or extended date of submission for such required studies has passed or if the request for an extension is pending. For a deferral that has expired prior to July 9, 2012, or that will expire prior to 270 days after July 9, 2012, a deferral extension shall be requested by

an applicant not later than 180 days after July 9, 2012. The Secretary shall respond to any such request as soon as practicable, but not later than 1 year after July 9, 2012. Nothing in this clause shall prevent the Secretary from updating the status of a study or studies publicly if components of such study or studies are late or delayed.

(C) Annual review

(i) In general

On an annual basis following the approval of a deferral under subparagraph (A), the applicant shall submit to the Secretary the following information:

(I) Information detailing the progress made in conducting pediatric studies.

(II) If no progress has been made in conducting such studies, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time.

(III) Projected completion date for pediatric studies.

(IV) The reason or reasons why a deferral or deferral extension continues to be necessary.

(ii) Public availability

Not later than 90 days after the submission to the Secretary of the information submitted through the annual review under clause (i), the Secretary shall make available to the public in an easily accessible manner, including through the Internet Web site of the Food and Drug Administration—

(I) such information;

(II) the name of the applicant for the product subject to the assessment or investigation;

(III) the date on which the product was approved; and

(IV) the date of each deferral or deferral extension under this paragraph for the product.

(5) Waivers

(A) Full waiver

On the initiative of the Secretary or at the request of an applicant, the Secretary shall grant a full waiver, as appropriate, of the requirement to submit assessments or reports on the investigation for a drug or biological product under this subsection if the applicant certifies and the Secretary finds that—

(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients is so small or the patients are geographically dispersed);

(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in all pediatric age groups; or

(iii) the drug or biological product—

(I) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients; and

(II) is not likely to be used in a substantial number of pediatric patients.

(B) Partial waiver

On the initiative of the Secretary or at the request of an applicant, the Secretary shall grant a partial waiver, as appropriate, of the requirement to submit assessments or reports on the investigation for a drug or biological product under this subsection with respect to a specific pediatric age group if the applicant certifies and the Secretary finds that—

(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients in that age group is so small or patients in that age group are geographically dispersed);

(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in that age group;

(iii) the drug or biological product—

(I) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in that age group; and

(II) is not likely to be used by a substantial number of pediatric patients in that age group; or

(iv) the applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for that age group have failed.

(C) Pediatric formulation not possible

If a partial waiver is granted on the ground that it is not possible to develop a pediatric formulation, the waiver shall cover only the pediatric groups requiring that formulation. An applicant seeking such a partial waiver shall submit to the Secretary documentation detailing why a pediatric formulation cannot be developed and, if the waiver is granted, the applicant's submission shall promptly be made available to the public in an easily accessible manner, including through posting on the Web site of the Food and Drug Administration.

(D) Labeling requirement

If the Secretary grants a full or partial waiver because there is evidence that a drug or biological product would be ineffective or unsafe in pediatric populations, the information shall be included in the labeling for the drug or biological product.

(b) Marketed drugs and biological products

(1) In general

The Secretary may (by order in the form of a letter) require the sponsor or holder of an approved application for a drug under section 355 of this title or the holder of a license for a biological product under section 262 of title 42 to submit by a specified date the assessments described in subsection (a)(2), if the Secretary finds that—

(A)(i) the drug or biological product is used for a substantial number of pediatric patients for the labeled indications; and

(ii) adequate pediatric labeling could confer a benefit on pediatric patients;

(B) there is reason to believe that the drug or biological product would represent a meaningful therapeutic benefit over existing therapies for pediatric patients for 1 or more of the claimed indications; or

(C) the absence of adequate pediatric labeling could pose a risk to pediatric patients.

(2) Waivers

(A) Full waiver

At the request of an applicant, the Secretary shall grant a full waiver, as appropriate, of the requirement to submit assessments under this subsection if the applicant certifies and the Secretary finds that—

(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients in that age group is so small or patients in that age group are geographically dispersed); or

(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in all pediatric age groups.

(B) Partial waiver

At the request of an applicant, the Secretary shall grant a partial waiver, as appropriate, of the requirement to submit assessments under this subsection with respect to a specific pediatric age group if the applicant certifies and the Secretary finds that—

(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients in that age group is so small or patients in that age group are geographically dispersed);

(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in that age group;

(iii)(I) the drug or biological product—

(aa) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in that age group; and

(bb) is not likely to be used in a substantial number of pediatric patients in that age group; and

(II) the absence of adequate labeling could not pose significant risks to pediatric patients; or

(iv) the applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for that age group have failed.

(C) Pediatric formulation not possible

If a waiver is granted on the ground that it is not possible to develop a pediatric formulation, the waiver shall cover only the pediatric groups requiring that formulation. An applicant seeking either a full or partial waiver shall submit to the Secretary documentation detailing why a pediatric formulation cannot be developed and, if the waiver is granted, the applicant's submission shall promptly be made available to the public in an easily accessible manner, including through posting on the Web site of the Food and Drug Administration.

(D) Labeling requirement

If the Secretary grants a full or partial waiver because there is evidence that a drug or biological product would be ineffective or unsafe in pediatric populations, the information shall be included in the labeling for the drug or biological product.

(3) Effect of subsection

Nothing in this subsection alters or amends section 331(j) of this title or section 552 of title 5 or section 1905 of title 18.

(c) Meaningful therapeutic benefit

For the purposes of paragraph (4)(A)(iii)(I) and (4)(B)(iii)(I) of subsection (a) and paragraphs (1)(B) and (2)(B)(iii)(I)(aa) of subsection (b), a drug or biological product shall be considered to represent a meaningful therapeutic benefit over existing therapies if the Secretary determines that—

(1) if approved, the drug or biological product could represent an improvement in the treatment, diagnosis, or prevention of a disease, compared with marketed products adequately labeled for that use in the relevant pediatric population; or

(2) the drug or biological product is in a class of products or for an indication for which there is a need for additional options.

(d) Submission of assessments and reports on the investigation

If a person fails to submit a required assessment described in subsection (a)(2) or the investigation described in subsection (a)(3), fails to meet the applicable requirements in subsection (a)(4), or fails to submit a request for approval of a pediatric formulation described in subsection (a) or (b), in accordance with applicable provisions of subsections (a) and (b), the following shall apply:

(1) Beginning 270 days after July 9, 2012, the Secretary shall issue a non-compliance letter to such person informing them of such failure to submit or meet the requirements of the applicable subsection. Such letter shall require the person to respond in writing within 45 calendar days of issuance of such letter. Such response may include the person's request for a deferral extension if applicable. Such letter and the person's written response to such letter shall be made publicly available on the Internet Web site of the Food and Drug Administration 60 calendar days after issuance, with redactions for any trade secrets and confidential commercial information. If the Secretary determines that the letter was issued in error, the requirements of this paragraph shall not apply. The Secretary shall inform the Pediatric Advisory Committee of letters issued under this paragraph and responses to such letters.

(2) The drug or biological product that is the subject of an assessment described in subsection (a)(2) or the investigation described in subsection (a)(3), applicable requirements in subsection (a)(4), or request for approval of a pediatric formulation, may be considered misbranded solely because of that failure and subject to relevant enforcement action (except that the drug or biological product shall not be subject to action under section 333 of this title), but such failure shall not be the basis for a proceeding—

(A) to withdraw approval for a drug under section 355(e) of this title; or

(B) to revoke the license for a biological product under section 262 of title 42.

(e) Pediatric study plans

(1) In general

An applicant subject to subsection (a) shall submit to the Secretary an initial pediatric study plan prior to the submission of the assessments described under subsection (a)(2) or the investigation described in subsection (a)(3).

(2) Timing; content; meetings

(A) Timing

An applicant shall submit the initial pediatric study plan under paragraph (1)—

(i) before the date on which the applicant submits the assessments under subsection (a)(2) or the investigation described in subsection (a)(3); and

(ii) not later than—

(I) 60 calendar days after the date of the end-of-Phase 2 meeting (as such term is used in section 312.47 of title 21, Code of Federal Regulations, or successor regulations); or

(II) such other time as may be agreed upon between the Secretary and the applicant.

Nothing in this section shall preclude the Secretary from accepting the submission of an initial pediatric study plan earlier than the date otherwise applicable under this subparagraph.

(B) Content of initial pediatric study plan

The initial pediatric study plan shall include—

(i) an outline of the pediatric study or studies that the applicant plans to conduct (including, to the extent practicable study objectives and design, age groups, relevant endpoints, and statistical approach);

(ii) any request for a deferral, partial waiver, or waiver under this section, if applicable, along with any supporting information; and

(iii) other information specified in the regulations promulgated under paragraph (7).

(C) Meetings

The Secretary—

(i) shall meet with the applicant—

(I) if requested by the applicant with respect to a drug or biological product that is intended to treat a serious or life-threatening disease or condition, to discuss preparation of the initial pediatric study plan, not later than the end-of-Phase 1 meeting (as such term is used in section 312.82(b) of title 21, Code of Federal Regulations, or successor regulations) or within 30 calendar days of receipt of such request, whichever is later;

(II) to discuss the initial pediatric study plan as soon as practicable, but not later than 90 calendar days after the receipt of such plan under subparagraph (A); and

(III) to discuss the bases for the deferral under subsection (a)(4) or a full or partial waiver under subsection (a)(5);

(ii) may determine that a written response to the initial pediatric study plan is sufficient to communicate comments on the initial pediatric study plan, and that no meeting under clause (i)(II) is necessary; and

(iii) if the Secretary determines that no meeting under clause (i)(II) is necessary, shall so notify the applicant and provide written comments of the Secretary as soon as practicable, but not later than 90 calendar days after the receipt of the initial pediatric study plan.

(3) Agreed initial pediatric study plan

Not later than 90 calendar days following the meeting under paragraph (2)(C)(i)(II) or the receipt of a written response from the Secretary under paragraph (2)(C)(iii), the applicant shall document agreement on the initial pediatric study plan in a submission to the Secretary marked ''Agreed Initial Pediatric Study Plan'', and the Secretary shall confirm such agreement to the applicant in writing not later than 30 calendar days of receipt of such agreed initial pediatric study plan.

(4) Deferral and waiver

If the agreed initial pediatric study plan contains a request from the applicant for a deferral, partial waiver, or waiver under this section, the written confirmation under paragraph (3) shall include a recommendation from the Secretary as to whether such request meets the standards under paragraphs (3) or (4) of subsection (a).

(5) Amendments to the agreed initial pediatric study plan

At the initiative of the Secretary or the applicant, the agreed initial pediatric study plan may be amended at any time. The requirements of paragraph (2)(C) shall apply to any such proposed amendment in the same manner and to the same extent as such requirements apply to an initial pediatric study plan under paragraph (1). The requirements of paragraphs (3) and (4) shall apply to any agreement resulting from such proposed amendment in the same manner and to the same extent as such requirements apply to an agreed initial pediatric study plan.

(6) Internal committee

The Secretary shall consult the internal committee under section 355d of this title on the review of the initial pediatric study plan, agreed initial pediatric study plan, and any significant amendments to such plans.

(7) Required rulemaking

Not later than 1 year after July 9, 2012, the Secretary shall promulgate proposed regulations and issue guidance to implement the provisions of this subsection.

(f) Review of pediatric study plans, assessments, deferrals, deferral extensions, and waivers

(1) Review

Beginning not later than 30 days after September 27, 2007, the Secretary shall utilize the internal committee established under section 355d of this title to provide consultation to reviewing divisions on initial pediatric study plans, agreed initial pediatric study plans, and

any significant amendments to such plans, and assessments prior to approval of an application or supplement for which a pediatric assessment is required under this section and all deferral, deferral extension, and waiver requests granted pursuant to this section.

(2) Activity by committee

The committee referred to in paragraph (1) may operate using appropriate members of such committee and need not convene all members of the committee.

(3) Documentation of committee action

For each drug or biological product, the committee referred to in paragraph (1) shall document, for each activity described in paragraph (4) or (5), which members of the committee participated in such activity.

(4) Review of pediatric study plans, assessments, deferrals, deferral extensions, and waivers

Consultation on initial pediatric study plans, agreed initial pediatric study plans, and assessments by the committee referred to in paragraph (1) pursuant to this section shall occur prior to approval of an application or supplement for which a pediatric assessment is required under this section. The committee shall review all requests for deferrals, deferral extensions, and waivers from the requirement to submit a pediatric assessment granted under this section and shall provide recommendations as needed to reviewing divisions, including with respect to whether such a supplement, when submitted, shall be considered for priority review.

(5) Retrospective review of pediatric assessments, deferrals, and waivers

Not later than 1 year after September 27, 2007, the committee referred to in paragraph (1) shall conduct a retrospective review and analysis of a representative sample of assessments submitted and deferrals and waivers approved under this section since December 3, 2003. Such review shall include an analysis of the quality and consistency of pediatric information in pediatric assessments and the appropriateness of waivers and deferrals granted. Based on such review, the Secretary shall issue recommendations to the review divisions for improvements and initiate guidance to industry related to the scope of pediatric studies required under this section.

(6) Tracking of assessments and labeling changes

The Secretary, in consultation with the committee referred to in paragraph (1), shall track and make available to the public in an easily accessible manner, including through posting on the Web site of the Food and Drug Administration—

(A) the number of assessments conducted under this section;

(B) the specific drugs and biological products and their uses assessed under this section;

(C) the types of assessments conducted under this section, including trial design, the number of pediatric patients studied, and the number of centers and countries involved;

(D) aggregated on an annual basis—

(i) the total number of deferrals and deferral extensions requested and granted under this section and, if granted, the reasons for each such deferral or deferral extension;

(ii) the timeline for completion of the assessments;

(iii) the number of assessments completed and pending; and

(iv) the number of postmarket non-compliance letters issued pursuant to subsection (d), and the recipients of such letters;

(E) the number of waivers requested and granted under this section and, if granted, the reasons for the waivers;

(F) the number of pediatric formulations developed and the number of pediatric formulations not developed and the reasons any such formulation was not developed;

(G) the labeling changes made as a result of assessments conducted under this section;

(H) an annual summary of labeling changes made as a result of assessments conducted under this section for distribution pursuant to subsection (h)(2);

(I) an annual summary of information submitted pursuant to subsection (a)(4)(C); and

(J) the number of times the committee referred to in paragraph (1) made a recommendation to the Secretary under paragraph (4) regarding priority review, the number of times the Secretary followed or did not follow such a recommendation, and, if not followed, the reasons why such a recommendation was not followed.

(g) Labeling changes

(1) Dispute resolution

(A) Request for labeling change and failure to agree

If, on or after September 27, 2007, the Commissioner determines that a sponsor and the Commissioner have been unable to reach agreement on appropriate changes to the labeling for the drug that is the subject of the application or supplement, not later than 180 days after the date of the submission of the application or supplement that receives a priority review or 330 days after the date of the submission of an application or supplement that receives a standard review—

(i) the Commissioner shall request that the sponsor of the application make any labeling change that the Commissioner determines to be appropriate; and

(ii) if the sponsor does not agree within 30 days after the Commissioner's request to make a labeling change requested by the Commissioner, the Commissioner shall refer the matter to the Pediatric Advisory Committee.

(B) Action by the Pediatric Advisory Committee

Not later than 90 days after receiving a referral under subparagraph (A)(ii), the Pediatric Advisory Committee shall—

(i) review the pediatric study reports; and

(ii) make a recommendation to the Commissioner concerning appropriate labeling changes, if any.

(C) Consideration of recommendations

The Commissioner shall consider the recommendations of the Pediatric Advisory Committee and, if appropriate, not later than 30 days after receiving the recommendation, make a request to the sponsor of the application or supplement to make any labeling changes that the Commissioner determines to be appropriate.

(D) Misbranding

If the sponsor of the application or supplement, within 30 days after receiving a request under subparagraph (C), does not agree to make a labeling change requested by the Commissioner, the Commissioner may deem the drug that is the subject of the application or supplement to be misbranded.

(E) No effect on authority

Nothing in this subsection limits the authority of the United States to bring an enforcement action under this chapter when a drug lacks appropriate pediatric labeling. Neither course of action (the Pediatric Advisory Committee process or an enforcement action referred to in the preceding sentence) shall preclude, delay, or serve as the basis to stay the other course of action.

(2) Other labeling changes

If, on or after September 27, 2007, the Secretary makes a determination that a pediatric assessment conducted under this section does or does not demonstrate that the drug that is the subject of such assessment is safe and effective in pediatric populations or subpopulations, including whether such assessment results are inconclusive, the Secretary shall order the labeling of such product to include information about the results of the assessment and a statement of the Secretary's determination.

(h) Dissemination of pediatric information

(1) In general

Not later than 210 days after the date of submission of an application (or supplement to an application) that contains a pediatric assessment under this section, if the application (or supplement) receives a priority review, or not later than 330 days after the date of submission of an application (or supplement to an application) that contains a pediatric assessment under this section, if the application (or supplement) receives a standard review, the Secretary shall make available to the public in an easily accessible manner the medical, statistical, and clinical pharmacology reviews of such pediatric assessments, and shall post such assessments on the Web site of the Food and Drug Administration.

(2) Dissemination of information regarding labeling changes

Beginning on September 27, 2007, the Secretary shall require that the sponsors of the assessments that result in labeling changes that are reflected in the annual summary developed pursuant to subsection (f)(6)(H) distribute such information to physicians and other health care providers.

(3) Effect of subsection

Nothing in this subsection shall alter or amend section 331(j) of this title or section 552 of title 5 or section 1905 of title 18.

(i) Adverse event reporting

(1) Reporting in first 18-month period

Beginning on September 27, 2007, during the 18-month period beginning on the date a labeling change is made pursuant to subsection (g), the Secretary shall ensure that all adverse event reports that have been received for such drug (regardless of when such report was received) are referred to the Office of Pediatric Therapeutics. In considering such reports, the Director of such Office shall provide for the review of such reports by the Pediatric Advisory Committee, including obtaining any recommendations of such committee regarding whether the Secretary should take action under this chapter in response to such reports.

(2) Reporting in subsequent periods

Following the 18-month period described in paragraph (1), the Secretary shall, as appropriate, refer to the Office of Pediatric Therapeutics all pediatric adverse event reports for a drug for which a pediatric study was conducted under this section. In considering such reports, the Director of such Office may provide for the review of such reports by the Pediatric Advisory Committee, including obtaining any recommendation of such Committee regarding whether the Secretary should take action in response to such reports.

(3) Preservation of authority

Nothing in this subsection shall prohibit the Office of Pediatric Therapeutics from providing for the review of adverse event reports by the Pediatric Advisory Committee prior to the 18-month period referred to in paragraph (1), if such review is necessary to ensure safe use of a drug in a pediatric population.

(4) Effect

The requirements of this subsection shall supplement, not supplant, other review of such adverse event reports by the Secretary.

(j) Scope of authority

Nothing in this section provides to the Secretary any authority to require a pediatric assessment of any drug or biological product, or any assessment regarding other populations or uses of a drug or biological product, other than the pediatric assessments described in this section.

(k) Relation to orphan drugs

(1) In general; exemption for orphan indications

Unless the Secretary requires otherwise by regulation and except as provided in paragraph (2), this section does not apply to any drug or biological product for an indication for which orphan designation has been granted under section 360bb of this title.

(2) Applicability despite orphan designation of certain indications

This section shall apply with respect to a drug or biological product for which an indication has been granted orphan designation under 360bb[1] of this title if the investigation described in subsection (a)(3) applies to the drug or biological product as described in subsection (a)(1)(B).

(*l*) New active ingredient

(1) Non-interchangeable biosimilar biological product

A biological product that is biosimilar to a reference product under section 262 of title 42, and that the Secretary has not determined to meet the standards described in subsection (k)(4) of such section for interchangeability with the reference product, shall be considered to have a new active ingredient under this section.

(2) Interchangeable biosimilar biological product

A biological product that is interchangeable with a reference product under section 262 of title 42 shall not be considered to have a new active ingredient under this section.

(m) List of primary molecular targets

(1) In general

Within one year of August 18, 2017, the Secretary shall establish and update regularly, and shall publish on the internet website of the Food and Drug Administration—

(A) a list of molecular targets considered, on the basis of data the Secretary determines to be adequate, to be substantially relevant to the growth and progression of a pediatric cancer, and that may trigger the requirements under this section; and

(B) a list of molecular targets of new cancer drugs and biological products in development for which pediatric cancer study requirements under this section will be automatically waived.

(2) Consultation

In establishing the lists described in paragraph (1), the Secretary shall consult the National Cancer Institute, members of the internal committee under section 355d of this title, and the Pediatric Oncology Subcommittee of the Oncologic Drugs Advisory Committee, and shall take into account comments from the meeting under subsection (c).

(3) Rule of construction

Nothing in paragraph (1) shall be construed—

(A) to require the inclusion of a molecular target on the list published under such paragraph as a condition for triggering the requirements under subsection (a)(1)(B) with respect to a drug or biological product directed at such molecular target; or

(B) to authorize the disclosure of confidential commercial information, as prohibited under section 331(j) of this title or section 1905 of title 18.

[1] So in original. Probably should be preceded by ''section''.

(June 25, 1938, ch. 675, § 505B, as added Pub. L. 108–155, § 2(a), Dec. 3, 2003, 117 Stat. 1936; amended Pub. L. 110–85, title IV, § 402(a), Sept. 27, 2007, 121 Stat. 866; Pub. L. 111–148, title VII, § 7002(d)(2), Mar. 23, 2010, 124 Stat. 816; Pub. L. 112–144, title V, §§ 501(b), 505–506(b), 509(b), July 9, 2012, 126 Stat. 1040–1044, 1048; Pub. L. 114–255, div. A, title III, §§ 3101(a)(2)(D), 3102(3), Dec. 13, 2016, 130 Stat. 1153, 1156; Pub. L. 115–52, title V, §§ 503–504(b), 505(e), Aug. 18, 2017, 131 Stat. 1038–1041, 1047; Pub. L. 117–328, div. FF, title II, § 2515(c), Dec. 29, 2022, 136 Stat. 5806.)

Editorial Notes

AMENDMENTS

2022—Subsec. (f)(6)(I). Pub. L. 117–328 substituted ''subsection (a)(4)(C)'' for ''subsection (a)(3)(B)''.

2017—Subsec. (a)(1). Pub. L. 115–52, § 504(a)(1)(A), designated existing provisions as subpar. (A) and inserted heading, substituted ''Except with respect to an application for which subparagraph (B) applies, a person'' for ''A person'', redesignated former subpars. (A) and (B) as cls. (i) and (ii), respectively, of subpar. (A) and realigned margins, substituted ''; or'' for '', or'' at end of subpar. (A)(i), and added subpar. (B).

Subsec. (a)(2)(A). Pub. L. 115–52, § 504(a)(1)(B), substituted ''paragraph (1)(A)'' for ''paragraph (1)'' in introductory provisions.

Subsec. (a)(3). Pub. L. 115–52, § 504(a)(1)(D), added par. (3). Former par. (3) redesignated (4).

Subsec. (a)(4). Pub. L. 115–52, § 504(a)(1)(C), redesignated par. (3) as (4). Former par. (4) redesignated (5).

Subsec. (a)(4)(A). Pub. L. 115–52, § 504(a)(1)(E)(i), substituted ''assessments required under paragraph (1)(A) or reports on the investigation required under paragraph (1)(B)'' for ''assessments required under paragraph (1)'' in introductory provisions.

Subsec. (a)(4)(A)(ii)(I). Pub. L. 115–52, § 504(a)(1)(E)(ii), inserted ''or reports on the investigation'' after ''assessments''.

Subsec. (a)(4)(B)(i). Pub. L. 115–52, § 504(a)(1)(E)(i), substituted ''assessments required under paragraph (1)(A) or reports on the investigation required under paragraph (1)(B)'' for ''assessments required under paragraph (1)'' in introductory provisions.

Subsec. (a)(4)(B)(ii). Pub. L. 115–52, § 504(a)(1)(E)(iii), substituted ''assessment under paragraph (1)(A) or reports on the investigation under paragraph (1)(B)'' for ''assessment under paragraph (1)''.

Subsec. (a)(4)(C)(ii)(II). Pub. L. 115–52, § 504(a)(1)(E)(iv), inserted ''or investigation'' after ''assessment''.

Subsec. (a)(5). Pub. L. 115–52, § 504(a)(1)(C), redesignated par. (4) as (5).

Subsec. (a)(5)(A), (B). Pub. L. 115–52, § 504(a)(1)(F), inserted ''or reports on the investigation'' after ''assessments'' in introductory provisions.

Subsec. (d). Pub. L. 115–52, § 504(a)(2), inserted ''and reports on the investigation'' after ''Submission of assessments'' in heading and, in introductory provisions, inserted ''or the investigation described in subsection (a)(3)'' after ''assessment described in subsection (a)(2)'' and substituted ''subsection (a)(4)'' for ''subsection (a)(3)''.

Subsec. (d)(1). Pub. L. 115–52, § 505(e), inserted at end ''The Secretary shall inform the Pediatric Advisory Committee of letters issued under this paragraph and responses to such letters.''

Subsec. (d)(2). Pub. L. 115–52, § 504(a)(2)(A), (C), in introductory provisions, inserted ''or the investigation described in subsection (a)(3)'' after ''assessment described in subsection (a)(2)'' and substituted ''subsection (a)(4)'' for ''subsection (a)(3)''.

Subsec. (e)(1). Pub. L. 115–52, § 504(a)(3)(A), inserted ''or the investigation described in subsection (a)(3)'' after ''under subsection (a)(2)''.

Subsec. (e)(2). Pub. L. 115–52, § 503(b)(1), substituted ''meetings'' for ''meeting'' in heading.

Subsec. (e)(2)(A)(i). Pub. L. 115–52, § 504(a)(3)(B), inserted ''or the investigation described in subsection (a)(3)'' after ''under subsection (a)(2)''.

Subsec. (e)(2)(C). Pub. L. 115–52, § 503(b)(2), substituted ''Meetings'' for ''Meeting'' in heading.

Subsec. (e)(2)(C)(i). Pub. L. 115–52, § 503(a), amended cl. (i) generally. Prior to amendment, cl. (i) read as follows: ''shall meet with the applicant to discuss the initial pediatric study plan as soon as practicable, but not later than 90 calendar days after the receipt of such plan under subparagraph (A);''.

Subsec. (e)(2)(C)(ii), (iii). Pub. L. 115–52, § 503(b)(3), substituted ''no meeting under clause (i)(II)'' for ''no meeting''.

Subsec. (e)(3). Pub. L. 115–52, § 503(b)(4), substituted ''meeting under paragraph (2)(C)(i)(II)'' for ''meeting under paragraph (2)(C)(i)''.

Subsec. (k). Pub. L. 115–52, § 504(b), amended subsec. (k) generally. Prior to amendment, text read as follows: ''Unless the Secretary requires otherwise by regulation, this section does not apply to any drug for an indication for which orphan designation has been granted under section 360bb of this title.''

Subsec. (m). Pub. L. 115–52, § 504(a)(4), added subsec. (m).

2016—Subsec. (e)(2)(A). Pub. L. 114–255, § 3101(a)(2)(D)(i)(I)(aa), inserted ''study'' after ''initial pediatric'' in introductory and concluding provisions.

Subsec. (e)(2)(B). Pub. L. 114–255, § 3101(a)(2)(D)(i)(I)(bb), substituted ''Content of initial pediatric study plan'' for ''Content of initial plan'' in heading.

Subsec. (e)(5). Pub. L. 114–255, § 3101(a)(2)(D)(i)(II), inserted ''agreed initial pediatric study'' before ''plan'' in heading.

Subsec. (e)(6). Pub. L. 114–255, § 3101(a)(2)(D)(i)(III), substituted ''agreed initial pediatric study plan'' for ''agreed initial pediatric plan''.

Subsec. (f)(1). Pub. L. 114–255, § 3101(a)(2)(D)(ii), inserted ''and any significant amendments to such plans,'' after ''agreed initial pediatric study plans,''.

Subsecs. (*l*), (m). Pub. L. 114–255, § 3102(3), redesignated subsec. (m) as (*l*) and struck out former subsec. (*l*) which related to Institute of Medicine study.

2012—Subsec. (a)(1). Pub. L. 112–144, § 509(b)(1)(A), inserted ''for a drug'' after ''(or supplement to an application)'' in introductory provisions.

Subsec. (a)(3)(A)(ii)(II). Pub. L. 112–144, § 506(b)(1), amended subcl. (II) generally. Prior to amendment, subcl. (II) read as follows: ''a description of the planned or ongoing studies;''.

Subsec. (a)(3)(B), (C). Pub. L. 112–144, § 505(a)(1)(A), (B), added subpar. (B) and redesignated former subpar. (B) as (C).

Subsec. (a)(3)(C)(i)(III), (IV). Pub. L. 112–144, § 505(a)(1)(C)(i), added subcls. (III) and (IV).

Subsec. (a)(3)(C)(ii). Pub. L. 112–144, § 505(a)(1)(C)(ii), amended cl. (ii) generally. Prior to amendment, text read as follows: ''The information submitted through the annual review under clause (i) shall promptly be made available to the public in an easily accessible manner, including through the Web site of the Food and Drug Administration.''

Subsec. (a)(4)(C). Pub. L. 112–144, § 509(b)(1)(B), inserted ''partial'' after ''If a'' in first sentence and substituted ''such a'' for ''either a full or'' in second sentence.

Subsec. (b)(1). Pub. L. 112–144, § 509(b)(2), substituted ''The'' for ''After providing notice in the form of a letter (that, for a drug approved under section 355 of this title, references a declined written request under section 355a of this title for a labeled indication which written request is not referred under section 355a(n)(1)(A) of this title to the Foundation of the National Institutes of Health for the pediatric studies), the'' in introductory provisions.

Subsec. (d). Pub. L. 112–144, § 505(c)(1), amended subsec. (d) generally. Prior to amendment, subsec. (d) related to submission of assessments.

Subsec. (e). Pub. L. 112–144, § 506(a), amended subsec. (e) generally. Prior to amendment, text read as follows: ''Before and during the investigational process for a new drug or biological product, the Secretary shall meet at appropriate times with the sponsor of the new drug or biological product to discuss—

''(1) information that the sponsor submits on plans and timelines for pediatric studies; or

''(2) any planned request by the sponsor for waiver or deferral of pediatric studies.''

Subsec. (f). Pub. L. 112–144, § 506(b)(2)(A), substituted ''pediatric study plans,'' for ''pediatric plans,'' in heading.

Pub. L. 112–144, § 505(a)(2)(A), inserted ''deferral extensions,'' after ''deferrals,'' in heading.

Subsec. (f)(1). Pub. L. 112–144, § 506(b)(2)(B), substituted ''initial pediatric study plans, agreed initial pediatric study plans,'' for ''all pediatric plans''.

Pub. L. 112–144, § 505(a)(2)(B), inserted '', deferral extension,'' after ''deferral''.

Subsec. (f)(4). Pub. L. 112–144, § 506(b)(2)(C), substituted ''pediatric study plans,'' for ''pediatric plans,'' in heading and ''initial pediatric study plans, agreed initial pediatric study plans,'' for ''pediatric plans'' in text.

Pub. L. 112–144, § 505(a)(2)(C), inserted ''deferral extensions,'' after ''deferrals,'' in heading and '', deferral extensions,'' after ''deferrals'' in text.

Subsec. (f)(6)(D). Pub. L. 112–144, § 505(b), amended subpar. (D) generally. Prior to amendment, subpar. (D) read as follows: ''the total number of deferrals requested and granted under this section and, if granted, the reasons for such deferrals, the timeline for completion, and the number completed and pending by the specified date, as outlined in subsection (a)(3);''.

Subsec. (f)(6)(D)(iv). Pub. L. 112–144, § 505(c)(2), added cl. (iv).

Subsec. (g)(1)(A). Pub. L. 112–144, § 509(b)(3)(A), inserted ''that receives a priority review or 330 days after the date of the submission of an application or supplement that receives a standard review'' after ''after the date of the submission of the application or supplement'' in introductory provisions.

Subsec. (g)(2). Pub. L. 112–144, § 509(b)(3)(B), substituted ''the labeling of such product'' for ''the label of such product''.

Subsec. (h)(1). Pub. L. 112–144, § 509(b)(4), inserted ''an application (or supplement to an application) that contains'' after ''date of submission of'' and ''if the application (or supplement) receives a priority review, or not later than 330 days after the date of submission of an application (or supplement to an application) that contains a pediatric assessment under this section, if the application (or supplement) receives a standard review,'' after ''under this section,''.

Subsec. (i)(1). Pub. L. 112–144, § 509(b)(5)(A), substituted ''first 18-month period'' for ''year one'' in heading and ''18-month'' for ''one-year'' in text.

Subsec. (i)(2). Pub. L. 112–144, § 509(b)(5)(B), substituted ''periods'' for ''years'' in heading and ''18-month period'' for ''one-year period'' in text.

Subsec. (i)(3), (4). Pub. L. 112–144, § 509(b)(5)(C), (D), added par. (3) and redesignated former par. (3) as (4).

Subsecs. (m), (n). Pub. L. 112–144, § 501(b), redesignated subsec. (n) as (m) and struck out former subsec. (m). Prior to amendment, text of subsec. (m) read as follows: ''The authority under this section shall remain in effect so long as an application subject to this section may be accepted for filing by the Secretary on or before the date specified in section 355a(q) of this title.''

2010—Subsec. (n). Pub. L. 111–148 added subsec. (n).

2007—Pub. L. 110–85 amended section generally. Prior to amendment, section related to required submission of assessments with an application for a new drug or new biological product and by order of the Secretary for certain marketed drugs and biological products used for pediatric patients, a definition of meaningful therapeutic benefit, consequences of failure to submit required assessments, meetings of the Secretary and the sponsor of a new drug or biological product, a limitation of the scope of the Secretary's authority, appli-

cation to orphan drugs, and integration with other pediatric studies.

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 2012 AMENDMENT

Pub. L. 112–144, title V, § 506(c), July 9, 2012, 126 Stat. 1045, provided that:

''(1) IN GENERAL.—Subject to paragraph (2), the amendments made by this section [amending this section] shall take effect 180 calendar days after the date of enactment of this Act [July 9, 2012], irrespective of whether the Secretary [of Health and Human Services] has promulgated final regulations to carry out such amendments.

''(2) RULE OF CONSTRUCTION.—Paragraph (1) shall not be construed to affect the deadline for promulgation of proposed regulations under section 505B(e)(7) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355c(e)(7)], as added by subsection (a) of this section.''

Notwithstanding any provision of this section stating that a provision applies beginning on Sept. 27, 2007, any amendment made by Pub. L. 112–144 to such a provision applies beginning on July 9, 2012, subject to a transitional rule, see section 509(g) of Pub. L. 112–144, set out as a note under section 355a of this title.

EFFECTIVE DATE OF 2007 AMENDMENT

Pub. L. 110–85, title IV, § 402(b), Sept. 27, 2007, 121 Stat. 875, provided that:

''(1) IN GENERAL.—Notwithstanding subsection (h) of section 505B of the Federal Food, Drug and Cosmetic Act [21 U.S.C. 355c(h)], as in effect on the day before the date of the enactment of this Act [Sept. 27, 2007], a pending assessment, including a deferred assessment, required under such section 505B shall be deemed to have been required under section 505B of the Federal Food, Drug and Cosmetic Act as in effect on or after the date of the enactment of this Act.

''(2) CERTAIN ASSESSMENTS AND WAIVER REQUESTS.—An assessment pending on or after the date that is 1 year prior to the date of the enactment of this Act shall be subject to the tracking and disclosure requirements established under such section 505B, as in effect on or after such date of enactment, except that any such assessments submitted or waivers of such assessments requested before such date of enactment shall not be subject to subsections (a)(4)(C), (b)(2)(C), (f)(6)(F), and (h) of such section 505B.''

EFFECTIVE DATE

Pub. L. 108–155, § 4, Dec. 3, 2003, 117 Stat. 1942, provided that:

''(a) IN GENERAL.—Subject to subsection (b), this Act [enacting this section, amending sections 355, 355a, and 355b of this title and sections 262 and 284m of Title 42, The Public Health and Welfare, enacting provisions set out as a note under section 301 of this title, and amending provisions set out as notes under section 355a of this title and section 284m of Title 42] and the amendments made by this Act take effect on the date of enactment of this Act [Dec. 3, 2003].

''(b) APPLICABILITY TO NEW DRUGS AND BIOLOGICAL PRODUCTS.—

''(1) IN GENERAL.—Subsection (a) of section 505B of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355c(a)] (as added by section 2) shall apply to an application described in paragraph (1) of that subsection submitted to the Secretary of Health and Human Services on or after April 1, 1999.

''(2) WAIVERS AND DEFERRALS.—

''(A) WAIVER OR DEFERRAL GRANTED.—If, with respect to an application submitted to the Secretary of Health and Human Services between April 1, 1999, and the date of enactment of this Act [Dec. 3, 2003], a waiver or deferral of pediatric assessments was granted under regulations of the Secretary then in effect, the waiver or deferral shall be a waiver or deferral under subsection (a) of section 505B of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355c(a)], except that any date specified in such a deferral shall be extended by the number of days that is equal to the number of days between October 17, 2002, and the date of enactment of this Act.

''(B) WAIVER AND DEFERRAL NOT GRANTED.—If, with respect to an application submitted to the Secretary of Health and Human Services between April 1, 1999, and the date of enactment of this Act [Dec. 3, 2003], neither a waiver nor deferral of pediatric assessments was granted under regulations of the Secretary then in effect, the person that submitted the application shall be required to submit assessments under subsection (a)(2) of section 505B of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355c(a)(2)] on the date that is the later of—

''(i) the date that is 1 year after the date of enactment of this Act; or

''(ii) such date as the Secretary may specify under subsection (a)(3) of that section;

unless the Secretary grants a waiver under subsection (a)(4) of that section.

''(c) NO LIMITATION OF AUTHORITY.—Neither the lack of guidance or regulations to implement this Act or the amendments made by this Act nor the pendency of the process for issuing guidance or regulations shall limit the authority of the Secretary of Health and Human Services under, or defer any requirement under, this Act or those amendments.''

RULE OF CONSTRUCTION

Pub. L. 115–52, title V, § 504(e), Aug. 18, 2017, 131 Stat. 1045, provided that: ''Nothing in this section [amending this section and section 355c–1 of this title and enacting provisions set out as a note below], including the amendments made by this section, shall limit the authority of the Secretary of Health and Human Services to issue written requests under section 505A of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a) or section 351(m) of the Public Health Service Act (42 U.S.C. 262(m)), or to negotiate or implement amendments to such requests proposed by the an [sic] applicant.''

MEETING, CONSULTATION, AND GUIDANCE

Pub. L. 115–52, title V, § 504(c), Aug. 18, 2017, 131 Stat. 1041, provided that:

''(1) MEETING.—The Secretary of Health and Human Services (referred to in this subsection as the 'Secretary'), acting through the Commissioner of Food and Drugs and in collaboration with the Director of the National Cancer Institute, shall convene a public meeting not later than 1 year after the date of enactment of this Act [Aug. 18, 2017] to solicit feedback from physicians and researchers (including pediatric oncologists and rare disease specialists), patients, and other stakeholders to provide input on development of the guidance under paragraph (2) and the list under subsection (m) of section 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355c), as added by subsection (a). The Secretary shall seek input at such meeting on—

''(A) the data necessary to determine that there is scientific evidence that a drug or biological product is directed at a molecular target that is considered to be substantially relevant to the growth or progression of a pediatric cancer;

''(B) the data necessary to determine that there is scientific evidence that a molecular target is considered to be substantially relevant to the growth or progression of a pediatric cancer;

''(C) the data needed to meet the requirement of conducting an investigation described in section 505B(a)(3) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355c(a)(3)], as amended by subsection (a);

''(D) considerations when developing the list under section 505B(m) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355c(m)] that contains molecular targets shared between different tumor types;

''(E) the process the Secretary shall utilize to update regularly a list of molecular targets that may trigger a pediatric study under section 505B of the Federal Food, Drug, and Cosmetic Act, as so amended, and how often such updates shall occur;

''(F) how to overcome the challenges related to pediatric cancer drug and biological product development, including issues related to the ethical, practical, and other barriers to conducting clinical trials in pediatric cancer with small patient populations;

''(G) scientific or operational challenges associated with performing an investigation described in section 505B(a)(1)(B) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355c(a)(1)(B)], including the effect on pediatric studies currently underway in a pediatric patient population, treatment of a pediatric patient population, and the ability to complete adult clinical trials;

''(H) the advantages and disadvantages of innovative clinical trial designs in addressing the development of cancer drugs or biological products directed at molecular targets in pediatric cancer patients;

''(I) the ways in which the Secretary can improve the current process outlined under sections 505A and 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a, 355c) to encourage additional research and development of pediatric cancer treatments;

''(J) the ways in which the Secretary might streamline and improve the written request process, including when studies contained in a request under such section 505A are not feasible due to the ethical, practical, or other barriers to conducting clinical trials in pediatric cancer populations;

''(K) how the Secretary will facilitate collaboration among pediatric networks, academic centers and experts in pediatric cancer to conduct an investigation described in such section 505B(a)(3);

''(L) how the Secretary may facilitate collaboration among sponsors of same-in-class drugs and biological products that would be subject to the requirements for an investigation under such section 505B based on shared molecular targets; and

''(M) the ways in which the Secretary will help to mitigate the risks, if any, of discouraging the research and development of orphan drugs when implementing such section 505B as amended.

''(2) GUIDANCE.—Not later than 2 years after the date of enactment of this Act [Aug. 18, 2017], the Secretary, acting through the Commissioner of Food and Drugs, shall issue final guidance on implementation of the amendments to section 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355c) regarding molecularly targeted cancer drugs made by this section, including—

''(A) the scientific criteria, types of data, and regulatory considerations for determining whether a molecular target is substantially relevant to the growth or progression of a pediatric cancer and would trigger an investigation under section 505B of the Federal Food, Drug, and Cosmetic Act, as amended;

''(B) the process by which the Secretary will engage with sponsors to discuss determinations, investigation requirements, deferrals, waivers, and any other issues that need to be resolved to ensure that any required investigation based on a molecular target can be reasonably conducted;

''(C) the scientific or operational challenges for which the Secretary may issue deferrals or waivers for an investigation described in subsection (a)(3) of such section 505B, including adverse impacts on current pediatric studies underway in a pediatric patient population, studies involving drugs designated as orphan drugs, treatment of a pediatric patient population, or the ability to complete adult clinical trials;

''(D) how the Secretary and sponsors will facilitate collaboration among pediatric networks, academic centers, and experts in pediatric cancer to conduct an investigation described in subsection (a)(3) of such section 505B;

''(E) scientific and regulatory considerations for study designs, including the applicability of innovative clinical trial designs for pediatric cancer drug and biological product developments under sections 505A and 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a, 355c);

''(F) approaches to streamline and improve the amendment process, including when studies contained in a request under such section 505A are not feasible due to the ethical, practical, or other barriers to conducting clinical trials in pediatric cancer populations;

''(G) the process for submission of an initial pediatric study plan for the investigation described in section 505B(a)(3) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355c(a)(3)), including the process for a sponsor to meet and reach agreement with the Secretary on the initial pediatric study plan; and

''(H) considerations for implementation of such section 505B, as so amended, and waivers of the requirements of such section 505B with regard to molecular targets for which several drugs or biological products may be under investigation.''

§ 355c–1. Report

(a) In general

Not later than four years after July 9, 2012, and every five years thereafter, the Secretary shall prepare and submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives, and make publicly available, including through posting on the Internet Web site of the Food and Drug Administration, a report on the implementation of sections 355a and 355c of this title.

(b) Contents

Each report under subsection (a) shall include—

(1) an assessment of the effectiveness of sections 355a and 355c of this title in improving information about pediatric uses for approved drugs and biological products, including the number and type of labeling changes made since July 9, 2012, and the importance of such uses in the improvement of the health of children;

(2) the number of required studies under such section 355c of this title that have not met the initial deadline provided under such section 355c of this title, including—

(A) the number of deferrals and deferral extensions granted and the reasons such extensions were granted;

(B) the number of waivers and partial waivers granted; and

(C) the number of letters issued under subsection (d) of such section 355c of this title;

(3) an assessment of the timeliness and effectiveness of pediatric study planning since July 9, 2012, including the number of initial pediatric study plans not submitted in accordance with the requirements of subsection (e) of such section 355c of this title and any resulting rulemaking;

(4) the number of written requests issued, accepted, and declined under such section 355a of this title since July 9, 2012, and a listing of any important gaps in pediatric information as a result of such declined requests;

(5) a description and current status of referrals made under subsection (n) of such section 355a of this title;

(6) an assessment of the effectiveness of studying biological products in pediatric popu-

lations under such sections 355a and 355c of this title and section 284m of title 42;

(7)(A) the efforts made by the Secretary to increase the number of studies conducted in the neonatal population (including efforts made to encourage the conduct of appropriate studies in neonates by companies with products that have sufficient safety and other information to make the conduct of the studies ethical and safe); and

(B) the results of such efforts;

(8)(A) the number and importance of drugs and biological products for children with cancer that are being tested as a result of the programs under such sections 355a and 355c of this title and under section 284m of title 42; and

(B) any recommendations for modifications to such programs that would lead to new and better therapies for children with cancer, including a detailed rationale for each recommendation;

(9) any recommendations for modification to such programs that would improve pediatric drug research and increase pediatric labeling of drugs and biological products;

(10) an assessment of the successes of and limitations to studying drugs for rare diseases under such sections 355a and 355c of this title;

(11) an assessment of the impact of the amendments to such section 355c of this title made by the FDA Reauthorization Act of 2017 on pediatric research and labeling of drugs and biological products and pediatric labeling of molecularly targeted drugs and biological products for the treatment of cancer;

(12) an assessment of the efforts of the Secretary to implement the plan developed under section 505C–1 of the Federal Food, Drug, and Cosmetic Act,[1] regarding earlier submission of pediatric studies under sections 355a and 355c of this title and section 262(m) of title 42, including—

(A) the average length of time after the approval of an application under section 355(b)(1) of this title or section 262(a) of title 42 before studies conducted pursuant to such section 355a of this title, 355c of this title, or section 262(m) of title 42 are completed, submitted, and incorporated into labeling;

(B) the average length of time after the receipt of a proposed pediatric study request before the Secretary responds to such request;

(C) the average length of time after the submission of a proposed pediatric study request before the Secretary issues a written request for such studies;

(D) the number of written requests issued for each investigational new drug or biological product prior to the submission of an application under section 355(b)(1) of this title or section 262(a) of title 42; and

(E) the average number, and range of numbers, of amendments to written requests issued, and the time the Secretary requires to review and act on proposed amendments to written requests;

(13) a list of sponsors of applications or holders of approved applications who received exclusivity under such section 355a of this title or such section 262(m) of title 42 after receiving a letter issued under such section 355c(d)(1) of this title for any drug or biological product before the studies referred to in such letter were completed and submitted;

(14) a list of assessments and investigations required under such section 355c of this title;

(15) how many requests under such section 355a of this title for molecular targeted cancer drugs, as defined by subsection (a)(1)(B) of such section 355c of this title, approved prior to 3 years after August 18, 2017, have been issued by the Food and Drug Administration, and how many such requests have been completed; and

(16) the Secretary's assessment of the overall impact of the amendments made by section 504 of the FDA Reauthorization Act of 2017 on the conduct and effectiveness of pediatric cancer research and the orphan drug program, as well any subsequent recommendations.

(c) Stakeholder comment

At least 180 days prior to the submission of each report under subsection (a), the Secretary shall consult with representatives of patient groups (including pediatric patient groups), consumer groups, regulated industry, academia, and other interested parties to obtain any recommendations or information relevant to the report including suggestions for modifications that would improve pediatric drug research and pediatric labeling of drugs and biological products.

(Pub. L. 112–144, title V, § 508, July 9, 2012, 126 Stat. 1045; Pub. L. 115–52, title V, § 504(d), Aug. 18, 2017, 131 Stat. 1044.)

Editorial Notes

REFERENCES IN TEXT

The FDA Reauthorization Act of 2017, referred to in subsec. (b)(11), (16), is Pub. L. 115–52, Aug. 18, 2017, 131 Stat. 1005. Section 504 of the Act amended this section and section 355c of this title. For complete classification of this Act to the Code, see Short Title of 2017 Amendment note set out under section 301 of this title and Tables.

Section 505C–1 of the Federal Food, Drug, and Cosmetic Act, referred to in subsec. (b)(12), probably means section 505(c) of Pub. L. 115–52, the FDA Reauthorization Act of 2017, which is set out as a note under section 355a of this title. The Federal Food, Drug, and Cosmetic Act does not contain a section 505C–1, and section 505(c) of the FDA Reauthorization Act of 2017 relates to the development and implementation of a plan for earlier submission of pediatric studies under sections 355a and 355c of this title and section 262(m) of Title 42, The Public Health and Welfare.

CODIFICATION

Section was enacted as part of the Food and Drug Administration Safety and Innovation Act, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

AMENDMENTS

2017—Subsec. (b)(11) to (16). Pub. L. 115–52 added pars. (11) to (16) and struck out former par. (11) which read as follows: ''an assessment of the Secretary's efforts to address the suggestions and options described in any prior report issued by the Comptroller General, Institute of Medicine, or the Secretary, and any subsequent

[1] See References in Text note below.

reports, including recommendations therein, regarding the topics addressed in the reports under this section, including with respect to—

''(A) improving public access to information from pediatric studies conducted under such sections 355a and 355c of this title; and

''(B) improving the timeliness of pediatric studies and pediatric study planning under such sections 355a and 355c of this title.''

Statutory Notes and Related Subsidiaries

RULE OF CONSTRUCTION

Nothing in amendment by Pub. L. 115–52 to limit the authority of the Secretary of Health and Human Services to issue written requests under section 355a of this title or section 262(m) of Title 42, The Public Health and Welfare, or to negotiate or implement amendments to such requests proposed by applicants, see section 504(e) of Pub. L. 115–52, set out as a note under section 355c of this title.

DEFINITION OF ''SECRETARY''

The term ''Secretary'' as used in this section means the Secretary of Health and Human Services, see section 503 of Pub. L. 112–144, set out as a note under section 355a of this title.

§ 355d. Internal committee for review of pediatric plans, assessments, deferrals, deferral extensions, and waivers

The Secretary shall establish an internal committee within the Food and Drug Administration to carry out the activities as described in sections 355a(f) and 355c(f) of this title. Such internal committee shall include employees of the Food and Drug Administration, with expertise in pediatrics (including representation from the Office of Pediatric Therapeutics), biopharmacology, statistics, chemistry, legal issues, pediatric ethics, neonatology, and the appropriate expertise pertaining to the pediatric product under review, such as expertise in child and adolescent psychiatry or pediatric rare diseases, and other individuals designated by the Secretary.

(June 25, 1938, ch. 675, § 505C, as added Pub. L. 110–85, title IV, § 403, Sept. 27, 2007, 121 Stat. 875; amended Pub. L. 112–144, title V, § 509(c), July 9, 2012, 126 Stat. 1049; Pub. L. 115–52, title V, § 505(f), Aug. 18, 2017, 131 Stat. 1047.)

Editorial Notes

AMENDMENTS

2017—Pub. L. 115–52 inserted ''or pediatric rare diseases'' after ''psychiatry''.

2012—Pub. L. 112–144 inserted ''deferral extensions,'' after ''deferrals,'' in section catchline and ''neonatology,'' after ''pediatric ethics,'' in text.

§ 355e. Pharmaceutical security

(a) In general

The Secretary shall develop standards and identify and validate effective technologies for the purpose of securing the drug supply chain against counterfeit, diverted, subpotent, substandard, adulterated, misbranded, or expired drugs.

(b) Standards development

(1) In general

The Secretary shall, in consultation with the agencies specified in paragraph (4), manufacturers, distributors, pharmacies, and other supply chain stakeholders, prioritize and develop standards for the identification, validation, authentication, and tracking and tracing of prescription drugs.

(2) Standardized numeral identifier

Not later than 30 months after September 27, 2007, the Secretary shall develop a standardized numerical identifier (which, to the extent practicable, shall be harmonized with international consensus standards for such an identifier) to be applied to a prescription drug at the point of manufacturing and repackaging (in which case the numerical identifier shall be linked to the numerical identifier applied at the point of manufacturing) at the package or pallet level, sufficient to facilitate the identification, validation, authentication, and tracking and tracing of the prescription drug.

(3) Promising technologies

The standards developed under this subsection shall address promising technologies, which may include—

(A) radio frequency identification technology;

(B) nanotechnology;

(C) encryption technologies; and

(D) other track-and-trace or authentication technologies.

(4) Interagency collaboration

In carrying out this subsection, the Secretary shall consult with Federal health and security agencies, including—

(A) the Department of Justice;

(B) the Department of Homeland Security;

(C) the Department of Commerce; and

(D) other appropriate Federal and State agencies.

(c) Inspection and enforcement

(1) In general

The Secretary shall expand and enhance the resources and facilities of agency components of the Food and Drug Administration involved with regulatory and criminal enforcement of this chapter to secure the drug supply chain against counterfeit, diverted, subpotent, substandard, adulterated, misbranded, or expired drugs including biological products and active pharmaceutical ingredients from domestic and foreign sources.

(2) Activities

The Secretary shall undertake enhanced and joint enforcement activities with other Federal and State agencies, and establish regional capacities for the validation of prescription drugs and the inspection of the prescription drug supply chain.

(d) Definition

In this section, the term ''prescription drug'' means a drug subject to section 353(b)(1) of this title.

(June 25, 1938, ch. 675, § 505D, as added Pub. L. 110–85, title IX, § 913, Sept. 27, 2007, 121 Stat. 952.)

§ 355f. Extension of exclusivity period for new qualified infectious disease products

(a) Extension

If the Secretary approves an application pursuant to section 355 of this title for a drug that

has been designated as a qualified infectious disease product under subsection (d), the 4- and 5-year periods described in subsections (c)(3)(E)(ii) and (j)(5)(F)(ii) of section 355 of this title, the 3-year periods described in clauses (iii) and (iv) of subsection (c)(3)(E) and clauses (iii) and (iv) of subsection (j)(5)(F) of section 355 of this title, or the 7-year period described in section 360cc of this title, as applicable, shall be extended by 5 years.

(b) Relation to pediatric exclusivity

Any extension under subsection (a) of a period shall be in addition to any extension of the period under section 355a of this title with respect to the drug.

(c) Limitations

Subsection (a) does not apply to the approval of—

(1) a supplement to an application under section 355(b) of this title for any qualified infectious disease product for which an extension described in subsection (a) is in effect or has expired;

(2) a subsequent application filed with respect to a product approved under section 355 of this title for a change that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength;

(3) a product that does not meet the definition of a qualified infectious disease product under subsection (g) based upon its approved uses; or

(4) an application pursuant to section 262(a) of title 42.

(d) Designation

(1) In general

The manufacturer or sponsor of a drug may request the Secretary to designate a drug as a qualified infectious disease product at any time before the submission of an application under section 355(b) of this title or section 262(a) of title 42 for such drug. The Secretary shall, not later than 60 days after the submission of such a request, determine whether the drug is a qualified infectious disease product.

(2) Limitation

Except as provided in paragraph (3), a designation under this subsection shall not be withdrawn for any reason, including modifications to the list of qualifying pathogens under subsection (f)(2)(C).

(3) Revocation of designation

The Secretary may revoke a designation of a drug as a qualified infectious disease product if the Secretary finds that the request for such designation contained an untrue statement of material fact.

(e) Regulations

(1) In general

Not later than 2 years after July 9, 2012, the Secretary shall adopt final regulations implementing this section, including developing the list of qualifying pathogens described in subsection (f).

(2) Procedure

In promulgating a regulation implementing this section, the Secretary shall—

(A) issue a notice of proposed rulemaking that includes the proposed regulation;

(B) provide a period of not less than 60 days for comments on the proposed regulation; and

(C) publish the final regulation not less than 30 days before the effective date of the regulation.

(3) Restrictions

Notwithstanding any other provision of law, the Secretary shall promulgate regulations implementing this section only as described in paragraph (2), except that the Secretary may issue interim guidance for sponsors seeking designation under subsection (d) prior to the promulgation of such regulations.

(4) Designation prior to regulations

The Secretary shall designate drugs as qualified infectious disease products under subsection (d) prior to the promulgation of regulations under this subsection, if such drugs meet the definition of a qualified infectious disease product described in subsection (g).

(f) Qualifying pathogen

(1) Definition

In this section, the term ''qualifying pathogen'' means a pathogen identified and listed by the Secretary under paragraph (2) that has the potential to pose a serious threat to public health, such as—

(A) resistant gram positive pathogens, including methicillin-resistant Staphylococcus aureus, vancomycin-resistant Staphylococcus aureus, and vancomycin-resistant enterococcus;

(B) multi-drug resistant gram negative bacteria, including Acinetobacter, Klebsiella, Pseudomonas, and E. coli species;

(C) multi-drug resistant tuberculosis; and

(D) Clostridium difficile.

(2) List of qualifying pathogens

(A) In general

The Secretary shall establish and maintain a list of qualifying pathogens, and shall make public the methodology for developing such list.

(B) Considerations

In establishing and maintaining the list of pathogens described under this section, the Secretary shall—

(i) consider—

(I) the impact on the public health due to drug-resistant organisms in humans;

(II) the rate of growth of drug-resistant organisms in humans;

(III) the increase in resistance rates in humans; and

(IV) the morbidity and mortality in humans; and

(ii) consult with experts in infectious diseases and antibiotic resistance, including the Centers for Disease Control and Prevention, the Food and Drug Administration, medical professionals, and the clinical research community.

(C) Review

Every 5 years, or more often as needed, the Secretary shall review, provide modifica-

tions to, and publish the list of qualifying pathogens under subparagraph (A) and shall by regulation revise the list as necessary, in accordance with subsection (e).

(g) Qualified infectious disease product

The term ''qualified infectious disease product'' means a drug (including a biological product), including an antibacterial or antifungal drug, for human use that—

(1) acts on bacteria or fungi or on substances produced by such bacteria or fungi; and

(2) is intended to treat a serious or life-threatening infection, including such an infection caused by—

(A) an antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens; or

(B) qualifying pathogens listed by the Secretary under subsection (f).

(June 25, 1938, ch. 675, § 505E, as added Pub. L. 112–144, title VIII, § 801(a), July 9, 2012, 126 Stat. 1077; amended Pub. L. 117–328, div. FF, title III, § 3212(a), Dec. 29, 2022, 136 Stat. 5826.)

Editorial Notes

AMENDMENTS

2022—Subsec. (c)(4). Pub. L. 117–328, § 3212(a)(1), added par. (4).

Subsec. (d)(1). Pub. L. 117–328, § 3212(a)(2), inserted ''or section 262(a) of title 42'' after ''section 355(b) of this title''.

Subsec. (g). Pub. L. 117–328, § 3212(a)(3), amended subsec. (g) generally. Prior to amendment, text read as follows: ''The term 'qualified infectious disease product' means an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections, including those caused by—

''(1) an antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens; or

''(2) qualifying pathogens listed by the Secretary under subsection (f).''

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE

Pub. L. 112–144, title VIII, § 801(b), July 9, 2012, 126 Stat. 1079, provided that: ''Section 505E of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355f], as added by subsection (a), applies only with respect to a drug that is first approved under section 505(c) of such Act (21 U.S.C. 355(c)) on or after the date of the enactment of this Act [July 9, 2012].''

§ 355g. Utilizing real world evidence

(a) In general

The Secretary shall establish a program to evaluate the potential use of real world evidence—

(1) to help to support the approval of a new indication for a drug approved under section 355(c) of this title; and

(2) to help to support or satisfy postapproval study requirements.

(b) Real world evidence defined

In this section, the term ''real world evidence'' means data regarding the usage, or the potential benefits or risks, of a drug derived from sources other than traditional clinical trials.

(c) Program framework

(1) In general

Not later than 2 years after December 13, 2016, the Secretary shall establish a draft framework for implementation of the program under this section.

(2) Contents of framework

The framework shall include information describing—

(A) the sources of real world evidence, including ongoing safety surveillance, observational studies, registries, claims, and patient-centered outcomes research activities;

(B) the gaps in data collection activities;

(C) the standards and methodologies for collection and analysis of real world evidence; and

(D) the priority areas, remaining challenges, and potential pilot opportunities that the program established under this section will address.

(3) Consultation

(A) In general

In developing the program framework under this subsection, the Secretary shall consult with regulated industry, academia, medical professional organizations, representatives of patient advocacy organizations, consumer organizations, disease research foundations, and other interested parties.

(B) Process

The consultation under subparagraph (A) may be carried out through approaches such as—

(i) a public-private partnership with the entities described in such subparagraph in which the Secretary may participate;

(ii) a contract, grant, or other arrangement, as the Secretary determines appropriate, with such a partnership or an independent research organization; or

(iii) public workshops with the entities described in such subparagraph.

(d) Program implementation

The Secretary shall, not later than 3 years after December 13, 2016, and in accordance with the framework established under subsection (c), implement the program to evaluate the potential use of real world evidence.

(e) Guidance for industry

The Secretary shall—

(1) utilize the program established under subsection (a), its activities, and any subsequent pilots or written reports, to inform a guidance for industry on—

(A) the circumstances under which sponsors of drugs and the Secretary may rely on real world evidence for the purposes described in paragraphs (1) and (2) of subsection (a); and

(B) the appropriate standards and methodologies for collection and analysis of real world evidence submitted for such purposes;

(2) not later than 5 years after December 13, 2016, issue draft guidance for industry as described in paragraph (1); and

(3) not later than 18 months after the close of the public comment period for the draft guidance described in paragraph (2), issue revised draft guidance or final guidance.

(f) Rule of construction

(1) In general

Subject to paragraph (2), nothing in this section prohibits the Secretary from using real world evidence for purposes not specified in this section, provided the Secretary determines that sufficient basis exists for any such nonspecified use.

(2) Standards of evidence and Secretary's authority

This section shall not be construed to alter—

(A) the standards of evidence under—

(i) subsection (c) or (d) of section 355 of this title, including the substantial evidence standard in such subsection (d); or

(ii) section 262(a) of title 42; or

(B) the Secretary's authority to require postapproval studies or clinical trials, or the standards of evidence under which studies or trials are evaluated.

(June 25, 1938, ch. 675, § 505F, as added Pub. L. 114–255, div. A, title III, § 3022, Dec. 13, 2016, 130 Stat. 1096; amended Pub. L. 115–52, title IX, § 901(c), (d), Aug. 18, 2017, 131 Stat. 1076.)

Editorial Notes

AMENDMENTS

2017—Subsec. (b). Pub. L. 115–52, § 901(c), substituted ''traditional'' for ''randomized''.

Subsec. (d). Pub. L. 115–52, § 901(d), substituted ''3 years'' for ''2 years''.

§ 355h. Regulation of certain nonprescription drugs that are marketed without an approved drug application

(a) Nonprescription drugs marketed without an approved application

Nonprescription drugs marketed without an approved drug application under section 355 of this title, as of March 27, 2020, shall be treated in accordance with this subsection.

(1) Drugs subject to a final monograph; category I drugs subject to a tentative final monograph

A drug is deemed to be generally recognized as safe and effective under section 321(p)(1) of this title, not a new drug under section 321(p) of this title, and not subject to section 353(b)(1) of this title, if—

(A) the drug is—

(i) in conformity with the requirements for nonprescription use of a final monograph issued under part 330 of title 21, Code of Federal Regulations (except as provided in paragraph (2)), the general requirements for nonprescription drugs, and conditions or requirements under subsections (b), (c), and (k); and

(ii) except as permitted by an order issued under subsection (b) or, in the case of a minor change in the drug, in conformity with an order issued under subsection (c), in a dosage form that, immediately prior to March 27, 2020, has been used to a material extent and for a material time under section 321(p)(2) of this title; or

(B) the drug is—

(i) classified in category I for safety and effectiveness under a tentative final monograph that is the most recently applicable proposal or determination issued under part 330 of title 21, Code of Federal Regulations;

(ii) in conformity with the proposed requirements for nonprescription use of such tentative final monograph, any applicable subsequent determination by the Secretary, the general requirements for nonprescription drugs, and conditions or requirements under subsections (b), (c), and (k); and

(iii) except as permitted by an order issued under subsection (b) or, in the case of a minor change in the drug, in conformity with an order issued under subsection (c), in a dosage form that, immediately prior to March 27, 2020, has been used to a material extent and for a material time under section 321(p)(2) of this title.

(2) Treatment of sunscreen drugs

With respect to sunscreen drugs subject to this section, the applicable requirements in terms of conformity with a final monograph, for purposes of paragraph (1)(A)(i), shall be the requirements specified in part 352 of title 21, Code of Federal Regulations, as published on May 21, 1999, beginning on page 27687 of volume 64 of the Federal Register, except that the applicable requirements governing effectiveness and labeling shall be those specified in section 201.327 of title 21, Code of Federal Regulations.

(3) Category III drugs subject to a tentative final monograph; category I drugs subject to proposed monograph or advance notice of proposed rulemaking

A drug that is not described in paragraph (1), (2), or (4) is not required to be the subject of an application approved under section 355 of this title, and is not subject to section 353(b)(1) of this title, if—

(A) the drug is—

(i) classified in category III for safety or effectiveness in the preamble of a proposed rule establishing a tentative final monograph that is the most recently applicable proposal or determination for such drug issued under part 330 of title 21, Code of Federal Regulations;

(ii) in conformity with—

(I) the conditions of use, including indication and dosage strength, if any, described for such category III drug in such preamble or in an applicable subsequent proposed rule;

(II) the proposed requirements for drugs classified in such tentative final monograph in category I in the most recently proposed rule establishing requirements related to such tentative final monograph and in any final rule es-

tablishing requirements that are applicable to the drug; and

(III) the general requirements for nonprescription drugs and conditions or requirements under subsection (b) or (k); and

(iii) in a dosage form that, immediately prior to March 27, 2020, had been used to a material extent and for a material time under section 321(p)(2) of this title; or

(B) the drug is—

(i) classified in category I for safety and effectiveness under a proposed monograph or advance notice of proposed rulemaking that is the most recently applicable proposal or determination for such drug issued under part 330 of title 21, Code of Federal Regulations;

(ii) in conformity with the requirements for nonprescription use of such proposed monograph or advance notice of proposed rulemaking, any applicable subsequent determination by the Secretary, the general requirements for nonprescription drugs, and conditions or requirements under subsection (b) or (k); and

(iii) in a dosage form that, immediately prior to March 27, 2020, has been used to a material extent and for a material time under section 321(p)(2) of this title.

(4) Category II drugs deemed new drugs

A drug that is classified in category II for safety or effectiveness under a tentative final monograph or that is subject to a determination to be not generally recognized as safe and effective in a proposed rule that is the most recently applicable proposal issued under part 330 of title 21, Code of Federal Regulations, shall be deemed to be a new drug under section 321(p) of this title, misbranded under section 352(ee) of this title, and subject to the requirement for an approved new drug application under section 355 of this title beginning on the day that is 180 calendar days after March 27, 2020, unless, before such day, the Secretary determines that it is in the interest of public health to extend the period during which the drug may be marketed without such an approved new drug application.

(5) Drugs not GRASE deemed new drugs

A drug that the Secretary has determined not to be generally recognized as safe and effective under section 321(p)(1) of this title under a final determination issued under part 330 of title 21, Code of Federal Regulations, shall be deemed to be a new drug under section 321(p) of this title, misbranded under section 352(ee) of this title, and subject to the requirement for an approved new drug application under section 355 of this title.

(6) Other drugs deemed new drugs

Except as provided in subsection (m), a drug is deemed to be a new drug under section 321(p) of this title and misbranded under section 352(ee) of this title if the drug—

(A) is not subject to section 353(b)(1) of this title; and

(B) is not described in paragraph (1), (2), (3), (4), or (5), or subsection (b)(1)(B).

(b) Administrative orders

(1) In general

(A) Determination

The Secretary may, on the initiative of the Secretary or at the request of one or more requestors, issue an administrative order determining whether there are conditions under which a specific drug, a class of drugs, or a combination of drugs, is determined to be—

(i) not subject to section 353(b)(1) of this title; and

(ii) generally recognized as safe and effective under section 321(p)(1) of this title.

(B) Effect

A drug or combination of drugs shall be deemed to not require approval under section 355 of this title if such drug or combination of drugs—

(i) is determined by the Secretary to meet the conditions specified in clauses (i) and (ii) of subparagraph (A);

(ii) is marketed in conformity with an administrative order under this subsection;

(iii) meets the general requirements for nonprescription drugs; and

(iv) meets the requirements under subsections (c) and (k).

(C) Standard

The Secretary shall find that a drug is not generally recognized as safe and effective under section 321(p)(1) of this title if—

(i) the evidence shows that the drug is not generally recognized as safe and effective under section 321(p)(1) of this title; or

(ii) the evidence is inadequate to show that the drug is generally recognized as safe and effective under section 321(p)(1) of this title.

(2) Administrative orders initiated by the Secretary

(A) In general

In issuing an administrative order under paragraph (1) upon the Secretary's initiative, the Secretary shall—

(i) make reasonable efforts to notify informally, not later than 2 business days before the issuance of the proposed order, the sponsors of drugs who have a listing in effect under section 360(j) of this title for the drugs or combination of drugs that will be subject to the administrative order;

(ii) after any such reasonable efforts of notification—

(I) issue a proposed administrative order by publishing it on the website of the Food and Drug Administration and include in such order the reasons for the issuance of such order; and

(II) publish a notice of availability of such proposed order in the Federal Register;

(iii) except as provided in subparagraph (B), provide for a public comment period with respect to such proposed order of not less than 45 calendar days; and

(iv) if, after completion of the proceedings specified in clauses (i) through (iii), the Secretary determines that it is appropriate to issue a final administrative order—

(I) issue the final administrative order, together with a detailed statement of reasons, which order shall not take effect until the time for requesting judicial review under paragraph (3)(D)(ii) has expired;

(II) publish a notice of such final administrative order in the Federal Register;

(III) afford requestors of drugs that will be subject to such order the opportunity for formal dispute resolution up to the level of the Director of the Center for Drug Evaluation and Research, which initially must be requested within 45 calendar days of the issuance of the order, and, for subsequent levels of appeal, within 30 calendar days of the prior decision; and

(IV) except with respect to drugs described in paragraph (3)(B), upon completion of the formal dispute resolution procedure, inform the persons which sought such dispute resolution of their right to request a hearing.

(B) Exceptions

When issuing an administrative order under paragraph (1) on the Secretary's initiative proposing to determine that a drug described in subsection (a)(3) is not generally recognized as safe and effective under section 321(p)(1) of this title, the Secretary shall follow the procedures in subparagraph (A), except that—

(i) the proposed order shall include notice of—

(I) the general categories of data the Secretary has determined necessary to establish that the drug is generally recognized as safe and effective under section 321(p)(1) of this title; and

(II) the format for submissions by interested persons;

(ii) the Secretary shall provide for a public comment period of no less than 180 calendar days with respect to such proposed order, except when the Secretary determines, for good cause, that a shorter period is in the interest of public health; and

(iii) any person who submits data in such comment period shall include a certification that the person has submitted all evidence created, obtained, or received by that person that is both within the categories of data identified in the proposed order and relevant to a determination as to whether the drug is generally recognized as safe and effective under section 321(p)(1) of this title.

(3) Hearings; judicial review

(A) In general

Only a person who participated in each stage of formal dispute resolution under subclause (III) of paragraph (2)(A)(iv) of an administrative order with respect to a drug may request a hearing concerning a final administrative order issued under such paragraph with respect to such drug. If a hearing is sought, such person must submit a request for a hearing, which shall be based solely on information in the administrative record, to the Secretary not later than 30 calendar days after receiving notice of the final decision of the formal dispute resolution procedure.

(B) No hearing required with respect to orders relating to certain drugs

(i) In general

The Secretary shall not be required to provide notice and an opportunity for a hearing pursuant to paragraph (2)(A)(iv) if the final administrative order involved relates to a drug—

(I) that is described in subsection (a)(3)(A); and

(II) with respect to which no human or non-human data studies relevant to the safety or effectiveness of such drug have been submitted to the administrative record since the issuance of the most recent tentative final monograph relating to such drug.

(ii) Human data studies and non-human data defined

In this subparagraph:

(I) The term ''human data studies'' means clinical trials of safety or effectiveness (including actual use studies), pharmacokinetics studies, or bioavailability studies.

(II) The term ''non-human data'' means data from testing other than with human subjects which provides information concerning safety or effectiveness.

(C) Hearing procedures

(i) Denial of request for hearing

If the Secretary determines that information submitted in a request for a hearing under subparagraph (A) with respect to a final administrative order issued under paragraph (2)(A)(iv) does not identify the existence of a genuine and substantial question of material fact, the Secretary may deny such request. In making such a determination, the Secretary may consider only information and data that are based on relevant and reliable scientific principles and methodologies.

(ii) Single hearing for multiple related requests

If more than one request for a hearing is submitted with respect to the same administrative order under subparagraph (A), the Secretary may direct that a single hearing be conducted in which all persons whose hearing requests were granted may participate.

(iii) Presiding officer

The presiding officer of a hearing requested under subparagraph (A) shall—

(I) be designated by the Secretary;

(II) not be an employee of the Center for Drug Evaluation and Research; and

(III) not have been previously involved in the development of the administrative order involved or proceedings relating to that administrative order.

(iv) Rights of parties to hearing

The parties to a hearing requested under subparagraph (A) shall have the right to present testimony, including testimony of expert witnesses, and to cross-examine witnesses presented by other parties. Where appropriate, the presiding officer may require that cross-examination by parties representing substantially the same interests be consolidated to promote efficiency and avoid duplication.

(v) Final decision

(I) At the conclusion of a hearing requested under subparagraph (A), the presiding officer of the hearing shall issue a decision containing findings of fact and conclusions of law. The decision of the presiding officer shall be final.

(II) The final decision may not take effect until the period under subparagraph (D)(ii) for submitting a request for judicial review of such decision expires.

(D) Judicial review of final administrative order

(i) In general

The procedures described in section 355(h) of this title shall apply with respect to judicial review of final administrative orders issued under this subsection in the same manner and to the same extent as such section applies to an order described in such section except that the judicial review shall be taken by filing in an appropriate district court of the United States in lieu of the appellate courts specified in such section.

(ii) Period to submit a request for judicial review

A person eligible to request a hearing under this paragraph and seeking judicial review of a final administrative order issued under this subsection shall file such request for judicial review not later than 60 calendar days after the latest of—

(I) the date on which notice of such order is published;

(II) the date on which a hearing with respect to such order is denied under subparagraph (B) or (C)(i);

(III) the date on which a final decision is made following a hearing under subparagraph (C)(v); or

(IV) if no hearing is requested, the date on which the time for requesting a hearing expires.

(4) Expedited procedure with respect to administrative orders initiated by the Secretary

(A) Imminent hazard to the public health

(i) In general

In the case of a determination by the Secretary that a drug, class of drugs, or combination of drugs subject to this section poses an imminent hazard to the public health, the Secretary, after first making reasonable efforts to notify, not later than 48 hours before issuance of such order under this subparagraph, sponsors who have a listing in effect under section 360(j) of this title for such drug or combination of drugs—

(I) may issue an interim final administrative order for such drug, class of drugs, or combination of drugs under paragraph (1), together with a detailed statement of the reasons for such order;

(II) shall publish in the Federal Register a notice of availability of any such order; and

(III) shall provide for a public comment period of at least 45 calendar days with respect to such interim final order.

(ii) Nondelegation

The Secretary may not delegate the authority to issue an interim final administrative order under this subparagraph.

(B) Safety labeling changes

(i) In general

In the case of a determination by the Secretary that a change in the labeling of a drug, class of drugs, or combination of drugs subject to this section is reasonably expected to mitigate a significant or unreasonable risk of a serious adverse event associated with use of the drug, the Secretary may—

(I) make reasonable efforts to notify informally, not later than 48 hours before the issuance of the interim final order, the sponsors of drugs who have a listing in effect under section 360(j) of this title for such drug or combination of drugs;

(II) after reasonable efforts of notification, issue an interim final administrative order in accordance with paragraph (1) to require such change, together with a detailed statement of the reasons for such order;

(III) publish in the Federal Register a notice of availability of such order; and

(IV) provide for a public comment period of at least 45 calendar days with respect to such interim final order.

(ii) Content of order

An interim final order issued under this subparagraph with respect to the labeling of a drug may provide for new warnings and other information required for safe use of the drug.

(C) Effective date

An order under subparagraph (A) or (B) shall take effect on a date specified by the Secretary.

(D) Final order

After the completion of the proceedings in subparagraph (A) or (B), the Secretary shall—

(i) issue a final order in accordance with paragraph (1);

(ii) publish a notice of availability of such final administrative order in the Federal Register; and

(iii) afford sponsors of such drugs that will be subject to such an order the opportunity for formal dispute resolution up to the level of the Director of the Center for Drug Evaluation and Research, which must initially be within 45 calendar days of the issuance of the order, and for subsequent levels of appeal, within 30 calendar days of the prior decision.

(E) Hearings

A sponsor of a drug subject to a final order issued under subparagraph (D) and that participated in each stage of formal dispute resolution under clause (iii) of such subparagraph may request a hearing on such order. The provisions of subparagraphs (A), (B), and (C) of paragraph (3), other than paragraph (3)(C)(v)(II), shall apply with respect to a hearing on such order in the same manner and to the same extent as such provisions apply with respect to a hearing on an administrative order issued under paragraph (2)(A)(iv).

(F) Timing

(i) Final order and hearing

The Secretary shall—

(I) not later than 6 months after the date on which the comment period closes under subparagraph (A) or (B), issue a final order in accordance with paragraph (1); and

(II) not later than 12 months after the date on which such final order is issued, complete any hearing under subparagraph (E).

(ii) Dispute resolution request

The Secretary shall specify in an interim final order issued under subparagraph (A) or (B) such shorter periods for requesting dispute resolution under subparagraph (D)(iii) as are necessary to meet the requirements of this subparagraph.

(G) Judicial review

A final order issued pursuant to subparagraph (F) shall be subject to judicial review in accordance with paragraph (3)(D).

(5) Administrative order initiated at the request of a requestor

(A) In general

In issuing an administrative order under paragraph (1) at the request of a requestor with respect to certain drugs, classes of drugs, or combinations of drugs—

(i) the Secretary shall, after receiving a request under this subparagraph, determine whether the request is sufficiently complete and formatted to permit a substantive review;

(ii) if the Secretary determines that the request is sufficiently complete and formatted to permit a substantive review, the Secretary shall—

(I) file the request; and

(II) initiate proceedings with respect to issuing an administrative order in accordance with paragraphs (2) and (3); and

(iii) except as provided in paragraph (6), if the Secretary determines that a request does not meet the requirements for filing or is not sufficiently complete and formatted to permit a substantive review, the requestor may demand that the request be filed over protest, and the Secretary shall initiate proceedings to review the request in accordance with paragraph (2)(A).

(B) Request to initiate proceedings

(i) In general

A requestor seeking an administrative order under paragraph (1) with respect to certain drugs, classes of drugs, or combinations of drugs, shall submit to the Secretary a request to initiate proceedings for such order in the form and manner as specified by the Secretary. Such requestor may submit a request under this subparagraph for the issuance of an administrative order—

(I) determining whether a drug is generally recognized as safe and effective under section 321(p)(1) of this title, exempt from section 353(b)(1) of this title, and not required to be the subject of an approved application under section 355 of this title; or

(II) determining whether a change to a condition of use of a drug is generally recognized as safe and effective under section 321(p)(1) of this title, exempt from section 353(b)(1) of this title, and not required to be the subject of an approved application under section 355 of this title, if, absent such a changed condition of use, such drug is—

(aa) generally recognized as safe and effective under section 321(p)(1) of this title in accordance with subsection (a)(1), (a)(2), or an order under this subsection; or

(bb) subject to subsection (a)(3), but only if such requestor initiates such request in conjunction with a request for the Secretary to determine whether such drug is generally recognized as safe and effective under section 321(p)(1) of this title, which is filed by the Secretary under subparagraph (A)(ii).

(ii) Exception

The Secretary is not required to complete review of a request for a change described in clause (i)(II) if the Secretary determines that there is an inadequate basis to find the drug is generally recognized as safe and effective under section 321(p)(1) of this title under paragraph (1) and issues a final order announcing that determination.

(iii) Withdrawal

The requestor may withdraw a request under this paragraph, according to the procedures set forth pursuant to subsection (d)(2)(B). Notwithstanding any other provision of this section, if such request is withdrawn, the Secretary may cease proceedings under this subparagraph.

(C) Exclusivity

(i) In general

A final administrative order issued in response to a request under this section shall have the effect of authorizing solely the order requestor (or the licensees, assignees, or successors in interest of such requestor with respect to the subject of such order), for a period of 18 months following the effective date of such final order and beginning on the date the requestor may lawfully market such drugs pursuant to the order, to market drugs—

(I) incorporating changes described in clause (ii); and

(II) subject to the limitations under clause (iv).

(ii) Changes described

A change described in this clause is a change subject to an order specified in clause (i), which—

(I) provides for a drug to contain an active ingredient (including any ester or salt of the active ingredient) not previously incorporated in a drug described in clause (iii); or

(II) provides for a change in the conditions of use of a drug, for which new human data studies conducted or sponsored by the requestor (or for which the requestor has an exclusive right of reference) were essential to the issuance of such order.

(iii) Drugs described

The drugs described in this clause are drugs—

(I) specified in subsection (a)(1), (a)(2), or (a)(3);

(II) subject to a final order issued under this section;

(III) subject to a final sunscreen order (as defined in section 360fff(2)(A) of this title); or

(IV) described in subsection (m)(1), other than drugs subject to an active enforcement action under subchapter III of this chapter.

(iv) Limitations on exclusivity

(I) In general

Only one 18-month period under this subparagraph shall be granted, under each order described in clause (i), with respect to changes (to the drug subject to such order) which are either—

(aa) changes described in clause (ii)(I), relating to active ingredients; or

(bb) changes described in clause (ii)(II), relating to conditions of use.

(II) No exclusivity allowed

No exclusivity shall apply to changes to a drug which are—

(aa) the subject of a Tier 2 OTC monograph order request (as defined in section 379j–71 of this title);

(bb) safety-related changes, as defined by the Secretary, or any other changes the Secretary considers necessary to assure safe use; or

(cc) changes related to methods of testing safety or efficacy.

(v) New human data studies defined

In this subparagraph, the term ''new human data studies'' means clinical trials of safety or effectiveness (including actual use studies), pharmacokinetics studies, or bioavailability studies, the results of which—

(I) have not been relied on by the Secretary to support—

(aa) a proposed or final determination that a drug described in subclause (I), (II), or (III) of clause (iii) is generally recognized as safe and effective under section 321(p)(1) of this title; or

(bb) approval of a drug that was approved under section 355 of this title; and

(II) do not duplicate the results of another study that was relied on by the Secretary to support—

(aa) a proposed or final determination that a drug described in subclause (I), (II), or (III) of clause (iii) is generally recognized as safe and effective under section 321(p)(1) of this title; or

(bb) approval of a drug that was approved under section 355 of this title.

(vi) Notification of drug not available for sale

A requestor that is granted exclusivity with respect to a drug under this subparagraph shall notify the Secretary in writing within 1 year of the issuance of the final administrative order if the drug that is the subject of such order will not be available for sale within 1 year of the date of issuance of such order. The requestor shall include with such notice the—

(I) identity of the drug by established name and by proprietary name, if any;

(II) strength of the drug;

(III) date on which the drug will be available for sale, if known; and

(IV) reason for not marketing the drug after issuance of the order.

(6) Information regarding safe nonprescription marketing and use as condition for filing a generally recognized as safe and effective request

(A) In general

In response to a request under this section that a drug described in subparagraph (B) be generally recognized as safe and effective, the Secretary—

(i) may file such request, if the request includes information specified under subparagraph (C) with respect to safe nonprescription marketing and use of such drug; or

(ii) if the request fails to include information specified under subparagraph (C), shall refuse to file such request and require that nonprescription marketing of the drug be pursuant to a new drug application as described in subparagraph (D).

(B) Drug described

A drug described in this subparagraph is a nonprescription drug which contains an ac-

tive ingredient not previously incorporated in a drug—

(i) specified in subsection (a)(1), (a)(2), or (a)(3);

(ii) subject to a final order under this section; or

(iii) subject to a final sunscreen order (as defined in section 360fff(2)(A) of this title).

(C) Information demonstrating prima facie safe nonprescription marketing and use

Information specified in this subparagraph, with respect to a request described in subparagraph (A)(i), is—

(i) information sufficient for a prima facie demonstration that the drug subject to such request has a verifiable history of being marketed and safely used by consumers in the United States as a nonprescription drug under comparable conditions of use;

(ii) if the drug has not been previously marketed in the United States as a nonprescription drug, information sufficient for a prima facie demonstration that the drug was marketed and safely used under comparable conditions of marketing and use in a country listed in section 382(b)(1)(A) of this title or designated by the Secretary in accordance with section 382(b)(1)(B) of this title—

(I) for such period as needed to provide reasonable assurances concerning the safe nonprescription use of the drug; and

(II) during such time was subject to sufficient monitoring by a regulatory body considered acceptable by the Secretary for such monitoring purposes, including for adverse events associated with nonprescription use of the drug; or

(iii) if the Secretary determines that information described in clause (i) or (ii) is not needed to provide a prima facie demonstration that the drug can be safely marketed and used as a nonprescription drug, such other information the Secretary determines is sufficient for such purposes.

(D) Marketing pursuant to new drug application

In the case of a request described in subparagraph (A)(ii), the drug subject to such request may be resubmitted for filing only if—

(i) the drug is marketed as a nonprescription drug, under conditions of use comparable to the conditions specified in the request, for such period as the Secretary determines appropriate (not to exceed 5 consecutive years) pursuant to an application approved under section 355 of this title; and

(ii) during such period, 1,000,000 retail packages of the drug, or an equivalent quantity as determined by the Secretary, were distributed for retail sale, as determined in such manner as the Secretary finds appropriate.

(E) Rule of application

Except in the case of a request involving a drug described in section 360fff(9) of this title, as in effect on January 1, 2017, if the Secretary refuses to file a request under this paragraph, the requestor may not file such request over protest under paragraph (5)(A)(iii).

(7) Packaging

An administrative order issued under paragraph (2), (4)(A), or (5) may include requirements for the packaging of a drug to encourage use in accordance with labeling. Such requirements may include unit dose packaging, requirements for products intended for use by pediatric populations, requirements to reduce risk of harm from unsupervised ingestion, and other appropriate requirements. This paragraph does not authorize the Food and Drug Administration to require standards or testing procedures as described in part 1700 of title 16, Code of Federal Regulations.

(8) Final and tentative final monographs for category I drugs deemed final administrative orders

(A) In general

A final monograph or tentative final monograph described in subparagraph (B) shall be deemed to be a final administrative order under this subsection and may be amended, revoked, or otherwise modified in accordance with the procedures of this subsection.

(B) Monographs described

For purposes of subparagraph (A), a final monograph or tentative final monograph is described in this subparagraph if it—

(i) establishes conditions of use for a drug described in paragraph (1) or (2) of subsection (a); and

(ii) represents the most recently promulgated version of such conditions, including as modified, in whole or in part, by any proposed or final rule.

(C) Deemed orders include harmonizing technical amendments

The deemed establishment of a final administrative order under subparagraph (A) shall be construed to include any technical amendments to such order as the Secretary determines necessary to ensure that such order is appropriately harmonized, in terms of terminology or cross-references, with the applicable provisions of this chapter (and regulations thereunder) and any other orders issued under this section.

(c) Procedure for minor changes

(1) In general

Minor changes in the dosage form of a drug that is described in paragraph (1) or (2) of subsection (a) or the subject of an order issued under subsection (b) may be made by a requestor without the issuance of an order under subsection (b) if—

(A) the requestor maintains such information as is necessary to demonstrate that the change—

(i) will not affect the safety or effectiveness of the drug; and

(ii) will not materially affect the extent of absorption or other exposure to the ac-

tive ingredient in comparison to a suitable reference product; and

(B) the change is in conformity with the requirements of an applicable administrative order issued by the Secretary under paragraph (3).

(2) Additional information

(A) Access to records

A sponsor shall submit records requested by the Secretary relating to such a minor change under section 374(a)(4) of this title, within 15 business days of receiving such a request, or such longer period as the Secretary may provide.

(B) Insufficient information

If the Secretary determines that the information contained in such records is not sufficient to demonstrate that the change does not affect the safety or effectiveness of the drug or materially affect the extent of absorption or other exposure to the active ingredient, the Secretary—

(i) may so inform the sponsor of the drug in writing; and

(ii) if the Secretary so informs the sponsor, shall provide the sponsor of the drug with a reasonable opportunity to provide additional information.

(C) Failure to submit sufficient information

If the sponsor fails to provide such additional information within a time prescribed by the Secretary, or if the Secretary determines that such additional information does not demonstrate that the change does not—

(i) affect the safety or effectiveness of the drug; or

(ii) materially affect the extent of absorption or other exposure to the active ingredient in comparison to a suitable reference product,

the drug as modified is a new drug under section 321(p) of this title and shall be deemed to be misbranded under section 352(ee) of this title.

(3) Determining whether a change will affect safety or effectiveness

(A) In general

The Secretary shall issue one or more administrative orders specifying requirements for determining whether a minor change made by a sponsor pursuant to this subsection will affect the safety or effectiveness of a drug or materially affect the extent of absorption or other exposure to an active ingredient in the drug in comparison to a suitable reference product, together with guidance for applying those orders to specific dosage forms.

(B) Standard practices

The orders and guidance issued by the Secretary under subparagraph (A) shall take into account relevant public standards and standard practices for evaluating the quality of drugs, and may take into account the special needs of populations, including children.

(d) Confidentiality of information submitted to the Secretary

(1) In general

Subject to paragraph (2), any information, including reports of testing conducted on the drug or drugs involved, that is submitted by a requestor in connection with proceedings on an order under this section (including any minor change under subsection (c)) and is a trade secret or confidential information subject to section 552(b)(4) of title 5 or section 1905 of title 18 shall not be disclosed to the public unless the requestor consents to that disclosure.

(2) Public availability

(A) In general

Except as provided in subparagraph (B), the Secretary shall—

(i) make any information submitted by a requestor in support of a request under subsection (b)(5)(A) available to the public not later than the date on which the proposed order is issued; and

(ii) make any information submitted by any other person with respect to an order requested (or initiated by the Secretary) under subsection (b), available to the public upon such submission.

(B) Limitations on public availability

Information described in subparagraph (A) shall not be made public if—

(i) the information pertains to pharmaceutical quality information, unless such information is necessary to establish standards under which a drug is generally recognized as safe and effective under section 321(p)(1) of this title;

(ii) the information is submitted in a requestor-initiated request, but the requestor withdraws such request, in accordance with withdrawal procedures established by the Secretary, before the Secretary issues the proposed order;

(iii) the Secretary requests and obtains the information under subsection (c) and such information is not submitted in relation to an order under subsection (b); or

(iv) the information is of the type contained in raw datasets.

(e) Updates to drug listing information

A sponsor who makes a change to a drug subject to this section shall submit updated drug listing information for the drug in accordance with section 360(j) of this title within 30 calendar days of the date when the drug is first commercially marketed, except that a sponsor who was the order requestor with respect to an order subject to subsection (b)(5)(C) (or a licensee, assignee, or successor in interest of such requestor) shall submit updated drug listing information on or before the date when the drug is first commercially marketed.

(f) Approvals under section 355 of this title

The provisions of this section shall not be construed to preclude a person from seeking or maintaining the approval of an application for a drug under sections 355(b)(1), 355(b)(2), and 355(j)

of this title. A determination under this section that a drug is not subject to section 353(b)(1) of this title, is generally recognized as safe and effective under section 321(p)(1) of this title, and is not a new drug under section 321(p) of this title shall constitute a finding that the drug is safe and effective that may be relied upon for purposes of an application under section 355(b)(2) of this title, so that the applicant shall be required to submit for purposes of such application only information needed to support any modification of the drug that is not covered by such determination under this section.

(g) Public availability of administrative orders

The Secretary shall establish, maintain, update (as determined necessary by the Secretary but no less frequently than annually), and make publicly available, with respect to orders issued under this section—

(1) a repository of each final order and interim final order in effect, including the complete text of the order; and

(2) a listing of all orders proposed and under development under subsection (b)(2), including—

(A) a brief description of each such order; and

(B) the Secretary's expectations, if resources permit, for issuance of proposed orders over a 3-year period.

(h) Development advice to sponsors or requestors

The Secretary shall establish procedures under which sponsors or requestors may meet with appropriate officials of the Food and Drug Administration to obtain advice on the studies and other information necessary to support submissions under this section and other matters relevant to the regulation of nonprescription drugs and the development of new nonprescription drugs under this section.

(i) Participation of multiple sponsors or requestors

The Secretary shall establish procedures to facilitate efficient participation by multiple sponsors or requestors in proceedings under this section, including provision for joint meetings with multiple sponsors or requestors or with organizations nominated by sponsors or requestors to represent their interests in a proceeding.

(j) Electronic format

All submissions under this section shall be in electronic format.

(k) Effect on existing regulations governing nonprescription drugs

(1) Regulations of general applicability to nonprescription drugs

Except as provided in this subsection, nothing in this section supersedes regulations establishing general requirements for nonprescription drugs, including regulations of general applicability contained in parts 201, 250, and 330 of title 21, Code of Federal Regulations, or any successor regulations. The Secretary shall establish or modify such regulations by means of rulemaking in accordance with section 553 of title 5.

(2) Regulations establishing requirements for specific nonprescription drugs

(A) The provisions of section 310.545 of title 21, Code of Federal Regulations, as in effect on the day before March 27, 2020, shall be deemed to be a final order under subsection (b).

(B) Regulations in effect on the day before March 27, 2020, establishing requirements for specific nonprescription drugs marketed pursuant to this section (including such requirements in parts 201 and 250 of title 21, Code of Federal Regulations), shall be deemed to be final orders under subsection (b), only as they apply to drugs—

(i) subject to paragraph (1), (2), (3), or (4) of subsection (a); or

(ii) otherwise subject to an order under this section.

(3) Withdrawal of regulations

The Secretary shall withdraw regulations establishing final monographs and the procedures governing the over-the-counter drug review under part 330 and other relevant parts of title 21, Code of Federal Regulations (as in effect on the day before March 27, 2020), or make technical changes to such regulations to ensure conformity with appropriate terminology and cross references. Notwithstanding subchapter II of chapter 5 of title 5, any such withdrawal or technical changes shall be made without public notice and comment and shall be effective upon publication through notice in the Federal Register (or upon such date as specified in such notice).

***(l)* Guidance**

The Secretary shall issue guidance that specifies—

(1) the procedures and principles for formal meetings between the Secretary and sponsors or requestors for drugs subject to this section;

(2) the format and content of data submissions to the Secretary under this section;

(3) the format of electronic submissions to the Secretary under this section;

(4) consolidated proceedings for appeal and the procedures for such proceedings where appropriate; and

(5) for minor changes in drugs, recommendations on how to comply with the requirements in orders issued under subsection (c)(3).

(m) Rule of construction

(1) In general

This section shall not affect the treatment or status of a nonprescription drug—

(A) that is marketed without an application approved under section 355 of this title as of March 27, 2020;

(B) that is not subject to an order issued under this section; and

(C) to which paragraph (1), (2), (3), (4), or (5) of subsection (a) do not apply.

(2) Treatment of products previously found to be subject to time and extent requirements

(A) Notwithstanding subsection (a), a drug described in subparagraph (B) may only be lawfully marketed, without an application approved under section 355 of this title, pursuant to an order issued under this section.

(B) A drug described in this subparagraph is a drug which, prior to March 27, 2020, the Secretary determined in a proposed or final rule to be ineligible for review under the OTC drug review (as such phrase ''OTC drug review'' was used in section 330.14 of title 21, Code of Federal Regulations, as in effect on the day before March 27, 2020).

(3) Preservation of authority

(A) Nothing in paragraph (1) shall be construed to preclude or limit the applicability of any provision of this chapter other than this section.

(B) Nothing in subsection (a) shall be construed to prohibit the Secretary from issuing an order under this section finding a drug to be not generally recognized as safe and effective under section 321(p)(1) of this title, as the Secretary determines appropriate.

(n) Investigational new drugs

A drug is not subject to this section if an exemption for investigational use under section 355(i) of this title is in effect for such drug.

***(o)* Inapplicability of Paperwork Reduction Act**

Chapter 35 of title 44 shall not apply to collections of information made under this section.

(p) Inapplicability of notice and comment rulemaking and other requirements

The requirements of subsection (b) shall apply with respect to orders issued under this section instead of the requirements of subchapter II of chapter 5 of title 5.

(q) Definitions

In this section:

(1) The term ''nonprescription drug'' refers to a drug not subject to the requirements of section 353(b)(1) of this title.

(2) The term ''sponsor'' refers to any person marketing, manufacturing, or processing a drug that—

(A) is listed pursuant to section 360(j) of this title; and

(B) is or will be subject to an administrative order under this section of the Food and Drug Administration.

(3) The term ''requestor'' refers to any person or group of persons marketing, manufacturing, processing, or developing a drug.

(June 25, 1938, ch. 675, §505G, as added Pub. L. 116–136, div. A, title III, §3851(a), Mar. 27, 2020, 134 Stat. 435.)

Statutory Notes and Related Subsidiaries

DRUGS EXCLUDED FROM THE OVER-THE-COUNTER DRUG REVIEW

Pub. L. 116–136, div. A, title III, §3853, Mar. 27, 2020, 134 Stat. 454, provided that:

''(a) IN GENERAL.—Nothing in this Act [probably should be ''this subtitle'', meaning subtitle F (§§3851–3862) of title III of div. A of Pub. L. 116–136, enacting this section, section 360fff–8 of this title, and subpart 10 of part C of subchapter VII of this chapter, amending sections 352, 360fff–3, 379j–52, 379r, and 381 of this title, repealing section 360fff–5 of this title, and enacting provisions set out as notes under this section and sections 360fff–3, 360fff–6, 379j–52, and 379j–71 of this title] (or the amendments made by this Act) shall apply to any nonprescription drug (as defined in section 505G(q) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355h(q)], as added by section 3851 of this subtitle) which was excluded by the Food and Drug Administration from the Over-the-Counter Drug Review in accordance with the paragraph numbered 25 on page 9466 of volume 37 of the Federal Register, published on May 11, 1972.

''(b) RULE OF CONSTRUCTION.—Nothing in this section shall be construed to preclude or limit the applicability of any other provision of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.).''

TREATMENT OF AUTHORITY REGARDING FINALIZATION OF SUNSCREEN MONOGRAPH

Pub. L. 116–136, div. A, title III, §3854(c), Mar. 27, 2020, 134 Stat. 456, provided that:

''(1) IN GENERAL.—

''(A) REVISION OF FINAL SUNSCREEN ORDER.—The Secretary of Health and Human Services (referred to in this subsection as the 'Secretary') shall amend and revise the final administrative order concerning nonprescription sunscreen (referred to in this subsection as the 'sunscreen order') for which the content, prior to the date of enactment of this Act [Mar. 27, 2020], was represented by the final monograph for sunscreen drug products set forth in part 352 of title 21, Code of Federal Regulations (as in effect on May 21, 1999).

''(B) ISSUANCE OF REVISED SUNSCREEN ORDER; EFFECTIVE DATE.—A revised sunscreen order described in subparagraph (A) shall be—

''(i) issued in accordance with the procedures described in section 505G(b)(2) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355h(b)(2)];

''(ii) issued in proposed form not later than 18 months after the date of enactment of this Act; and

''(iii) issued by the Secretary at least 1 year prior to the effective date of the revised order.

''(2) REPORTS.—If a revised sunscreen order issued under paragraph (1) does not include provisions related to the effectiveness of various sun protection factor levels, and does not address all dosage forms known to the Secretary to be used in sunscreens marketed in the United States without a new drug application approved under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355), the Secretary shall submit a report to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate on the rationale for omission of such provisions from such order, and a plan and timeline to compile any information necessary to address such provisions through such order.''

ANNUAL UPDATE TO CONGRESS ON APPROPRIATE PEDIATRIC INDICATION FOR CERTAIN OTC COUGH AND COLD DRUGS

Pub. L. 116–136, div. A, title III, §3855, Mar. 27, 2020, 134 Stat. 457, provided that:

''(a) IN GENERAL.—Subject to subsection (c), the Secretary of Health and Human Services shall, beginning not later than 1 year after the date of enactment of this Act [Mar. 27, 2020], annually submit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate a letter describing the progress of the Food and Drug Administration—

''(1) in evaluating the cough and cold monograph described in subsection (b) with respect to children under age 6; and

''(2) as appropriate, revising such cough and cold monograph to address such children through the order process under section 505G(b) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355h(b)], as added by section 3851 of this subtitle.

''(b) COUGH AND COLD MONOGRAPH DESCRIBED.—The cough and cold monograph described in this subsection consists of the conditions under which nonprescription drugs containing antitussive, expectorant, nasal decon-

gestant, or antihistamine active ingredients (or combinations thereof) are generally recognized as safe and effective, as specified in part 341 of title 21, Code of Federal Regulations (as in effect immediately prior to the date of enactment of this Act), and included in an order deemed to be established under section 505G(b) of the Federal Food, Drug, and Cosmetic Act, as added by section 3851 of this subtitle.

''(c) DURATION OF AUTHORITY.—The requirement under subsection (a) shall terminate as of the date of a letter submitted by the Secretary of Health and Human Services pursuant to such subsection in which the Secretary indicates that the Food and Drug Administration has completed its evaluation and revised, in a final order, as applicable, the cough and cold monograph as described in subsection (a)(2).''

§ 356. Expedited approval of drugs for serious or life-threatening diseases or conditions

(a) Designation of a drug as a breakthrough therapy

(1) In general

The Secretary shall, at the request of the sponsor of a drug, expedite the development and review of such drug if the drug is intended, alone or in combination with 1 or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on 1 or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. (In this section, such a drug is referred to as a ''breakthrough therapy''.)

(2) Request for designation

The sponsor of a drug may request the Secretary to designate the drug as a breakthrough therapy. A request for the designation may be made concurrently with, or at any time after, the submission of an application for the investigation of the drug under section 355(i) of this title or section 351(a)(3) of the Public Health Service Act [42 U.S.C. 262(a)(3)].

(3) Designation

(A) In general

Not later than 60 calendar days after the receipt of a request under paragraph (2), the Secretary shall determine whether the drug that is the subject of the request meets the criteria described in paragraph (1). If the Secretary finds that the drug meets the criteria, the Secretary shall designate the drug as a breakthrough therapy and shall take such actions as are appropriate to expedite the development and review of the application for approval of such drug.

(B) Actions

The actions to expedite the development and review of an application under subparagraph (A) may include, as appropriate—

(i) holding meetings with the sponsor and the review team throughout the development of the drug;

(ii) providing timely advice to, and interactive communication with, the sponsor regarding the development of the drug to ensure that the development program to gather the nonclinical and clinical data necessary for approval is as efficient as practicable;

(iii) involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review;

(iv) assigning a cross-disciplinary project lead for the Food and Drug Administration review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor; and

(v) taking steps to ensure that the design of the clinical trials is as efficient as practicable, when scientifically appropriate, such as by minimizing the number of patients exposed to a potentially less efficacious treatment.

(b) Designation of drug as fast track product

(1) In general

The Secretary shall, at the request of the sponsor of a new drug, facilitate the development and expedite the review of such drug if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition, or if the Secretary designates the drug as a qualified infectious disease product under section 355f(d) of this title. (In this section, such a drug is referred to as a ''fast track product''.)

(2) Request for designation

The sponsor of a new drug may request the Secretary to designate the drug as a fast track product. A request for the designation may be made concurrently with, or at any time after, submission of an application for the investigation of the drug under section 355(i) of this title or section 351(a)(3) of the Public Health Service Act [42 U.S.C. 262(a)(3)].

(3) Designation

Within 60 calendar days after the receipt of a request under paragraph (2), the Secretary shall determine whether the drug that is the subject of the request meets the criteria described in paragraph (1). If the Secretary finds that the drug meets the criteria, the Secretary shall designate the drug as a fast track product and shall take such actions as are appropriate to expedite the development and review of the application for approval of such product.

(c) Accelerated approval of a drug for a serious or life-threatening disease or condition, including a fast track product

(1) In general

(A) Accelerated approval

The Secretary may approve an application for approval of a product for a serious or life-threatening disease or condition, including a fast track product, under section 355(c) of this title or section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)] upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a

clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. The approval described in the preceding sentence is referred to in this section as ''accelerated approval''.

(B) Evidence

The evidence to support that an endpoint is reasonably likely to predict clinical benefit under subparagraph (A) may include epidemiological, pathophysiological, therapeutic, pharmacologic, or other evidence developed using biomarkers, for example, or other scientific methods or tools.

(2) Limitation

(A) In general

Approval of a product under this subsection may be subject to 1 or both of the following requirements:

(i) That the sponsor conduct an appropriate postapproval study or studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical benefit.

(ii) That the sponsor submit copies of all promotional materials related to the product during the preapproval review period and, following approval and for such period thereafter as the Secretary determines to be appropriate, at least 30 days prior to dissemination of the materials.

(B) Studies not required

If the Secretary does not require that the sponsor of a product approved under accelerated approval conduct a postapproval study under this paragraph, the Secretary shall publish on the website of the Food and Drug Administration the rationale for why such study is not appropriate or necessary.

(C) Postapproval study conditions

Not later than the date of approval of a product under accelerated approval, the Secretary shall specify the conditions for a postapproval study or studies required to be conducted under this paragraph with respect to such product, which may include enrollment targets, the study protocol, and milestones, including the target date of study completion.

(D) Studies begun before approval

The Secretary may require, as appropriate, a study or studies to be underway prior to approval, or within a specified time period after the date of approval, of the applicable product.

(3) Expedited withdrawal of approval

(A) In general

The Secretary may withdraw approval of a product approved under accelerated approval using expedited procedures described in subparagraph (B) if—

(i) the sponsor fails to conduct any required postapproval study of the product with due diligence, including with respect to conditions specified by the Secretary under paragraph (2)(C);

(ii) a study required to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical benefit of the product fails to verify and describe such effect or benefit;

(iii) other evidence demonstrates that the product is not shown to be safe or effective under the conditions of use; or

(iv) the sponsor disseminates false or misleading promotional materials with respect to the product.

(B) Expedited procedures described

Expedited procedures described in this subparagraph shall consist of, prior to the withdrawal of accelerated approval—

(i) providing the sponsor with—

(I) due notice;

(II) an explanation for the proposed withdrawal;

(III) an opportunity for a meeting with the Commissioner or the Commissioner's designee; and

(IV) an opportunity for written appeal to—

(aa) the Commissioner; or

(bb) a designee of the Commissioner who has not participated in the proposed withdrawal of approval (other than a meeting pursuant to subclause (III)) and is not subordinate of an individual (other than the Commissioner) who participated in such proposed withdrawal;

(ii) providing an opportunity for public comment on the proposal to withdraw approval;

(iii) the publication of a summary of the public comments received, and the Secretary's response to such comments, on the website of the Food and Drug Administration; and

(iv) convening and consulting an advisory committee on issues related to the proposed withdrawal, if requested by the sponsor and if no such advisory committee has previously advised the Secretary on such issues with respect to the withdrawal of the product prior to the sponsor's request.

(d) Review of incomplete applications for approval of a fast track product

(1) In general

If the Secretary determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective, the Secretary shall evaluate for filing, and may commence review of portions of, an application for the approval of the product before the sponsor submits a complete application. The Secretary shall commence such review only if the applicant—

(A) provides a schedule for submission of information necessary to make the application complete; and

(B) pays any fee that may be required under section 379h of this title.

(2) Exception

Any time period for review of human drug applications that has been agreed to by the Secretary and that has been set forth in goals identified in letters of the Secretary (relating to the use of fees collected under section 379h of this title to expedite the drug development process and the review of human drug applications) shall not apply to an application submitted under paragraph (1) until the date on which the application is complete.

(e) Construction

(1) Purpose

The amendments made by the Food and Drug Administration Safety and Innovation Act and the 21st Century Cures Act to this section are intended to encourage the Secretary to utilize innovative and flexible approaches to the assessment of products under accelerated approval for treatments for patients with serious or life-threatening diseases or conditions and unmet medical needs.

(2) Construction

Nothing in this section shall be construed to alter the standards of evidence under subsection (c) or (d) of section 355 of this title (including the substantial evidence standard in section 355(d) of this title) or under section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)]. Such sections and standards of evidence apply to the review and approval of products under this section, including whether a product is safe and effective. Nothing in this section alters the ability of the Secretary to rely on evidence that does not come from adequate and well-controlled investigations for the purpose of determining whether an endpoint is reasonably likely to predict clinical benefit as described in subsection (b)(1)(B).

(f) Awareness efforts

The Secretary shall—

(1) develop and disseminate to physicians, patient organizations, pharmaceutical and biotechnology companies, and other appropriate persons a description of the provisions of this section applicable to breakthrough therapies, accelerated approval, and and[1] fast track products; and

(2) establish a program to encourage the development of surrogate and clinical endpoints, including biomarkers, and other scientific methods and tools that can assist the Secretary in determining whether the evidence submitted in an application is reasonably likely to predict clinical benefit for serious or life-threatening conditions for which significant unmet medical needs exist.

(g) Regenerative advanced therapy

(1) In general

The Secretary, at the request of the sponsor of a drug, shall facilitate an efficient development program for, and expedite review of, such drug if the drug qualifies as a regenerative advanced therapy under the criteria described in paragraph (2).

[1] So in original.

(2) Criteria

A drug is eligible for designation as a regenerative advanced therapy under this subsection if—

(A) the drug is a regenerative medicine therapy (as defined in paragraph (8));

(B) the drug is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and

(C) preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such a disease or condition.

(3) Request for designation

The sponsor of a drug may request the Secretary to designate the drug as a regenerative advanced therapy concurrently with, or at any time after, submission of an application for the investigation of the drug under section 355(i) of this title or section 351(a)(3) of the Public Health Service Act [42 U.S.C. 262(a)(3)].

(4) Designation

Not later than 60 calendar days after the receipt of a request under paragraph (3), the Secretary shall determine whether the drug that is the subject of the request meets the criteria described in paragraph (2). If the Secretary determines that the drug meets the criteria, the Secretary shall designate the drug as a regenerative advanced therapy and shall take such actions as are appropriate under paragraph (1). If the Secretary determines that a drug does not meet the criteria for such designation, the Secretary shall include with the determination a written description of the rationale for such determination.

(5) Actions

The sponsor of a regenerative advanced therapy shall be eligible for the actions to expedite development and review of such therapy under subsection (a)(3)(B), including early interactions to discuss any potential surrogate or intermediate endpoint to be used to support the accelerated approval of an application for the product under subsection (c).

(6) Access to expedited approval pathways

An application for a regenerative advanced therapy under section 355(b)(1) of this title or section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)] may be—

(A) eligible for priority review, as described in the Manual of Policies and Procedures of the Food and Drug Administration and goals identified in the letters described in section 101(b) of the Prescription Drug User Fee Amendments of 2012; and

(B) eligible for accelerated approval under subsection (c), as agreed upon pursuant to subsection (a)(3)(B), through, as appropriate—

(i) surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit; or

(ii) reliance upon data obtained from a meaningful number of sites, including through expansion to additional sites, as appropriate.

(7) Postapproval requirements

The sponsor of a regenerative advanced therapy that is granted accelerated approval and

is subject to the postapproval requirements under subsection (c) may, as appropriate, fulfill such requirements, as the Secretary may require, through—

(A) the submission of clinical evidence, clinical studies, patient registries, or other sources of real world evidence, such as electronic health records;

(B) the collection of larger confirmatory data sets, as agreed upon pursuant to subsection (a)(3)(B); or

(C) postapproval monitoring of all patients treated with such therapy prior to approval of the therapy.

(8) Definition

For purposes of this section, the term ''regenerative medicine therapy'' includes cell therapy, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products, except for those regulated solely under section 361 of the Public Health Service Act [42 U.S.C. 264] and part 1271 of title 21, Code of Federal Regulations.

(h) Limited population pathway for antibacterial and antifungal drugs

(1) In general

The Secretary may approve an antibacterial or antifungal drug, alone or in combination with one or more other drugs, as a limited population drug pursuant to this subsection only if—

(A) the drug is intended to treat a serious or life-threatening infection in a limited population of patients with unmet needs;

(B) the standards for approval under section 355(c) and (d) of this title, or the standards for licensure under section 351 of the Public Health Service Act [42 U.S.C. 262], as applicable, are met; and

(C) the Secretary receives a written request from the sponsor to approve the drug as a limited population drug pursuant to this subsection.

(2) Benefit-risk consideration

The Secretary's determination of safety and effectiveness of an antibacterial or antifungal drug shall reflect the benefit-risk profile of such drug in the intended limited population, taking into account the severity, rarity, or prevalence of the infection the drug is intended to treat and the availability or lack of alternative treatment in such limited population. Such drug may be approved under this subsection notwithstanding a lack of evidence to fully establish a favorable benefit-risk profile in a population that is broader than the intended limited population.

(3) Additional requirements

A drug approved under this subsection shall be subject to the following requirements, in addition to any other applicable requirements of this chapter:

(A) Labeling

To indicate that the safety and effectiveness of a drug approved under this subsection has been demonstrated only with respect to a limited population—

(i) all labeling and advertising of an antibacterial or antifungal drug approved under this subsection shall contain the statement ''Limited Population'' in a prominent manner and adjacent to, and not more prominent than—

(I) the proprietary name of such drug, if any; or

(II) if there is no proprietary name, the established name of the drug, if any, as defined in section 353(e)(3) of this title, or, in the case of a drug that is a biological product, the proper name, as defined by regulation; and

(ii) the prescribing information for the drug required by section 201.57 of title 21, Code of Federal Regulations (or any successor regulation) shall also include the following statement: ''This drug is indicated for use in a limited and specific population of patients.''.

(B) Promotional material

The sponsor of an antibacterial or antifungal drug subject to this subsection shall submit to the Secretary copies of all promotional materials related to such drug at least 30 calendar days prior to dissemination of the materials.

(4) Other programs

A sponsor of a drug that seeks approval of a drug under this subsection may also seek designation or approval, as applicable, of such drug under other applicable sections or subsections of this chapter or the Public Health Service Act [42 U.S.C. 201 et seq.].

(5) Guidance

Not later than 18 months after December 13, 2016, the Secretary shall issue draft guidance describing criteria, processes, and other general considerations for demonstrating the safety and effectiveness of limited population antibacterial and antifungal drugs. The Secretary shall publish final guidance within 18 months of the close of the public comment period on such draft guidance. The Secretary may approve antibacterial and antifungal drugs under this subsection prior to issuing guidance under this paragraph.

(6) Advice

The Secretary shall provide prompt advice to the sponsor of a drug for which the sponsor seeks approval under this subsection to enable the sponsor to plan a development program to obtain the necessary data for such approval, and to conduct any additional studies that would be required to gain approval of such drug for use in a broader population.

(7) Termination of limitations

If, after approval of a drug under this subsection, the Secretary approves a broader indication for such drug under section 355(b) of this title or section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)], the Secretary may remove any postmarketing conditions, including requirements with respect to labeling and review of promotional materials under paragraph (3), applicable to the approval of the drug under this subsection.

(8) Rules of construction

Nothing in this subsection shall be construed to alter the authority of the Secretary to approve drugs pursuant to this chapter or section 351 of the Public Health Service Act [42 U.S.C. 262], including the standards of evidence and applicable conditions for approval under such chapter or Act, the standards of approval of a drug under such chapter or Act, or to alter the authority of the Secretary to monitor drugs pursuant to such chapter or Act.

(9) Reporting and accountability

(A) Biennial reporting

The Secretary shall report to Congress not less often than once every 2 years on the number of requests for approval, and the number of approvals, of an antibacterial or antifungal drug under this subsection.

(B) GAO report

Not later than December 2021, the Comptroller General of the United States shall submit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor and Pensions of the Senate a report on the coordination of activities required under section 319E of the Public Health Service Act [42 U.S.C. 247d–5]. Such report shall include a review of such activities, and the extent to which the use of the pathway established under this subsection has streamlined premarket approval for antibacterial or antifungal drugs for limited populations, if such pathway has functioned as intended, if such pathway has helped provide for safe and effective treatment for patients, if such premarket approval would be appropriate for other categories of drugs, and if the authorities under this subsection have affected antibacterial or antifungal resistance.

(June 25, 1938, ch. 675, § 506, as added Pub. L. 105–115, title I, § 112(a), Nov. 21, 1997, 111 Stat. 2309; amended Pub. L. 112–144, title VIII, § 803, title IX, §§ 901(b), 902(a), July 9, 2012, 126 Stat. 1079, 1083, 1086; Pub. L. 114–255, div. A, title III, §§ 3033(a), (c), 3042, Dec. 13, 2016, 130 Stat. 1101, 1103, 1112; Pub. L. 117–328, div. FF, title III, § 3210(a), Dec. 29, 2022, 136 Stat. 5822.)

Editorial Notes

REFERENCES IN TEXT

The Food and Drug Administration Safety and Innovation Act, referred to in subsec. (e)(1), is Pub. L. 112–144. For the amendments made to this section by the Act, see 2012 Amendment notes below.

The 21st Century Cures Act, referred to in subsec. (e)(1), is Pub. L. 114–255. For the amendments made to this section by the Act, see 2016 Amendment notes below.

Section 101(b) of the Prescription Drug User Fee Amendments of 2012, referred to in subsec. (g)(6)(A), is section 101(b) of Pub. L. 112–144, which is set out as a note under section 379g of this title.

The Public Health Service Act, referred to in subsec. (h)(4), is act July 1, 1944, ch. 373, 58 Stat. 682, which is classified generally to chapter 6A (§ 201 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 201 of Title 42 and Tables.

PRIOR PROVISIONS

A prior section 356, act June 25, 1938, ch. 675, § 506, as added Dec. 22, 1941, ch. 613, § 3, 55 Stat. 851; amended Pub. L. 102–300, § 6(b)(2), June 16, 1992, 106 Stat. 240; Pub. L. 103–80, § 3(*o*), Aug. 13, 1993, 107 Stat. 777, related to certification of drugs containing insulin, prior to repeal by Pub. L. 105–115, title I, § 125(a)(1), Nov. 21, 1997, 111 Stat. 2325.

AMENDMENTS

2022—Subsec. (c)(2). Pub. L. 117–328, § 3210(a)(1)(A), (B), (D), designated existing provisions as subpar. (A), inserted heading, redesignated former subpars. (A) and (B) as cls. (i) and (ii), respectively, of subpar. (A) and realigned margins, and added subpars. (B) to (D).

Subsec. (c)(2)(A)(i). Pub. L. 117–328, § 3210(a)(1)(C), substituted ''an appropriate postapproval study or studies'' for ''appropriate postapproval studies''.

Subsec. (c)(3). Pub. L. 117–328, § 3210(a)(2)(B), (C), (F), designated existing provisions as subpar. (A), inserted heading, redesignated former subpars. (A) to (D) as cls. (i) to (iv), respectively, of subpar. (A) and realigned margins, and added subpar. (B).

Pub. L. 117–328, § 3210(a)(2)(A), substituted ''described in subparagraph (B)'' for ''(as prescribed by the Secretary in regulations which shall include an opportunity for an informal hearing)'' in introductory provisions.

Subsec. (c)(3)(A)(i). Pub. L. 117–328, § 3210(a)(2)(D), substituted ''product with due diligence, including with respect to conditions specified by the Secretary under paragraph (2)(C)'' for ''drug with due diligence''.

Subsec. (c)(3)(A)(iii). Pub. L. 117–328, § 3210(a)(2)(E), inserted ''shown to be'' after ''product is not''.

2016—Subsec. (e). Pub. L. 114–255, § 3033(a)(1), transferred subsec. (e) to appear before subsec. (f).

Subsec. (e)(1). Pub. L. 114–255, § 3033(c), inserted ''and the 21st Century Cures Act'' after ''Food and Drug Administration Safety and Innovation Act''.

Subsec. (g). Pub. L. 114–255, § 3033(a)(2), added subsec. (g).

Subsec. (h). Pub. L. 114–255, § 3042, added subsec. (h).

2012—Pub. L. 112–144, § 901(b), amended section generally. Prior to amendment, section consisted of subsecs. (a) to (d) relating to designation of drugs as fast track products, approval of applications for fast track products, review of incomplete applications for approval of fast track products, and awareness efforts, respectively.

Subsec. (a). Pub. L. 112–144, § 902(a)(3), added subsec. (a). Former subsec. (a) redesignated (b).

Subsec. (a)(1). Pub. L. 112–144, § 803, amended subsec. (a)(1), as amended by Pub. L. 112–144, § 901(b), by inserting '', or if the Secretary designates the drug as a qualified infectious disease product under section 355f(d) of this title'' after ''such a disease or condition''.

Subsecs. (b) to (d). Pub. L. 112–144, § 902(a)(1), redesignated subsecs. (a) to (c) as (b) to (d), respectively. Former subsec. (d) relating to awareness efforts redesignated (f).

Subsec. (f). Pub. L. 112–144, § 902(a)(2), which directed the redesignation of subsec. (d) as (f), was executed by redesignating the subsec. (d) relating to awareness efforts as (f), to reflect the probable intent of Congress and the subsequent amendment by Pub. L. 114–255, § 3033(a)(1), which transferred subsec. (e) to appear before subsec. (f) ''relating to awareness efforts''.

Subsec. (f)(1). Pub. L. 112–144, § 902(a)(4), substituted ''applicable to breakthrough therapies, accelerated approval, and'' for ''applicable to accelerated approval''.

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE

Section effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115,

set out as an Effective Date of 1997 Amendment note under section 321 of this title.

CONSTRUCTION OF 2022 AMENDMENT

Pub. L. 117–328, div. FF, title III, §3210(f), Dec. 29, 2022, 136 Stat. 5825, provided that: ''Nothing in this section [enacting section 356–2 of this title, amending this section and sections 331 and 356b of this title, and enacting provisions set out as a note under this section] (including the amendments made by this section) shall be construed to affect ongoing withdrawal proceedings for products approved pursuant to section 506(c) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356(c)) for which a notice of proposed withdrawal has been published in the Federal Register prior to the date of enactment of this Act [Dec. 29, 2022]. Such proceedings may continue under procedures in effect prior to the date of enactment of this Act.''

CONSTRUCTION OF 2016 AMENDMENTS

Pub. L. 114–255, div. A, title III, §3033(b), Dec. 13, 2016, 130 Stat. 1103, provided that: ''Nothing in this section [amending this section] and the amendments made by this section shall be construed to alter the authority of the Secretary of Health and Human Services—

''(1) to approve drugs pursuant to the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.) and section 351 of the Public Health Service Act (42 U.S.C. 262) as authorized prior to the date of enactment of the 21st Century Cures Act [Dec. 13, 2016], including the standards of evidence, and applicable conditions, for approval under such Acts; or

''(2) to alter the authority of the Secretary to require postapproval studies pursuant to such Acts, as authorized prior to the date of enactment of the 21st Century Cures Act.''

Pub. L. 114–255, div. A, title III, §3043, Dec. 13, 2016, 130 Stat. 1114, provided that: ''Nothing in this subtitle [subtitle E (§§3041–3044) of title III of div. A of Pub. L. 114–255, enacting section 360a–2 of this title, amending this section, sections 352 and 360d of this title, and section 247d–5 of Title 42, The Public Health and Welfare, repealing section 247d–5a of Title 42, and enacting provisions set out as notes under section 360a–2 of this title and section 247d–5 of Title 42], or an amendment made by this subtitle, shall be construed to restrict the prescribing of antimicrobial drugs or other products, including drugs approved under subsection (h) of section 506 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356[(h)]) (as added by section 3042), by health care professionals, or to limit the practice of health care.''

GUIDANCE

Pub. L. 117–328, div. FF, title III, §3210(d), Dec. 29, 2022, 136 Stat. 5824, provided that:

''(1) IN GENERAL.—The Secretary [of Health and Human Services] shall issue guidance describing—

''(A) how sponsor questions related to the identification of novel surrogate or intermediate clinical endpoints may be addressed in early-stage development meetings with the Food and Drug Administration;

''(B) the use of novel clinical trial designs that may be used to conduct appropriate postapproval studies as may be required under section 506(c)(2)(A) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356(c)(2)(A)), as amended by subsection (a);

''(C) the expedited procedures described in section 506(c)(3)(B) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356(c)(3)(B)); and

''(D) considerations related to the use of surrogate or intermediate clinical endpoints that may support the accelerated approval of an application under 506(c)(1)(A) of such Act (21 U.S.C. 356(c)(1)(A)), including considerations in evaluating the evidence related to any such endpoints.

''(2) FINAL GUIDANCE.—The Secretary shall issue—

''(A) draft guidance under paragraph (1) not later than 18 months after the date of enactment of this Act [Dec. 29, 2022]; and

''(B) final guidance not later than 1 year after the close of the public comment period on such draft guidance.''

REPORT ON REGENERATIVE ADVANCED THERAPIES

Pub. L. 114–255, div. A, title III, §3035, Dec. 13, 2016, 130 Stat. 1103, provided that:

''(a) REPORT TO CONGRESS.—Before March 1 of each calendar year, the Secretary of Health and Human Services shall, with respect to the previous calendar year, submit a report to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives on—

''(1) the number and type of applications for approval of regenerative advanced therapies filed, approved or licensed as applicable, withdrawn, or denied; and

''(2) how many of such applications or therapies, as applicable, were granted accelerated approval or priority review.

''(b) REGENERATIVE ADVANCED THERAPY.—In this section, the term 'regenerative advanced therapy' has the meaning given such term in section 506(g) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 356(g)], as added by section 3033 of this Act.''

FINDINGS AND SENSE OF CONGRESS ON ENHANCEMENT OF ACCELERATED PATIENT ACCESS TO NEW MEDICAL TREATMENTS

Pub. L. 112–144, title IX, §901(a), July 9, 2012, 126 Stat. 1082, as amended by Pub. L. 114–255, div. A, title III, §3101(b)(1), Dec. 13, 2016, 130 Stat. 1156, provided that:

''(1) FINDINGS.—Congress finds as follows:

''(A) The Food and Drug Administration (referred to in this section as the 'FDA') serves a critical role in helping to assure that new medicines are safe and effective. Regulatory innovation is 1 element of the Nation's strategy to address serious or life-threatening diseases or conditions by promoting investment in and development of innovative treatments for unmet medical needs.

''(B) During the 2 decades following the establishment of the accelerated approval mechanism, advances in medical sciences, including genomics, molecular biology, and bioinformatics, have provided an unprecedented understanding of the underlying biological mechanism and pathogenesis of disease. A new generation of modern, targeted medicines is under development to treat serious and life-threatening diseases, some applying drug development strategies based on biomarkers or pharmacogenomics, predictive toxicology, clinical trial enrichment techniques, and novel clinical trial designs, such as adaptive clinical trials.

''(C) As a result of these remarkable scientific and medical advances, the FDA should be encouraged to implement more broadly effective processes for the expedited development and review of innovative new medicines intended to address unmet medical needs for serious or life-threatening diseases or conditions, including those for rare diseases or conditions, using a broad range of surrogate or clinical endpoints and modern scientific tools earlier in the drug development cycle when appropriate. This may result in fewer, smaller, or shorter clinical trials for the intended patient population or targeted subpopulation without compromising or altering the high standards of the FDA for the approval of drugs.

''(D) Patients benefit from expedited access to safe and effective innovative therapies to treat unmet medical needs for serious or life-threatening diseases or conditions.

''(E) For these reasons, the statutory authority in effect on the day before the date of enactment of this Act [July 9, 2012] governing expedited approval of drugs for serious or life-threatening diseases or conditions should be amended in order to enhance the authority of the FDA to consider appropriate scientific

data, methods, and tools, and to expedite development and access to novel treatments for patients with a broad range of serious or life-threatening diseases or conditions.

''(2) SENSE OF CONGRESS.—It is the sense of Congress that the Food and Drug Administration should apply the accelerated approval and fast track provisions set forth in section 506 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356), as amended by this section, to help expedite the development and availability to patients of treatments for serious or life-threatening diseases or conditions while maintaining safety and effectiveness standards for such treatments.''

GUIDANCE; AMENDED REGULATIONS

Pub. L. 112–144, title IX, § 901(c), July 9, 2012, 126 Stat. 1085, provided that:

''(1) DRAFT GUIDANCE.—Not later than 1 year after the date of enactment of this Act [July 9, 2012], the Secretary of Health and Human Services (referred to in this section as the 'Secretary') shall issue draft guidance to implement the amendments made by this section [amending this section]. In developing such guidance, the Secretary shall specifically consider issues arising under the accelerated approval and fast track processes under section 506 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 356], as amended by subsection (b), for drugs designated for a rare disease or condition under section 526 of such Act (21 U.S.C. 360bb) and shall also consider any unique issues associated with very rare diseases.

''(2) FINAL GUIDANCE.—Not later than 1 year after the issuance of draft guidance under paragraph (1), and after an opportunity for public comment, the Secretary shall—

''(A) issue final guidance; and

''(B) amend the regulations governing accelerated approval in parts 314 and 601 of title 21, Code of Federal Regulations, as necessary to conform such regulations with the amendment made by subsection (b).

''(3) CONSIDERATION.—In developing the guidance under paragraphs (1) and (2)(A) and the amendments under paragraph (2)(B), the Secretary shall consider how to incorporate novel approaches to the review of surrogate endpoints based on pathophysiologic and pharmacologic evidence in such guidance, especially in instances where the low prevalence of a disease renders the existence or collection of other types of data unlikely or impractical.

''(4) CONFORMING CHANGES.—The Secretary shall issue, as necessary, conforming amendments to the applicable regulations under title 21, Code of Federal Regulations, governing accelerated approval.

''(5) NO EFFECT OF INACTION ON REQUESTS.—The issuance (or nonissuance) of guidance or conforming regulations implementing the amendment made by subsection (b) shall not preclude the review of, or action on, a request for designation or an application for approval submitted pursuant to section 506 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 356], as amended by subsection (b).''

Pub. L. 112–144, title IX, § 902(b), July 9, 2012, 126 Stat. 1087, provided that:

''(1) IN GENERAL.—

''(A) GUIDANCE.—Not later than 18 months after the date of enactment of this Act [July 9, 2012], the Secretary of Health and Human Services (referred to in this section as the 'Secretary') shall issue draft guidance on implementing the requirements with respect to breakthrough therapies, as set forth in section 506(a) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356(a)), as amended by this section. The Secretary shall issue final guidance not later than 1 year after the close of the comment period for the draft guidance.

''(B) AMENDED REGULATIONS.—

''(i) IN GENERAL.—If the Secretary determines that it is necessary to amend the regulations under title 21, Code of Federal Regulations in order to implement the amendments made by this section to section 506(a) of the Federal Food, Drug, and Cosmetic Act, the Secretary shall amend such regulations not later than 2 years after the date of enactment of this Act.

''(ii) PROCEDURE.—In amending regulations under clause (i), the Secretary shall—

''(I) issue a notice of proposed rulemaking that includes the proposed regulation;

''(II) provide a period of not less than 60 days for comments on the proposed regulation; and

''(III) publish the final regulation not less than 30 days before the effective date of the regulation.

''(iii) RESTRICTIONS.—Notwithstanding any other provision of law, the Secretary shall promulgate regulations implementing the amendments made by this section only as described in clause (ii).

''(2) REQUIREMENTS.—Guidance issued under this section shall—

''(A) specify the process and criteria by which the Secretary makes a designation under section 506(a)(3) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 356(a)(3)]; and

''(B) specify the actions the Secretary shall take to expedite the development and review of a breakthrough therapy pursuant to such designation under such section 506(a)(3), including updating good review management practices to reflect breakthrough therapies.''

Pub. L. 105–115, title I, § 112(b), Nov. 21, 1997, 111 Stat. 2310, provided that: ''Within 1 year after the date of enactment of this Act [Nov. 21, 1997], the Secretary of Health and Human Services shall issue guidance for fast track products (as defined in [former] section 506(a)(1) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 356(a)(1)]) that describes the policies and procedures that pertain to section 506 of such Act.''

§ 356–1. Accelerated approval of priority countermeasures

(a) In general

The Secretary of Health and Human Services may designate a priority countermeasure as a fast-track product pursuant to section 356 of this title or as a device granted review priority pursuant to section 360e(d)(5)[1] of this title. Such a designation may be made prior to the submission of—

(1) a request for designation by the sponsor or applicant; or

(2) an application for the investigation of the drug under section 355(i) of this title or section 262(a)(3) of title 42.

Nothing in this subsection shall be construed to prohibit a sponsor or applicant from declining such a designation.

(b) Use of animal trials

A drug for which approval is sought under section 355(b) of this title or section 262 of title 42 on the basis of evidence of effectiveness that is derived from animal studies pursuant to section 123[1] may be designated as a fast track product for purposes of this section.

(c) Priority review of drugs and biological products

A priority countermeasure that is a drug or biological product shall be considered a priority drug or biological product for purposes of performance goals for priority drugs or biological products agreed to by the Commissioner of Food and Drugs.

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[1] See References in Text note below.

(d) Definitions

For purposes of this title: [1]

(1) The term ''priority countermeasure'' has the meaning given such term in section 247d–6(h)(4) [1] of title 42.

(2) The term ''priority drugs or biological products'' means a drug or biological product that is the subject of a drug or biologics application referred to in section 101(4) of the Food and Drug Administration Modernization Act of 1997.

(Pub. L. 107–188, title I, § 122, June 12, 2002, 116 Stat. 613.)

Editorial Notes

REFERENCES IN TEXT

Section 360e(d)(5) of this title, referred to in subsec. (a), was struck out and former subsec. (d)(6) redesignated subsec. (d)(5) of section 360e by Pub. L. 114–255, div. A, title III, § 3051(c)(1), Dec. 13, 2016, 130 Stat. 1124. Section 360e(d)(5) no longer relates to grants of review priority.

Section 123, referred to in subsec. (b), is section 123 of Pub. L. 107–188, title I, June 12, 2002, 116 Stat. 613, which is not classified to the Code.

This title, referred to in subsec. (d), is title I of Pub. L. 107–188, June 12, 2002, 116 Stat. 596, which enacted this section, section 669a of Title 29, Labor, and sections 244, 245, 247d–3a, 247d–3b, 247d–7a to 247d–7d, 300hh, 300hh–11 to 300hh–13, 1320b–5, and 7257d of Title 42, The Public Health and Welfare, amended sections 247d to 247d–6, 264, 266, 290hh–1, and 5196b of Title 42, and enacted provisions set out as notes preceding section 8101 of Title 38, Veterans' Benefits, and under sections 201, 244, 247d, 247d–6, 300hh, 300hh–12, and 1320b–5 of Title 42. For complete classification of this title to the Code, see Tables.

Section 247d–6(h)(4) of title 42, referred to in subsec. (d)(1), was redesignated section 247d–6(e)(4) by Pub. L. 109–417, title III, § 304(3), Dec. 19, 2006, 120 Stat. 2861.

Section 101(4) of the Food and Drug Administration Modernization Act of 1997, referred to in subsec. (d)(2), is section 101(4) of Pub. L. 105–115, which is set out as a note under section 379g of this title.

CODIFICATION

Section was enacted as part of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

§ 356–2. Accelerated approval Council

(1) In general

Not later than 1 year after December 29, 2022, the Secretary shall establish an intra-agency coordinating council (referred to in this subsection as the ''Council'') within the Food and Drug Administration to ensure the consistent and appropriate use of accelerated approval across the Food and Drug Administration, pursuant to section 356(c) of this title.

(2) Membership

The members of the Council shall consist of the following senior officials, or a designee of such official, from the Food and Drug Administration and relevant Centers:

(A) The Director of the Center for Drug Evaluation and Research.

(B) The Director of the Center for Biologics Evaluation and Research.

(C) The Director of the Oncology Center of Excellence.

(D) The Director of the Office of New Drugs.

(E) The Director of the Office of Orphan Products Development.

(F) The Director of the Office of Tissues and Advanced Therapies.

(G) The Director of the Office of Medical Policy.

(H) At least 3 directors of review divisions or offices overseeing products approved under accelerated approval, including at least one director within the Office of Neuroscience.

(3) Duties of the Council

(A) Meetings

The Council shall convene not fewer than 3 times per calendar year to discuss issues related to accelerated approval, including any relevant cross-disciplinary approaches related to product review with respect to accelerated approval.

(B) Policy development

The Council shall directly engage with product review teams to support the consistent and appropriate use of accelerated approval across the Food and Drug Administration. Such engagement may include—

(i) developing guidance for Food and Drug Administration staff and best practices for, and across, product review teams, including with respect to communication between sponsors and the Food and Drug Administration and the review of products under accelerated approval;

(ii) providing training for product review teams; and

(iii) advising review divisions on best practices with respect to product-specific development, review, and withdrawal of products under accelerated approval.

(4) Publication of a report

Not later than 1 year after December 29, 2022, and annually thereafter, the Council shall publish on the public website of the Food and Drug Administration a report on the activities of the Council.

(Pub. L. 117–328, div. FF, title III, § 3210(e), Dec. 29, 2022, 136 Stat. 5824.)

Editorial Notes

CODIFICATION

Section was enacted as part of the Food and Drug Omnibus Reform Act of 2022, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

Statutory Notes and Related Subsidiaries

CONSTRUCTION

Nothing in section 3210(e) of Pub. L. 117–328, which enacted this section, to be construed to affect ongoing withdrawal proceedings for products approved pursuant to section 356(c) of this title for which a notice of proposed withdrawal has been published in the Federal Register prior to Dec. 29, 2022, see section 3210(f) of Pub. L. 117–328, set out as a Construction of 2022 Amendment note under section 356 of this title.

DEFINITION OF ''SECRETARY''

Secretary as used in this section means the Secretary of Health and Human Services, see section 3002 of div.

FF of Pub. L. 117–328, set out as a note under section 350a–1 of this title.

§ 356a. Manufacturing changes

(a) In general

With respect to a drug for which there is in effect an approved application under section 355 or 360b of this title or a license under section 262 of title 42, a change from the manufacturing process approved pursuant to such application or license may be made, and the drug as made with the change may be distributed, if—

(1) the holder of the approved application or license (referred to in this section as a ''holder'') has validated the effects of the change in accordance with subsection (b); and

(2)(A) in the case of a major manufacturing change, the holder has complied with the requirements of subsection (c); or

(B) in the case of a change that is not a major manufacturing change, the holder complies with the applicable requirements of subsection (d).

(b) Validation of effects of changes

For purposes of subsection (a)(1), a drug made with a manufacturing change (whether a major manufacturing change or otherwise) may be distributed only if, before distribution of the drug as so made, the holder involved validates the effects of the change on the identity, strength, quality, purity, and potency of the drug as the identity, strength, quality, purity, and potency may relate to the safety or effectiveness of the drug.

(c) Major manufacturing changes

(1) Requirement of supplemental application

For purposes of subsection (a)(2)(A), a drug made with a major manufacturing change may be distributed only if, before the distribution of the drug as so made, the holder involved submits to the Secretary a supplemental application for such change and the Secretary approves the application. The application shall contain such information as the Secretary determines to be appropriate, and shall include the information developed under subsection (b) by the holder in validating the effects of the change.

(2) Changes qualifying as major changes

For purposes of subsection (a)(2)(A), a major manufacturing change is a manufacturing change that is determined by the Secretary to have substantial potential to adversely affect the identity, strength, quality, purity, or potency of the drug as they may relate to the safety or effectiveness of a drug. Such a change includes a change that—

(A) is made in the qualitative or quantitative formulation of the drug involved or in the specifications in the approved application or license referred to in subsection (a) for the drug (unless exempted by the Secretary by regulation or guidance from the requirements of this subsection);

(B) is determined by the Secretary by regulation or guidance to require completion of an appropriate clinical study demonstrating equivalence of the drug to the drug as manufactured without the change; or

(C) is another type of change determined by the Secretary by regulation or guidance to have a substantial potential to adversely affect the safety or effectiveness of the drug.

(d) Other manufacturing changes

(1) In general

For purposes of subsection (a)(2)(B), the Secretary may regulate drugs made with manufacturing changes that are not major manufacturing changes as follows:

(A) The Secretary may in accordance with paragraph (2) authorize holders to distribute such drugs without submitting a supplemental application for such changes.

(B) The Secretary may in accordance with paragraph (3) require that, prior to the distribution of such drugs, holders submit to the Secretary supplemental applications for such changes.

(C) The Secretary may establish categories of such changes and designate categories to which subparagraph (A) applies and categories to which subparagraph (B) applies.

(2) Changes not requiring supplemental application

(A) Submission of report

A holder making a manufacturing change to which paragraph (1)(A) applies shall submit to the Secretary a report on the change, which shall contain such information as the Secretary determines to be appropriate, and which shall include the information developed under subsection (b) by the holder in validating the effects of the change. The report shall be submitted by such date as the Secretary may specify.

(B) Authority regarding annual reports

In the case of a holder that during a single year makes more than one manufacturing change to which paragraph (1)(A) applies, the Secretary may in carrying out subparagraph (A) authorize the holder to comply with such subparagraph by submitting a single report for the year that provides the information required in such subparagraph for all the changes made by the holder during the year.

(3) Changes requiring supplemental application

(A) Submission of supplemental application

The supplemental application required under paragraph (1)(B) for a manufacturing change shall contain such information as the Secretary determines to be appropriate, which shall include the information developed under subsection (b) by the holder in validating the effects of the change.

(B) Authority for distribution

In the case of a manufacturing change to which paragraph (1)(B) applies:

(i) The holder involved may commence distribution of the drug involved 30 days after the Secretary receives the supplemental application under such paragraph, unless the Secretary notifies the holder within such 30-day period that prior approval of the application is required before distribution may be commenced.

(ii) The Secretary may designate a category of such changes for the purpose of providing that, in the case of a change that is in such category, the holder involved may commence distribution of the drug involved upon the receipt by the Secretary of a supplemental application for the change.

(iii) If the Secretary disapproves the supplemental application, the Secretary may order the manufacturer to cease the distribution of the drugs that have been made with the manufacturing change.

(June 25, 1938, ch. 675, § 506A, as added Pub. L. 105–115, title I, § 116(a), Nov. 21, 1997, 111 Stat. 2313.)

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE

Pub. L. 105–115, title I, § 116(b), Nov. 21, 1997, 111 Stat. 2315, provided that: ''The amendment made by subsection (a) [enacting this section] takes effect upon the effective date of regulations promulgated by the Secretary of Health and Human Services to implement such amendment, or upon the expiration of the 24-month period beginning on the date of the enactment of this Act [Nov. 21, 1997], whichever occurs first.''

§ 356b. Reports of postmarketing studies

(a) Submission

(1) In general

A sponsor of a drug that has entered into an agreement with the Secretary to conduct a postmarketing study of a drug shall submit to the Secretary, within 1 year after the approval of such drug and annually thereafter until the study is completed or terminated, a report of the progress of the study or the reasons for the failure of the sponsor to conduct the study. The report shall be submitted in such form as is prescribed by the Secretary in regulations issued by the Secretary.

(2) Accelerated approval

Notwithstanding paragraph (1), a sponsor of a drug approved pursuant to accelerated approval shall submit to the Secretary a report of the progress of any study required under section 356(c) of this title, including progress toward enrollment targets, milestones, and other information as required by the Secretary, not later than 180 days after the approval of such drug and not less frequently than every 180 days thereafter, until the study is completed or terminated. The Secretary shall promptly publish on the website of the Food and Drug Administration, in an easily searchable format, the information reported under this paragraph.

(3) Agreements prior to effective date

Any agreement entered into between the Secretary and a sponsor of a drug, prior to November 21, 1997, to conduct a postmarketing study of a drug shall be subject to the requirements of paragraph (1). An initial report for such an agreement shall be submitted within 6 months after the date of the issuance of the regulations under paragraph (1).

(b) Consideration of information as public information

Any information pertaining to a report described in subsection (a) shall be considered to be public information to the extent that the information is necessary—

(1) to identify the sponsor; and

(2) to establish the status of a study described in subsection (a) and the reasons, if any, for any failure to carry out the study.

(c) Status of studies and reports

The Secretary shall annually develop and publish in the Federal Register a report that provides information on the status of the postmarketing studies—

(1) that sponsors have entered into agreements to conduct; and

(2) for which reports have been submitted under subsection (a)(1).

(d) Disclosure

If a sponsor fails to complete an agreed upon study required by this section by its original or otherwise negotiated deadline, the Secretary shall publish a statement on the Internet site of the Food and Drug Administration stating that the study was not completed and, if the reasons for such failure to complete the study were not satisfactory to the Secretary, a statement that such reasons were not satisfactory to the Secretary.

(e) Notification

With respect to studies of the type required under section 356(c)(2)(A) of this title or under section 314.510 or 601.41 of title 21, Code of Federal Regulations, as each of such sections was in effect on the day before the effective date of this subsection, the Secretary may require that a sponsor who, for reasons not satisfactory to the Secretary, fails to complete by its deadline a study under any of such sections of such type for a drug or biological product (including such a study conducted after such effective date) notify practitioners who prescribe such drug or biological product of the failure to complete such study and the questions of clinical benefit, and, where appropriate, questions of safety, that remain unanswered as a result of the failure to complete such study. Nothing in this subsection shall be construed as altering the requirements of the types of studies required under section 356(c)(2)(A) of this title or under section 314.510 or 601.41 of title 21, Code of Federal Regulations, as so in effect, or as prohibiting the Secretary from modifying such sections of title 21 of such Code to provide for studies in addition to those of such type.

(June 25, 1938, ch. 675, § 506B, as added Pub. L. 105–115, title I, § 130(a), Nov. 21, 1997, 111 Stat. 2331; amended Pub. L. 107–188, title V, § 506, June 12, 2002, 116 Stat. 693; Pub. L. 112–144, title IX, § 902(c), July 9, 2012, 126 Stat. 1088; Pub. L. 117–328, div. FF, title III, § 3210(b), Dec. 29, 2022, 136 Stat. 5823.)

Editorial Notes

REFERENCES IN TEXT

The effective date of this subsection, referred to in subsec. (e), is Oct. 1, 2002, see Effective Date of 2002 Amendment note set out below.

AMENDMENTS

2022—Subsec. (a)(2), (3). Pub. L. 117–328 added par. (2) and redesignated former par. (2) as (3).

2012—Subsec. (e). Pub. L. 112–144 substituted ''section 356(c)(2)(A) of this title'' for ''section 356(b)(2)(A) of this title'' in two places.

2002—Subsecs. (d), (e). Pub. L. 107–188 added subsecs. (d) and (e).

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 2002 AMENDMENT

Pub. L. 107–188, title V, § 508, June 12, 2002, 116 Stat. 694, provided that: ''The amendments made by this subtitle [subtitle A (§§ 501–509) of title V of Pub. L. 107–188, amending this section and sections 379g and 379h of this title] shall take effect October 1, 2002.''

EFFECTIVE DATE

Section effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as an Effective Date of 1997 Amendment note under section 321 of this title.

CONSTRUCTION OF 2022 AMENDMENT

Nothing in amendment made by Pub. L. 117–328 to be construed to affect ongoing withdrawal proceedings for products approved pursuant to section 356(c) of this title for which a notice of proposed withdrawal has been published in the Federal Register prior to Dec. 29, 2022, see section 3210(f) of Pub. L. 117–328, set out as a note under section 356 of this title.

REPORT TO CONGRESSIONAL COMMITTEES

Pub. L. 105–115, title I, § 130(b), Nov. 21, 1997, 111 Stat. 2331, provided that not later than Oct. 1, 2001, the Secretary was to submit to Congress a report containing a summary of the reports submitted under section 356b of this title and an evaluation and legislative recommendations relating to postmarketing studies of drugs.

§ 356c. Discontinuance or interruption in the production of life-saving drugs

(a) In general

A manufacturer of a drug—

(1) that is—

(A) life-supporting;

(B) life-sustaining; or

(C) intended for use in the prevention or treatment of a debilitating disease or condition, including any such drug used in emergency medical care or during surgery or any such drug that is critical to the public health during a public health emergency declared by the Secretary under section 247d of title 42; and

(2) that is not a radio pharmaceutical drug product or any other product as designated by the Secretary,

shall notify the Secretary, in accordance with subsection (b), of a permanent discontinuance in the manufacture of the drug or an interruption of the manufacture of the drug that is likely to lead to a meaningful disruption in the supply of that drug in the United States, or a permanent discontinuance in the manufacture of an active pharmaceutical ingredient or an interruption in the manufacture of the active pharmaceutical ingredient of such drug that is likely to lead to a meaningful disruption in the supply of the active pharmaceutical ingredient of such drug, and the reasons for such discontinuance or interruption. Notification under this subsection shall include disclosure of reasons for the discontinuation or interruption, and if applicable, an active pharmaceutical ingredient is a reason for, or risk factor in, such discontinuation or interruption, the source of the active pharmaceutical ingredient and any alternative sources for the active pharmaceutical ingredient known by the manufacturer; whether any associated device used for preparation or administration included in the drug is a reason for, or a risk factor in, such discontinuation or interruption; the expected duration of the interruption; and such other information as the Secretary may require.

(b) Timing

A notice required under subsection (a) shall be submitted to the Secretary—

(1) at least 6 months prior to the date of the discontinuance or interruption; or

(2) if compliance with paragraph (1) is not possible, as soon as practicable.

(c) Distribution

To the maximum extent practicable, the Secretary shall distribute, through such means as the Secretary deems appropriate, information on the discontinuance or interruption of the manufacture of the drugs described in subsection (a) to appropriate organizations, including physician, health provider, and patient organizations, as described in section 356e of this title.

(d) Confidentiality

Nothing in this section shall be construed as authorizing the Secretary to disclose any information that is a trade secret or confidential information subject to section 552(b)(4) of title 5 or section 1905 of title 18.

(e) Coordination with Attorney General

Not later than 30 days after the receipt of a notification described in subsection (a), the Secretary shall—

(1) determine whether the notification pertains to a controlled substance subject to a production quota under section 826 of this title; and

(2) if necessary, as determined by the Secretary—

(A) notify the Attorney General that the Secretary has received such a notification;

(B) request that the Attorney General increase the aggregate and individual production quotas under section 826 of this title applicable to such controlled substance and any ingredient therein to a level the Secretary deems necessary to address a shortage of a controlled substance based on the best available market data; and

(C) if the Attorney General determines that the level requested is not necessary to address a shortage of a controlled substance, the Attorney General shall provide to the Secretary a written response detailing the basis for the Attorney General's determination.

The Secretary shall make the written response provided under subparagraph (C) available to the public on the Internet Web site of the Food and Drug Administration.

(f) Failure to meet requirements

If a person fails to submit information required under subsection (a) in accordance with subsection (b)—

(1) the Secretary shall issue a letter to such person informing such person of such failure;

(2) not later than 30 calendar days after the issuance of a letter under paragraph (1), the person who receives such letter shall submit to the Secretary a written response to such letter setting forth the basis for noncompliance and providing information required under subsection (a); and

(3) not later than 45 calendar days after the issuance of a letter under paragraph (1), the Secretary shall make such letter and any response to such letter under paragraph (2) available to the public on the Internet Web site of the Food and Drug Administration, with appropriate redactions made to protect information described in subsection (d), except that, if the Secretary determines that the letter under paragraph (1) was issued in error or, after review of such response, the person had a reasonable basis for not notifying as required under subsection (a), the requirements of this paragraph shall not apply.

(g) Expedited inspections and reviews

If, based on notifications described in subsection (a) or any other relevant information, the Secretary concludes that there is, or is likely to be, a drug shortage of a drug described in subsection (a), the Secretary shall, as appropriate—

(1) prioritize and expedite the review of a supplement to a new drug application submitted under section 355(b) of this title, an abbreviated new drug application submitted under section 355(j) of this title, or a supplement to such an application submitted under section 355(j) of this title, that could help mitigate or prevent such shortage; or

(2) prioritize and expedite an inspection or reinspection of an establishment that could help mitigate or prevent such drug shortage.

(h) Definitions

For purposes of this section—

(1) the term ''drug''—

(A) means a drug (as defined in section 321(g) of this title) that is intended for human use and that is subject to section 353(b)(1) of this title; and

(B) does not include biological products (as defined in section 262 of title 42), unless otherwise provided by the Secretary in the regulations promulgated under subsection (i);

(2) the term ''drug shortage'' or ''shortage'', with respect to a drug, means a period of time when the demand or projected demand for the drug within the United States exceeds the supply of the drug; and

(3) the term ''meaningful disruption''—

(A) means a change in production that is reasonably likely to lead to a reduction in the supply of a drug by a manufacturer that is more than negligible and affects the ability of the manufacturer to fill orders or meet expected demand for its product; and

(B) does not include interruptions in manufacturing due to matters such as routine maintenance or insignificant changes in manufacturing so long as the manufacturer expects to resume operations in a short period of time.

(i) Regulations

(1) In general

Not later than 18 months after July 9, 2012, the Secretary shall adopt a final regulation implementing this section.

(2) Contents

Such regulation shall define, for purposes of this section, the terms ''life-supporting'', ''life-sustaining'', and ''intended for use in the prevention or treatment of a debilitating disease or condition''.

(3) Inclusion of biological products

(A) In general

The Secretary may by regulation apply this section to biological products (as defined in section 262 of title 42), including plasma products derived from human plasma protein and their recombinant analogs, if the Secretary determines such inclusion would benefit the public health. Such regulation shall take into account any supply reporting programs and shall aim to reduce duplicative notification.

(B) Rule for vaccines

If the Secretary applies this section to vaccines pursuant to subparagraph (A), the Secretary shall—

(i) consider whether the notification requirement under subsection (a) may be satisfied by submitting a notification to the Centers for Disease Control and Prevention under the vaccine shortage notification program of such Centers; and

(ii) explain the determination made by the Secretary under clause (i) in the regulation.

(4) Procedure

In promulgating a regulation implementing this section, the Secretary shall—

(A) issue a notice of proposed rulemaking that includes the proposed regulation;

(B) provide a period of not less than 60 days for comments on the proposed regulation; and

(C) publish the final regulation not less than 30 days before the regulation's effective date.

(5) Restrictions

Notwithstanding any other provision of Federal law, in implementing this section, the Secretary shall only promulgate regulations as described in paragraph (4).

(j) Risk management plans

Each manufacturer of a drug described in subsection (a) or of any active pharmaceutical ingredient or any associated medical device used for preparation or administration included in the drug, shall develop, maintain, and implement, as appropriate, a redundancy risk management plan that identifies and evaluates risks to the supply of the drug, as applicable, for each establishment in which such drug or active

pharmaceutical ingredient of such drug is manufactured. A risk management plan under this section shall be subject to inspection and copying by the Secretary pursuant to an inspection or a request under section 374(a)(4) of this title.

(June 25, 1938, ch. 675, § 506C, as added Pub. L. 105–115, title I, § 131(a), Nov. 21, 1997, 111 Stat. 2332; amended Pub. L. 112–144, title X, § 1001(a), July 9, 2012, 126 Stat. 1099; Pub. L. 114–255, div. A, title III, § 3101(a)(2)(E), Dec. 13, 2016, 130 Stat. 1153; Pub. L. 116–136, div. A, title III, §§ 3111–3112(b), Mar. 27, 2020, 134 Stat. 361, 362; Pub. L. 117–328, div. FF, title II, § 2515(a)(1), (b)(1), Dec. 29, 2022, 136 Stat. 5806.)

Editorial Notes

Amendments

2022—Subsec. (a). Pub. L. 117–328, § 2515(b)(1), substituted ''in the United States,'' for ''in the United States,,'' in concluding provisions.

Subsec. (g). Pub. L. 117–328, § 2515(a)(1), made technical amendment to directory language of Pub. L. 116–136, § 3111(1). See 2020 Amendment note below.

2020—Subsec. (a). Pub. L. 116–136, § 3112(a)(2), in concluding provisions, inserted '', or a permanent discontinuance in the manufacture of an active pharmaceutical ingredient or an interruption in the manufacture of the active pharmaceutical ingredient of such drug that is likely to lead to a meaningful disruption in the supply of the active pharmaceutical ingredient of such drug,'' before ''and the reasons'' and inserted at end ''Notification under this subsection shall include disclosure of reasons for the discontinuation or interruption, and if applicable, an active pharmaceutical ingredient is a reason for, or risk factor in, such discontinuation or interruption, the source of the active pharmaceutical ingredient and any alternative sources for the active pharmaceutical ingredient known by the manufacturer; whether any associated device used for preparation or administration included in the drug is a reason for, or a risk factor in, such discontinuation or interruption; the expected duration of the interruption; and such other information as the Secretary may require.''

Subsec. (a)(1)(C). Pub. L. 116–136, § 3112(a)(1), inserted ''or any such drug that is critical to the public health during a public health emergency declared by the Secretary under section 247d of title 42'' after ''during surgery''.

Subsec. (g). Pub. L. 116–136, § 3111(1), as amended by Pub. L. 117–328, § 2515(a)(1), substituted ''the Secretary shall, as appropriate'' for ''the Secretary may'' in introductory provisions.

Subsec. (g)(1). Pub. L. 116–136, § 3111(2), inserted ''prioritize and'' before ''expedite the review''.

Subsec. (g)(2). Pub. L. 116–136, § 3111(3), inserted ''prioritize and'' before ''expedite an inspection''.

Subsec. (j). Pub. L. 116–136, § 3112(b), added subsec. (j).

2016—Subsec. (c). Pub. L. 114–255, § 3101(a)(2)(E)(i), substituted ''discontinuance'' for ''discontinuation''.

Subsec. (g)(1). Pub. L. 114–255, § 3101(a)(2)(E)(ii), substituted ''section 355(j) of this title, that could help'' for ''section 355(j) of this title that could help''.

2012—Pub. L. 112–144 amended section generally. Prior to amendment, section related to discontinuance of life saving products.

Statutory Notes and Related Subsidiaries

Effective Date of 2022 Amendment

Pub. L. 117–328, div. FF, title II, § 2515(b)(2), Dec. 29, 2022, 136 Stat. 5806, provided that: ''The amendment made by paragraph (1) [amending this section] shall take effect as if included in section 3112 of division A of the CARES Act (Public Law 116–136).''

Effective Date of 2020 Amendment

Pub. L. 116–136, div. A, title III, § 3112(g), Mar. 27, 2020, 134 Stat. 363, provided that: ''The amendments made by this section [amending this section and sections 356e, 360, and 374 of this title] and section 3111 [amending this section] shall take effect on the date that is 180 days after the date of enactment of this Act [Mar. 27, 2020].''

Effective Date

Section effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as an Effective Date of 1997 Amendment note under section 321 of this title.

Construction of 2020 Amendment: Confidentiality

Pub. L. 116–136, div. A, title III, § 3112(f), Mar. 27, 2020, 134 Stat. 363, provided that: ''Nothing in the amendments made by this section [see Effective Date of 2020 Amendment note set out above] shall be construed as authorizing the Secretary to disclose any information that is a trade secret or confidential information subject to section 552(b)(4) of title 5, United States Code, or section 1905 of title 18, United States Code.''

Effect of Notification

Pub. L. 112–144, title X, § 1001(b), July 9, 2012, 126 Stat. 1101, provided that: ''The submission of a notification to the Secretary of Health and Human Services (referred to in this title [see Tables for classification] as the 'Secretary') for purposes of complying with the requirement in section 506C(a) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 356c(a)] (as amended by subsection (a)) shall not be construed—

''(1) as an admission that any product that is the subject of such notification violates any provision of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.); or

''(2) as evidence of an intention to promote or market the product for an indication or use for which the product has not been approved by the Secretary.''

Executive Documents

Ex. Ord. No. 13588. Reducing Prescription Drug Shortages

Ex. Ord. No. 13588, Oct. 31, 2011, 76 F.R. 68295, provided:

By the authority vested in me as President by the Constitution and the laws of the United States of America, it is hereby ordered as follows:

Section 1. *Policy*. Shortages of pharmaceutical drugs pose a serious and growing threat to public health. While a very small number of drugs in the United States experience a shortage in any given year, the number of prescription drug shortages in the United States nearly tripled between 2005 and 2010, and shortages are becoming more severe as well as more frequent. The affected medicines include cancer treatments, anesthesia drugs, and other drugs that are critical to the treatment and prevention of serious diseases and life-threatening conditions.

For example, over approximately the last 5 years, data indicates that the use of sterile injectable cancer treatments has increased by about 20 percent, without a corresponding increase in production capacity. While manufacturers are currently in the process of expanding capacity, it may be several years before production capacity has been significantly increased. Interruptions in the supplies of these drugs endanger patient safety and burden doctors, hospitals, pharmacists, and patients. They also increase health care costs, particularly because some participants in the market may use shortages as opportunities to hoard scarce drugs or charge exorbitant prices.

The Food and Drug Administration (FDA) in the Department of Health and Human Services has been working diligently to address this problem through its exist-

ing regulatory framework. While the root problems and many of their solutions are outside of the FDA's control, the agency has worked cooperatively with manufacturers to prevent or mitigate shortages by expediting review of certain regulatory submissions and adopting a flexible approach to drug manufacturing and importation regulations where appropriate. As a result, the FDA prevented 137 drug shortages in 2010 and 2011. Despite these successes, however, the problem of drug shortages has continued to grow.

Many different factors contribute to drug shortages, and solving this critical public health problem will require a multifaceted approach. An important factor in many of the recent shortages appears to be an increase in demand that exceeds current manufacturing capacity. While manufacturers are in the process of expanding capacity, one important step is ensuring that the FDA and the public receive adequate advance notice of shortages whenever possible. The FDA cannot begin to work with manufacturers or use the other tools at its disposal until it knows there is a potential problem. Similarly, early disclosure of a shortage can help hospitals, doctors, and patients make alternative arrangements before a shortage becomes a crisis. However, drug manufacturers have not consistently provided the FDA with adequate notice of potential shortages.

As part of my Administration's broader effort to work with manufacturers, health care providers, and other stakeholders to prevent drug shortages, this order directs the FDA to take steps that will help to prevent and reduce current and future disruptions in the supply of lifesaving medicines.

SEC. 2. *Broader Reporting of Manufacturing Discontinuances*. To the extent permitted by law, the FDA shall use all appropriate administrative tools, including its authority to interpret and administer the reporting requirements in 21 U.S.C. 356c, to require drug manufacturers to provide adequate advance notice of manufacturing discontinuances that could lead to shortages of drugs that are life-supporting or life-sustaining, or that prevent debilitating disease.

SEC. 3. *Expedited Regulatory Review*. To the extent practicable, and consistent with its statutory responsibility to ensure the safety and effectiveness of the drug supply, the FDA shall take steps to expand its current efforts to expedite its regulatory reviews, including reviews of new drug suppliers, manufacturing sites, and manufacturing changes, whenever it determines that expedited review would help to avoid or mitigate existing or potential drug shortages. In prioritizing and allocating its limited resources, the FDA should consider both the severity of the shortage and the importance of the affected drug to public health.

SEC. 4. *Review of Certain Behaviors by Market Participants*. The FDA shall communicate to the Department of Justice (DOJ) any findings that shortages have led market participants to stockpile the affected drugs or sell them at exorbitant prices. The DOJ shall then determine whether these activities are consistent with applicable law. Based on its determination, DOJ, in coordination with other State and Federal regulatory agencies as appropriate, should undertake whatever enforcement actions, if any, it deems appropriate.

SEC. 5. *General Provisions*. (a) Nothing in this order shall be construed to impair or otherwise affect:

(i) authority granted by law to an agency, or the head thereof; or

(ii) functions of the Director of the Office of Management and Budget relating to budgetary, administrative, or legislative proposals.

(b) This order shall be implemented consistent with applicable law and subject to the availability of appropriations.

(c) This order is not intended to, and does not, create any right or benefit, substantive or procedural, enforceable at law or in equity by any party against the United States, its departments, agencies, or entities, its officers, employees, or agents, or any other person.

BARACK OBAMA.

§ 356c–1. Annual reporting on drug shortages

(a) Annual reports to Congress

Not later than March 31 of each calendar year, the Secretary shall submit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate a report, with respect to the preceding calendar year, on drug shortages that—

(1) specifies the number of manufacturers that submitted a notification to the Secretary under section 356c(a) of this title during such calendar year;

(2) describes the communication between the field investigators of the Food and Drug Administration and the staff of the Center for Drug Evaluation and Research's Office of Compliance and Drug Shortage Program, including the Food and Drug Administration's procedures for enabling and ensuring such communication;

(3) describes the coordination and alignment activities undertaken pursuant to section 356d(g) of this title;

(4) provides the number of reports that were required under section 374(b)(2) of this title to be sent to the appropriate offices of the Food and Drug Administration with expertise regarding drug shortages, and the number of such reports that were sent;

(5)(A) lists the major actions taken by the Secretary to prevent or mitigate the drug shortages described in paragraph (9);

(B) in the list under subparagraph (A), includes—

(i) the number of applications and supplements for which the Secretary expedited review under section 356c(g)(1) of this title during such calendar year; and

(ii) the number of establishment inspections or reinspections that the Secretary expedited under section 356c(g)(2) of this title during such calendar year;

(6) describes the coordination between the Food and Drug Administration and the Drug Enforcement Administration on efforts to prevent or alleviate drug shortages;

(7) identifies the number of and describes the instances in which the Food and Drug Administration exercised regulatory flexibility and discretion to prevent or alleviate a drug shortage;

(8) lists the names of manufacturers that were issued letters under section 356c(f) of this title; and

(9) specifies the number of drug shortages occurring during such calendar year, as identified by the Secretary.

(b) Trend analysis

The Secretary is authorized to retain a third party to conduct a study, if the Secretary believes such a study would help clarify the causes, trends, or solutions related to drug shortages.

(c) Definition

In this section, the term ''drug shortage'' or ''shortage'' has the meaning given such term in section 356c of this title.

(June 25, 1938, ch. 675, § 506C–1, as added Pub. L. 112–144, title X, § 1002, July 9, 2012, 126 Stat. 1102; amended Pub. L. 114–255, div. A, title III, § 3101(a)(2)(F), Dec. 13, 2016, 130 Stat. 1153; Pub. L. 117–328, div. FF, title III, § 3616(b)(1), Dec. 29, 2022, 136 Stat. 5875.)

Editorial Notes

AMENDMENTS

2022—Subsec. (a)(3) to (5). Pub. L. 117–328, § 3616(b)(1)(A), (B), added pars. (3) and (4) and redesignated former par. (3) as (5). Former pars. (4) and (5) redesignated (6) and (7), respectively.

Subsec. (a)(5)(A). Pub. L. 117–328, § 3616(b)(1)(C), substituted ''paragraph (9)'' for ''paragraph (7)''.

Subsec. (a)(6) to (9). Pub. L. 117–328, § 3616(b)(1)(A), redesignated pars. (4) to (7) as (6) to (9), respectively.

2016—Subsec. (a). Pub. L. 114–255, in introductory provisions, substituted ''Not later than March 31 of each calendar year,'' for ''Not later than the end of calendar year 2013, and not later than the end of each calendar year thereafter,'' and inserted '', with respect to the preceding calendar year,'' after ''a report''.

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 2022 AMENDMENT

Pub. L. 117–328, div. FF, title III, § 3616(b)(2), Dec. 29, 2022, 136 Stat. 5875, provided that: ''The amendments made by paragraph (1) [amending this section] shall apply with respect to reports submitted under section 506C–1 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356c–1) on or after March 31, 2024.''

§ 356d. Coordination; task force and strategic plan

(a) Task force and strategic plan

(1) In general

(A) Task force

As soon as practicable after July 9, 2012, the Secretary shall establish a task force to develop and implement a strategic plan for enhancing the Secretary's response to preventing and mitigating drug shortages.

(B) Strategic plan

The strategic plan described in subparagraph (A) shall include—

(i) plans for enhanced interagency and intra-agency coordination, communication, and decisionmaking;

(ii) plans for ensuring that drug shortages are considered when the Secretary initiates a regulatory action that could precipitate a drug shortage or exacerbate an existing drug shortage;

(iii) plans for effective communication with outside stakeholders, including who the Secretary should alert about potential or actual drug shortages, how the communication should occur, and what types of information should be shared;

(iv) plans for considering the impact of drug shortages on research and clinical trials; and

(v) an examination of whether to establish a ''qualified manufacturing partner program'', as described in subparagraph (C).

(C) Description of program

In conducting the examination of a ''qualified manufacturing partner program'' under subparagraph (B)(v), the Secretary—

(i) shall take into account that—

(I) a ''qualified manufacturer'', for purposes of such program, would need to have the capability and capacity to supply products determined or anticipated to be in shortage; and

(II) in examining the capability and capacity to supply products in shortage, the ''qualified manufacturer'' could have a site that manufactures a drug listed under section 356e of this title or have the capacity to produce drugs in response to a shortage within a rapid timeframe; and

(ii) shall examine whether incentives are necessary to encourage the participation of ''qualified manufacturers'' in such a program.

(D) Consultation

In carrying out this paragraph, the task force shall ensure consultation with the appropriate offices within the Food and Drug Administration, including the Office of the Commissioner, the Center for Drug Evaluation and Research, the Office of Regulatory Affairs, and employees within the Department of Health and Human Services with expertise regarding drug shortages. The Secretary shall engage external stakeholders and experts as appropriate.

(2) Timing

Not later than 1 year after July 9, 2012, the task force shall—

(A) publish the strategic plan described in paragraph (1); and

(B) submit such plan to Congress.

(b) Communication

The Secretary shall ensure that, prior to any enforcement action or issuance of a warning letter that the Secretary determines could reasonably be anticipated to lead to a meaningful disruption in the supply in the United States of a drug described under section 356c(a) of this title, there is communication with the appropriate office of the Food and Drug Administration with expertise regarding drug shortages regarding whether the action or letter could cause, or exacerbate, a shortage of the drug.

(c) Action

If the Secretary determines, after the communication described in subsection (b), that an enforcement action or a warning letter could reasonably cause or exacerbate a shortage of a drug described under section 356c(a) of this title, then the Secretary shall evaluate the risks associated with the impact of such shortage upon patients and those risks associated with the violation involved before taking such action or issuing such letter, unless there is imminent risk of serious adverse health consequences or death to humans.

(d) Reporting by other entities

The Secretary shall identify or establish a mechanism by which health care providers and other third-party organizations may report to the Secretary evidence of a drug shortage.

(e) Review and construction

No determination, finding, action, or omission of the Secretary under this section shall—

(1) be subject to judicial review; or

(2) be construed to establish a defense to an enforcement action by the Secretary.

(f) Temporary sunset

Subsection (a) shall cease to be effective on the date that is 5 years after July 9, 2012. Subsections (b), (c), and (e) shall not be in effect during the period beginning 5 years after July 9, 2012, and ending on December 29, 2022. Subsections (b), (c), and (e) shall be in effect beginning on December 29, 2022.

(g) Coordination

The Secretary shall ensure timely and effective internal coordination and alignment among the field investigators of the Food and Drug Administration and the staff of the Center for Drug Evaluation and Research's Office of Compliance and Drug Shortage Program regarding—

(1) the reviews of reports shared pursuant to section 374(b)(2) of this title; and

(2) any feedback or corrective or preventive actions in response to such reports.

(June 25, 1938, ch. 675, § 506D, as added Pub. L. 112–144, title X, § 1003, July 9, 2012, 126 Stat. 1103; amended Pub. L. 117–328, div. FF, title III, § 3616(a), Dec. 29, 2022, 136 Stat. 5874.)

Editorial Notes

AMENDMENTS

2022—Subsec. (f). Pub. L. 117–328, § 3616(a)(2), amended subsec. (f) generally. Prior to amendment, text read as follows: ''Subsections (a), (b), (c), and (e) shall cease to be effective on the date that is 5 years after July 9, 2012.''

Subsec. (g). Pub. L. 117–328, § 3616(a)(1), added subsec. (g).

§ 356e. Drug shortage list

(a) Establishment

The Secretary shall maintain an up-to-date list of drugs that are determined by the Secretary to be in shortage in the United States.

(b) Contents

For each drug on such list, the Secretary shall include the following information:

(1) The name of the drug in shortage, including the National Drug Code number for such drug.

(2) The name of each manufacturer of such drug.

(3) The reason for the shortage, as determined by the Secretary, selecting from the following categories:

(A) Requirements related to complying with good manufacturing practices.

(B) Regulatory delay.

(C) Shortage of an active ingredient.

(D) Shortage of an inactive ingredient component.

(E) Discontinuance of the manufacture of the drug.

(F) Delay in shipping of the drug.

(G) Demand increase for the drug.

(4) The estimated duration of the shortage as determined by the Secretary.

(c) Public availability

(1) In general

Subject to paragraphs (2) and (3), the Secretary shall make the information in such list publicly available.

(2) Trade secrets and confidential information

Nothing in this section alters or amends section 1905 of title 18 or section 552(b)(4) of title 5.

(3) Public health exception

The Secretary may choose not to make information collected under this section publicly available under paragraph (1) or section 356c(c) of this title if the Secretary determines that disclosure of such information would adversely affect the public health (such as by increasing the possibility of hoarding or other disruption of the availability of drug products to patients).

(d) Interagency notification

Not later than 180 days after March 27, 2020, and every 90 days thereafter, the Secretary shall transmit a report regarding the drugs of the current drug shortage list under this section to the Administrator of the Centers for Medicare & Medicaid Services.

(June 25, 1938, ch. 675, § 506E, as added Pub. L. 112–144, title X, § 1004, July 9, 2012, 126 Stat. 1104; amended Pub. L. 114–255, div. A, title III, § 3101(a)(2)(G), Dec. 13, 2016, 130 Stat. 1153; Pub. L. 116–136, div. A, title III, § 3112(c), Mar. 27, 2020, 134 Stat. 362.)

Editorial Notes

AMENDMENTS

2020—Subsec. (d). Pub. L. 116–136 added subsec. (d).

2016—Subsec. (b)(3)(E). Pub. L. 114–255, which directed substitution of ''discontinuance'' for ''discontinuation'', was executed by substituting ''Discontinuance'' for ''Discontinuation'' to reflect the probable intent of Congress.

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 2020 AMENDMENT

Amendment by Pub. L. 116–136 effective 180 days after Mar. 27, 2020, see section 3112(g) of Pub. L. 116–136, set out as a note under section 356c of this title.

§ 356f. Hospital repackaging of drugs in shortage

(a) Definitions

In this section:

(1) Drug

The term ''drug'' excludes any controlled substance (as such term is defined in section 802 of this title).

(2) Health system

The term ''health system'' means a collection of hospitals that are owned and operated by the same entity and that share access to databases with drug order information for their patients.

(3) Repackage

For the purposes of this section only, the term ''repackage'', with respect to a drug, means to divide the volume of a drug into smaller amounts in order to—

(A) extend the supply of a drug in response to the placement of the drug on a drug shortage list under section 356e of this title; and

(B) facilitate access to the drug by hospitals within the same health system.

(b) Exclusion from registration

Notwithstanding any other provision of this chapter, a hospital shall not be considered an establishment for which registration is required under section 360 of this title solely because it repackages a drug and transfers it to another hospital within the same health system in accordance with the conditions in subsection (c)—

(1) during any period in which the drug is listed on the drug shortage list under section 356e of this title; or

(2) during the 60-day period following any period described in paragraph (1).

(c) Conditions

Subsection (b) shall only apply to a hospital, with respect to the repackaging of a drug for transfer to another hospital within the same health system, if the following conditions are met:

(1) Drug for intrasystem use only

In no case may a drug that has been repackaged in accordance with this section be sold or otherwise distributed by the health system or a hospital within the system to an entity or individual that is not a hospital within such health system.

(2) Compliance with State rules

Repackaging of a drug under this section shall be done in compliance with applicable State requirements of each State in which the drug is repackaged and received.

(d) Termination

This section shall not apply on or after the date on which the Secretary issues final guidance that clarifies the policy of the Food and Drug Administration regarding hospital pharmacies repackaging and safely transferring repackaged drugs to other hospitals within the same health system during a drug shortage.

(June 25, 1938, ch. 675, § 506F, as added Pub. L. 112–144, title X, § 1007, July 9, 2012, 126 Stat. 1106.)

§ 356g. Standards for regenerative medicine and regenerative advanced therapies

(a) In general

Not later than 2 years after December 13, 2016, the Secretary, in consultation with the National Institute of Standards and Technology and stakeholders (including regenerative medicine and advanced therapies manufacturers and clinical trial sponsors, contract manufacturers, academic institutions, practicing clinicians, regenerative medicine and advanced therapies industry organizations, and standard setting organizations), shall facilitate an effort to coordinate and prioritize the development of standards and consensus definition of terms, through a public process, to support, through regulatory predictability, the development, evaluation, and review of regenerative medicine therapies and regenerative advanced therapies, including with respect to the manufacturing processes and controls of such products.

(b) Activities

(1) In general

In carrying out this section, the Secretary shall continue to—

(A) identify opportunities to help advance the development of regenerative medicine therapies and regenerative advanced therapies;

(B) identify opportunities for the development of laboratory regulatory science research and documentary standards that the Secretary determines would help support the development, evaluation, and review of regenerative medicine therapies and regenerative advanced therapies through regulatory predictability; and

(C) work with stakeholders, such as those described in subsection (a), as appropriate, in the development of such standards.

(2) Regulations and guidance

Not later than 1 year after the development of standards as described in subsection (a), the Secretary shall review relevant regulations and guidance and, through a public process, update such regulations and guidance as the Secretary determines appropriate.

(c) Definitions

For purposes of this section, the terms ''regenerative medicine therapy'' and ''regenerative advanced therapy'' have the meanings given such terms in section 356(g) of this title.

(June 25, 1938, ch. 675, § 506G, as added Pub. L. 114–255, div. A, title III, § 3036, Dec. 13, 2016, 130 Stat. 1104; amended Pub. L. 115–52, title IX, § 901(b), Aug. 18, 2017, 131 Stat. 1076.)

Editorial Notes

AMENDMENTS

2017—Subsec. (b)(1)(A). Pub. L. 115–52 substituted ''identify'' for ''identity''.

Statutory Notes and Related Subsidiaries

GUIDANCE REGARDING DEVICES USED IN THE RECOVERY, ISOLATION, OR DELIVERY OF REGENERATIVE ADVANCED THERAPIES

Pub. L. 114–255, div. A, title III, § 3034, Dec. 13, 2016, 130 Stat. 1103, provided that:

''(a) DRAFT GUIDANCE.—Not later than 1 year after the date of enactment of the 21st Century Cures Act [Dec. 13, 2016], the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs, shall issue draft guidance clarifying how, in the context of regenerative advanced therapies, the Secretary will evaluate devices used in the recovery, isolation, or delivery of regenerative advanced therapies. In doing so, the Secretary shall specifically address—

''(1) how the Food and Drug Administration intends to simplify and streamline regulatory requirements for combination device and cell or tissue products;

''(2) what, if any, intended uses or specific attributes would result in a device used with a regenerative therapy product to be classified as a class III device;

''(3) when the Food and Drug Administration considers it is necessary, if ever, for the intended use of a device to be limited to a specific intended use with only one particular type of cell; and

''(4) application of the least burdensome approach to demonstrate how a device may be used with more than one cell type.

''(b) FINAL GUIDANCE.—Not later than 12 months after the close of the period for public comment on the draft guidance under subsection (a), the Secretary of Health and Human Services shall finalize such guidance.''

§ 356h. Competitive generic therapies

(a) In general

The Secretary may, at the request of an applicant of a drug that is designated as a competitive generic therapy pursuant to subsection (b), expedite the development and review of an abbreviated new drug application under section 355(j) of this title for such drug.

(b) Designation process

(1) Request

The applicant may request the Secretary to designate the drug as a competitive generic therapy.

(2) Timing

A request under paragraph (1) may be made concurrently with, or at any time prior to, the submission of an abbreviated new drug application for the drug under section 355(j) of this title.

(3) Criteria

A drug is eligible for designation as a competitive generic therapy under this section if the Secretary determines that there is inadequate generic competition.

(4) Designation

Not later than 60 calendar days after the receipt of a request under paragraph (1), the Secretary may—

(A) determine whether the drug that is the subject of the request meets the criteria described in paragraph (3); and

(B) if the Secretary finds that the drug meets such criteria, designate the drug as a competitive generic therapy.

(c) Actions

In expediting the development and review of an application under subsection (a), the Secretary may, as requested by the applicant, take actions including the following:

(1) Hold meetings with the applicant and the review team throughout the development of the drug prior to submission of the application for such drug under section 355(j) of this title.

(2) Provide timely advice to, and interactive communication with, the applicant regarding the development of the drug to ensure that the development program to gather the data necessary for approval is as efficient as practicable.

(3) Involve senior managers and experienced review staff, as appropriate, in a collaborative, coordinated review of such application, including with respect to drug-device combination products and other complex products.

(4) Assign a cross-disciplinary project lead—

(A) to facilitate an efficient review of the development program and application, including manufacturing inspections; and

(B) to serve as a scientific liaison between the review team and the applicant.

(d) Reporting requirement

Not later than one year after the date of the approval of an application under section 355(j) of this title with respect to a drug for which the development and review is expedited under this section, the sponsor of such drug shall report to the Secretary on whether the drug has been marketed in interstate commerce since the date of such approval.

(e) Definitions

In this section:

(1) The term ''generic drug'' means a drug that is approved pursuant to section 355(j) of this title.

(2) The term ''inadequate generic competition'' means, with respect to a drug, there is not more than one approved drugs[1] on the list of drugs described in section 355(j)(7)(A) of this title (not including drugs on the discontinued section of such list) that is—

(A) the reference listed drug; or

(B) a generic drug with the same reference listed drug as the drug for which designation as a competitive generic therapy is sought.

(3) The term ''reference listed drug'' means the listed drug (as such term is used in section 355(j) of this title) for the drug involved.

(June 25, 1938, ch. 675, § 506H, as added Pub. L. 115–52, title VIII, § 803(a), Aug. 18, 2017, 131 Stat. 1070.)

Statutory Notes and Related Subsidiaries

GUIDANCE; AMENDED REGULATIONS

Pub. L. 115–52, title VIII, § 803(b), Aug. 18, 2017, 131 Stat. 1071, provided that:

''(1) IN GENERAL.—

''(A) ISSUANCE.—The Secretary of Health and Human Services shall—

''(i) not later than 18 months after the date of enactment of this Act [Aug. 18, 2017], issue draft guidance on section 506H of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 356h], as added by subsection (a); and

''(ii) not later than 1 year after the close of the comment period for the draft guidance, issue final guidance on such section 506H.

''(B) CONTENTS.—The guidance issued under this paragraph shall—

''(i) specify the process and criteria by which the Secretary makes a designation under section 506H of the Federal Food, Drug, and Cosmetic Act, as added by subsection (a);

''(ii) specify the actions the Secretary may take to expedite the development and review of a competitive generic therapy pursuant to such a designation; and

''(iii) include good review management practices for competitive generic therapies.

''(2) AMENDED REGULATIONS.—The Secretary of Health and Human Services shall issue or revise any regulations as may be necessary to carry out this section not later than 2 years after the date of enactment of this Act [Aug. 18, 2017].''

§ 356i. Prompt reports of marketing status

(a) Notification of withdrawal

The holder of an application approved under subsection (c) or (j) of section 355 of this title or subsection (a) or (k) of section 262 of title 42 shall notify the Secretary in writing 180 days prior to withdrawing the approved drug from sale, or if 180 days is not practicable as soon as

[1] So in original. Probably should be ''drug''.

practicable but not later than the date of withdrawal. The holder shall include with such notice the—

(1) National Drug Code;

(2) identity of the drug by established name (or, in the case of a biological product, the proper name) and by proprietary name, if any;

(3) new drug application number, abbreviated application number, or biologics license application number;

(4) strength of the drug;

(5) date on which the drug is expected to no longer be available for sale; and

(6) reason for withdrawal of the drug.

(b) Notification of drug not available for sale

The holder of an application approved under subsection (c) or (j) of section 355 of this title or subsection (a) or (k) of section 262 of title 42 shall notify the Secretary in writing within 180 calendar days of the date of approval of the drug if the drug will not be available for sale within 180 calendar days of such date of approval. The holder shall include with such notice the—

(1) identity of the drug by established name (or, in the case of a biological product, the proper name) and by proprietary name, if any;

(2) new drug application number, abbreviated application number, or biologics license application number;

(3) strength of the drug;

(4) date on which the drug will be available for sale, if known; and

(5) reason for not marketing the drug after approval.

(c) Additional one-time report

Within 180 days of December 29, 2022, all holders of applications approved under subsection (a) or (k) of section 262 of title 42 shall review the information in the list published under section 262(k)(9)(A) of title 42 and shall submit a written notice to the Secretary—

(1) stating that all of the application holder's biological products in the list published under such section 262(k)(9)(A) of title 42 that are not listed as discontinued are available for sale; or

(2) including the information required pursuant to subsection (a) or (b), as applicable, for each of the application holder's biological products that are in the list published under such section 262(k)(9)(A) of title 42 and not listed as discontinued, but have been discontinued from sale or never have been available for sale.

(d) Failure to meet requirements

If a holder of an approved application fails to submit the information required under subsection (a), (b), or (c), the Secretary may—

(1) move the application holder's drugs from the active section of the list published under section 355(j)(7)(A) of this title to the discontinued section of the list, except that the Secretary shall remove from the list in accordance with section 355(j)(7)(C) of this title drugs the Secretary determines have been withdrawn from sale for reasons of safety or effectiveness; and

(2) identify the application holder's biological products as discontinued in the list published under section 262(k)(9)(A) of title 42, except that the Secretary shall remove from the list in accordance with section 262(k)(9)(B) of such title biological products for which the license has been revoked or suspended for reasons of safety, purity, or potency.

(e) Updates

The Secretary shall update the list published under section 355(j)(7)(A) of this title based on the information provided under subsections (a), (b), and (c) by moving drugs that are not available for sale from the active section to the discontinued section of the list, except that drugs the Secretary determines have been withdrawn from sale for reasons of safety or effectiveness shall be removed from the list in accordance with section 355(j)(7)(C) of this title. The Secretary shall update the list published under section 262(k)(9)(A) of title 42 based on information provided under subsections (a), (b), and (c) by identifying as discontinued biological products that are not available for sale, except that biological products for which the license has been revoked or suspended for safety, purity, or potency reasons shall be removed from the list in accordance with section 262(k)(9)(B) of title 42. The Secretary shall make monthly updates to the lists referred to in the preceding sentences based on the information provided pursuant to subsections (a) and (b), and shall update such lists based on the information provided under subsection (c) as soon as practicable.

(f) Limitation on use of notices

Any notice submitted under this section shall not be made public by the Secretary and shall be used solely for the purpose of the updates described in subsection (e).

(June 25, 1938, ch. 675, § 506I, as added Pub. L. 115–52, title VIII, § 804, Aug. 18, 2017, 131 Stat. 1071; amended Pub. L. 117–328, div. FF, title III, § 3201, Dec. 29, 2022, 136 Stat. 5808.)

Editorial Notes

AMENDMENTS

2022—Subsec. (a). Pub. L. 117–328, § 3201(a)(1)(A), substituted ''The holder of an application approved under subsection (c) or (j) of section 355 of this title or subsection (a) or (k) of section 262 of title 42'' for ''The holder of an application approved under subsection (c) or (j) of section 355 of this title'' in introductory provisions.

Subsec. (a)(2). Pub. L. 117–328, § 3201(a)(1)(B), substituted ''established name (or, in the case of a biological product, the proper name)'' for ''established name''.

Subsec. (a)(3). Pub. L. 117–328, § 3201(a)(1)(C), substituted '', abbreviated application number, or biologics license application number'' for ''or abbreviated application number''.

Subsec. (b). Pub. L. 117–328, § 3201(a)(2)(A), substituted ''The holder of an application approved under subsection (c) or (j) of section 355 of this title or subsection (a) or (k) of section 262 of title 42'' for ''The holder of an application approved under subsection (c) or (j)'' in introductory provisions.

Subsec. (b)(1). Pub. L. 117–328, § 3201(a)(2)(B), substituted ''established name (or, in the case of a biological product, the proper name)'' for ''established name''.

Subsec. (b)(2). Pub. L. 117–328, § 3201(a)(2)(C), substituted '', abbreviated application number, or biologics license application number'' for ''or abbreviated application number''.

Subsec. (c). Pub. L. 117–328, § 3201(b), amended subsec. (c) generally. Prior to amendment, subsec. (c) related to an additional one-time report to be done within 180 days of Aug. 18, 2017.

Subsec. (d). Pub. L. 117–328, § 3201(c)(1), added subsec. (d) and struck out former subsec. (d). Prior to amendment, text read as follows: ''If a holder of an approved application fails to submit the information required under subsection (a), (b), or (c), the Secretary may move the application holder's drugs from the active section of the list published under subsection 355(j)(7)(A) of this title to the discontinued section of the list, except that the Secretary shall remove from the list in accordance with subsection 355(j)(7)(C) of this title drugs the Secretary determines have been withdrawn from sale for reasons of safety of effectiveness.''

Subsec. (e). Pub. L. 117–328, § 3201(d), substituted ''section 355(j)(7)(A) of this title'' for ''subsection 355(j)(7)(A) of this title'' and ''section 355(j)(7)(C) of this title'' for ''subsection 355(j)(7)(C) of this title''.

Pub. L. 117–328, § 3201(c)(2), inserted ''The Secretary shall update the list published under section 262(k)(9)(A) of title 42 based on information provided under subsections (a), (b), and (c) by identifying as discontinued biological products that are not available for sale, except that biological products for which the license has been revoked or suspended for safety, purity, or potency reasons shall be removed from the list in accordance with section 262(k)(9)(B) of title 42.'' before ''The Secretary shall make monthly updates'' and substituted ''monthly updates to the lists referred to in the preceding sentences'' for ''monthly updates to the list'' and ''and shall update such lists based on'' for ''and shall update the list based on''.

§ 356j. Discontinuance or interruption in the production of medical devices

(a) In general

A manufacturer of a device that—

(1) is critical to public health during a public health emergency, including devices that are life-supporting, life-sustaining, or intended for use in emergency medical care or during surgery; or

(2) for which the Secretary determines that information on potential meaningful supply disruptions of such device is needed during, or in advance of, a public health emergency;

shall, during, or in advance of, a public health emergency declared by the Secretary under section 247d of title 42, notify the Secretary, in accordance with subsection (b), of a permanent discontinuance in the manufacture of the device (except for discontinuances as a result of an approved modification of the device) or an interruption of the manufacture of the device that is likely to lead to a meaningful disruption in the supply of that device in the United States, and the reasons for such discontinuance or interruption.

(b) Timing

A notice required under subsection (a) shall be submitted to the Secretary—

(1) at least 6 months prior to the date of the discontinuance or interruption; or

(2) if compliance with paragraph (1) is not possible, as soon as practicable.

(c) Distribution

(1) Public availability

To the maximum extent practicable, subject to paragraph (2), the Secretary shall distribute, through such means as the Secretary determines appropriate, information on the discontinuance or interruption of the manufacture of devices reported under subsection (a) to appropriate organizations, including physician, health provider, patient organizations, and supply chain partners, as appropriate and applicable, as described in subsection (g).

(2) Public health exception

The Secretary may choose not to make information collected under this section publicly available pursuant to this section if the Secretary determines that disclosure of such information would adversely affect the public health, such as by increasing the possibility of unnecessary over purchase of product, component parts, or other disruption of the availability of medical products to patients.

(d) Confidentiality

Nothing in this section shall be construed as authorizing the Secretary to disclose any information that is a trade secret or confidential information subject to section 552(b)(4) of title 5 or section 1905 of title 18.

(e) Failure to meet requirements

If a person fails to submit information required under subsection (a) in accordance with subsection (b)—

(1) the Secretary shall issue a letter to such person informing such person of such failure;

(2) not later than 30 calendar days after the issuance of a letter under paragraph (1), the person who receives such letter shall submit to the Secretary a written response to such letter setting forth the basis for noncompliance and providing information required under subsection (a); and

(3) not later than 45 calendar days after the issuance of a letter under paragraph (1), the Secretary shall make such letter and any response to such letter under paragraph (2) available to the public on the internet website of the Food and Drug Administration, with appropriate redactions made to protect information described in subsection (d), except that, if the Secretary determines that the letter under paragraph (1) was issued in error or, after review of such response, the person had a reasonable basis for not notifying as required under subsection (a), the requirements of this paragraph shall not apply.

(f) Expedited inspections and reviews

If, based on notifications described in subsection (a) or (h) or any other relevant information, the Secretary concludes that there is, or is likely to be, a shortage of an[1] device, the Secretary shall, as appropriate—

(1) prioritize and expedite the review of a submission under section 360c(f)(2) of this title, 360e of this title, review of a notification under section 360(k) of this title, or 360j(m) of this title for a device that could help mitigate or prevent such shortage; or

(2) prioritize and expedite an inspection or reinspection of an establishment that could help mitigate or prevent such shortage.

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[1] So in original. Probably should be ''a''.

(g) Device shortage list

(1) Establishment

The Secretary shall establish and maintain an up-to-date list of devices that are determined by the Secretary to be in shortage in the United States.

(2) Contents

For each device included on the list under paragraph (1), the Secretary shall include the following information:

(A) The category or name of the device in shortage.

(B) The name of each manufacturer of such device.

(C) The reason for the shortage, as determined by the Secretary, selecting from the following categories:

(i) Requirements related to complying with good manufacturing practices.

(ii) Regulatory delay.

(iii) Shortage or discontinuance of a component or part.

(iv) Discontinuance of the manufacture of the device.

(v) Delay in shipping of the device.

(vi) Delay in sterilization of the device.

(vii) Demand increase for the device.

(viii) Facility closure.

(D) The estimated duration of the shortage as determined by the Secretary.

(3) Public availability

(A) In general

Subject to subparagraphs (B) and (C), the Secretary shall make the information in the list under paragraph (1) publicly available.

(B) Trade secrets and confidential information

Nothing in this subsection shall be construed to alter or amend section 1905 of title 18 or section 552(b)(4) of title 5.

(C) Public health exception

The Secretary may elect not to make information collected under this subsection publicly available if the Secretary determines that disclosure of such information would adversely affect the public health (such as by increasing the possibility of hoarding or other disruption of the availability of the device to patients).

(h) Additional notifications

The Secretary may receive voluntary notifications from a manufacturer of a device that is life-supporting, life-sustaining, or intended for use in emergency medical care or during surgery, or any other device the Secretary determines to be critical to the public health, pertaining to a permanent discontinuance in the manufacture of the device (except for any discontinuance as a result of an approved modification of the device) or an interruption of the manufacture of the device that is likely to lead to a meaningful disruption in the supply of that device in the United States, and the reasons for such discontinuance or interruption.

(i) Rule of construction

Nothing in this section shall be construed to affect the authority of the Secretary on March 27, 2020, to expedite the review of devices under section 360e of this title, section 360e–3 of this title relating to the priority review program for devices, and section 360bbb–3 of this title relating to the emergency use authorization authorities.

(j) Definitions

In this section:

(1) Meaningful disruption

The term ''meaningful disruption''—

(A) means a change in production that is reasonably likely to lead to a reduction in the supply of a device by a manufacturer that is more than negligible and affects the ability of the manufacturer to fill orders or meet expected demand for its product;

(B) does not include interruptions in manufacturing due to matters such as routine maintenance or insignificant changes in manufacturing so long as the manufacturer expects to resume operations in a short period of time, not to exceed 6 months;

(C) does not include interruptions in manufacturing of components or raw materials so long as such interruptions do not result in a shortage of the device and the manufacturer expects to resume operations in a reasonable period of time; and

(D) does not include interruptions in manufacturing that do not lead to a reduction in procedures or diagnostic tests associated with a medical device designed to perform more than one procedure or diagnostic test.

(2) Shortage

The term ''shortage'', with respect to a device, means a period of time when the demand or projected demand for the device within the United States exceeds the supply of the device.

(June 25, 1938, ch. 675, § 506J, as added Pub. L. 116–136, div. A, title III, § 3121, Mar. 27, 2020, 134 Stat. 363; amended Pub. L. 117–328, div. FF, title II, § 2514(a), Dec. 29, 2022, 136 Stat. 5805.)

Editorial Notes

AMENDMENTS

2022—Subsec. (f). Pub. L. 117–328, § 2514(a)(1), inserted ''or (h)'' after ''subsection (a)'' in introductory provisions.

Subsecs. (h) to (j). Pub. L. 117–328, § 2514(a)(2), (3), added subsec. (h) and redesignated former subsecs. (h) and (i) as (i) and (j), respectively.

Statutory Notes and Related Subsidiaries

GUIDANCE ON VOLUNTARY NOTIFICATIONS OF DISCONTINUANCE OR INTERRUPTION OF DEVICE MANUFACTURE

Pub. L. 117–328, div. FF, title II, § 2514(b), Dec. 29, 2022, 136 Stat. 5806, provided that: ''Not later than 1 year after the date of enactment of this Act [Dec. 29, 2022], the Secretary shall issue draft guidance to facilitate voluntary notifications under subsection (h) of section 506J of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356j), as added by subsection (a). Such guidance shall include a description of circumstances in which a voluntary notification under such subsection (h) may be appropriate, recommended timeframes for such a notification, the process for receiving such a notification, and actions the Secretary may take to mitigate or prevent a shortage resulting from a discontinuance or

interruption in the manufacture of a device for which such notification is received. The Secretary shall issue final guidance not later than 1 year after the close of the comment period for the draft guidance.''

GUIDANCE ON DEVICE SHORTAGE NOTIFICATION REQUIREMENT

Pub. L. 117–328, div. FF, title II, § 2514(c), Dec. 29, 2022, 136 Stat. 5806, provided that: ''Not later than 1 year after the date of enactment of this Act [Dec. 29, 2022], the Secretary shall issue or revise draft guidance regarding requirements under section 506J of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356j). Such guidance shall include a list of each device product code for which a manufacturer of such device is required to notify the Secretary in accordance with section 506J.''

§ 356k. Platform technologies

(a) In general

The Secretary shall establish a program for the designation of platform technologies that meet the criteria described in subsection (b).

(b) Criteria

A platform technology incorporated within or utilized by a drug or biological product is eligible for designation as a designated platform technology under this section if—

(1) the platform technology is incorporated in, or utilized by, a drug approved under section 355 of this title or a biological product licensed under section 351 of the Public Health Service Act [42 U.S.C. 262];

(2) preliminary evidence submitted by the sponsor of the approved or licensed drug described in paragraph (1), or a sponsor that has been granted a right of reference to data submitted in the application for such drug, demonstrates that the platform technology has the potential to be incorporated in, or utilized by, more than one drug without an adverse effect on quality, manufacturing, or safety; and

(3) data or information submitted by the applicable person under paragraph (2) indicates that incorporation or utilization of the platform technology has a reasonable likelihood to bring significant efficiencies to the drug development or manufacturing process and to the review process.

(c) Request for designation

A person may request the Secretary designate a platform technology as a designated platform technology concurrently with, or at any time after, submission under section 355(i) of this title or section 351(a)(3) of the Public Health Service Act [42 U.S.C. 262(a)(3)] for the investigation of a drug that incorporates or utilizes the platform technology that is the subject of the request.

(d) Designation

(1) In general

Not later than 90 calendar days after the receipt of a request under subsection (c), the Secretary shall determine whether the platform technology that is the subject of the request meets the criteria described in subsection (b).

(2) Designation

If the Secretary determines that the platform technology meets the criteria described in subsection (b), the Secretary shall designate the platform technology as a designated platform technology and may expedite the development and review of any subsequent application submitted under section 355(b) of this title or section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)] for a drug that uses or incorporates the platform technology pursuant to subsection (e), as appropriate.

(3) Determination not to designate

If the Secretary determines that the platform technology does not meet the criteria under subsection (b), the Secretary shall include with the determination not to designate the technology a written description of the rationale for such determination.

(4) Revocation of designation

The Secretary may revoke a designation made under paragraph (2), if the Secretary determines that the designated platform technology no longer meets the criteria described in subsection (b). The Secretary shall communicate the determination to revoke a designation to the requesting sponsor in writing, including a description of the rationale for such determination.

(5) Applicability

Nothing in this section shall prevent a product that uses or incorporates a designated platform technology from being eligible for expedited approval pathways if it is otherwise eligible under this chapter or the Public Health Service Act [42 U.S.C. 201 et seq.].

(e) Actions

The Secretary may take actions to expedite the development and review of an application for a drug that incorporates or utilizes a designated platform technology, including—

(1) engaging in early interactions with the sponsor to discuss the use of the designated platform technology and what is known about such technology, including data previously submitted that is relevant to establishing, as applicable, safety or efficacy under section 355(b) of this title or safety, purity, or potency under section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)];

(2) providing timely advice to, and interactive communication with, the sponsor regarding the development of the drug that proposes to use the designated platform technology to ensure that the development program designed to gather data necessary for approval or licensure is as efficient as practicable, which may include holding meetings with the sponsor and the review team throughout the development of the drug; and

(3) considering inspectional findings, including prior findings, related to the manufacture of a drug that incorporates or utilizes the designated platform technology.

(f) Leveraging data from designated platform technologies

The Secretary shall, consistent with applicable standards for approval, authorization, or licensure under this chapter and section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)], allow the sponsor of an application under sec-

tion 355(b) of this title or section 351(a) of the Public Health Service Act or a request for emergency use authorization under section 360bbb–3 of this title, in order to support approval, licensure, or authorization, to reference or rely upon data and information within an application or request for a drug or biological product that incorporates or utilizes the same platform technology designated under subsection (d), provided that—

(1) such data and information was submitted by the same sponsor, pursuant to the application for the drug with respect to which designation of the designated platform technology under subsection (d) was granted; or

(2) the sponsor relying on such data and information received a right of reference to such data and information from the sponsor described in paragraph (1).

(g) Changes to a designated platform technology

A sponsor of more than one application approved under section 355(b) of this title or section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)] for drugs that incorporate or utilize a designated platform technology may submit a single supplemental application for proposed changes to the designated platform technology that may be applicable to more than one such drug that incorporates or utilizes the same designated platform technology. Such supplemental application may cross-reference data and information submitted in other applications and may include one or more comparability protocols regarding how such changes to the platform technology would be made for each applicable drug or biological product.

(h) Definitions

For purposes of this section:

(1) The term ''platform technology'' means a well-understood and reproducible technology, which may include a nucleic acid sequence, molecular structure, mechanism of action, delivery method, vector, or a combination of any such technologies that the Secretary determines to be appropriate, that the sponsor demonstrates—

(A) is incorporated in or utilized by a drug or biological product and is essential to the structure or function of such drug or biological product;

(B) can be adapted for, incorporated into, or utilized by, more than one drug or biological product sharing common structural elements; and

(C) facilitates the manufacture or development of more than one drug or biological product through a standardized production or manufacturing process or processes.

(2) The term ''designated platform technology'' means a platform technology that is designated as a platform technology under subsection (d).

(i) Rule of construction

Nothing in this section shall be construed to—

(1) alter the authority of the Secretary to approve drugs pursuant to section 505 of this Act [21 U.S.C. 355] or license biological products pursuant to section 351 of the Public Health Service Act [42 U.S.C. 262], including standards of evidence and applicable conditions for approval or licensure under the applicable Act; or

(2) confer any new rights with respect to the permissibility of a sponsor of an application for a drug product or biological product referencing information contained in another application submitted by the holder of an approved application under section 355(c) of this title or of a license under section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)].

(June 25, 1938, ch. 675, § 506K, as added Pub. L. 117–328, div. FF, title II, § 2503(a), Dec. 29, 2022, 136 Stat. 5798.)

Editorial Notes

REFERENCES IN TEXT

The Public Health Service Act, referred to in subsec. (d)(5), is act July 1, 1944, ch. 373, 58 Stat. 682, which is classified generally to chapter 6A (§ 201 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 201 of Title 42 and Tables.

Statutory Notes and Related Subsidiaries

GUIDANCE

Pub. L. 117–328, div. FF, title II, § 2503(b), Dec. 29, 2022, 136 Stat. 5801, provided that: ''Not later than 1 year after the date of enactment of this Act [Dec. 29, 2022], the Secretary of Health and Human Services (referred to in this section as the 'Secretary') shall issue draft guidance on the implementation of this section. Such guidance shall include examples of drugs that can be manufactured using platform technologies, including drugs that contain or consist of vectors and nucleic acids, information about the Secretary's review of platform technologies, information regarding submitting for designation, considerations for persons submitting a request for designation who have been granted a right of reference, the implementation of the designated platform technology designation program, efficiencies that may be achieved in the development and review of products that incorporate or utilize designated platform technologies, and recommendations and requirements for making and reporting manufacturing changes to a designated platform technology in accordance with section 506K(g) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 356k(g)] (as added by subsection (a)) and section 506A of such Act (21 U.S.C. 356a), as applicable.''

§ 356*l*. Advanced manufacturing technologies designation program

(a) In general

Not later than 1 year after December 29, 2022, the Secretary shall initiate a program under which persons may request designation of an advanced manufacturing technology as described in subsection (b).

(b) Designation process

The Secretary shall establish a process for the designation under this section of methods of manufacturing drugs, including biological products, and active pharmaceutical ingredients of such drugs, as advanced manufacturing technologies. A method of manufacturing, or a combination of manufacturing methods, is eligible for designation as an advanced manufacturing technology if such method or combination of methods incorporates a novel technology, or uses an established technique or technology in a

novel way, that will substantially improve the manufacturing process for a drug while maintaining equivalent, or providing superior, drug quality, including by—

(1) reducing development time for a drug using the designated manufacturing method; or

(2) increasing or maintaining the supply of—

(A) a drug that is life-supporting, life-sustaining, or of critical importance to providing health care; or

(B) a drug that is on the drug shortage list under section 356e of this title.

(c) Evaluation and designation of an advanced manufacturing technology

(1) Submission

A person who requests designation of a method of manufacturing as an advanced manufacturing technology under this section shall submit to the Secretary data or information demonstrating that the method of manufacturing meets the criteria described in subsection (b) in a particular context of use. The Secretary may facilitate the development and review of such data or information by—

(A) providing timely advice to, and interactive communication with, such person regarding the development of the method of manufacturing; and

(B) involving senior managers and experienced staff of the Food and Drug Administration, as appropriate, in a collaborative, cross-disciplinary review of the method of manufacturing, as applicable.

(2) Evaluation and designation

Not later than 180 calendar days after the receipt of a request under paragraph (1), the Secretary shall determine whether to designate such method of manufacturing as an advanced manufacturing technology, in a particular context of use, based on the data and information submitted under paragraph (1) and the criteria described in subsection (b).

(d) Review of advanced manufacturing technologies

If the Secretary designates a method of manufacturing as an advanced manufacturing technology, the Secretary shall—

(1) expedite the development and review of an application submitted under section 355 of this title or section 262 of title 42, including supplemental applications, for drugs that are manufactured using a designated advanced manufacturing technology; and

(2) allow the holder of an advanced technology designation, or a person authorized by the advanced manufacturing technology designation holder, to reference or rely upon, in an application submitted under section 355 of this title or section 262 of title 42, including a supplemental application, data and information about the designated advanced manufacturing technology for use in manufacturing drugs in the same context of use for which the designation was granted.

(e) Implementation and evaluation of advanced manufacturing technologies program

(1) Public meeting

The Secretary shall publish in the Federal Register a notice of a public meeting, to be held not later than 180 days after December 29, 2022, to discuss, and obtain input and recommendations from relevant stakeholders regarding—

(A) the goals and scope of the program under this section, and the framework, procedures, and requirements suitable for such program; and

(B) ways in which the Food and Drug Administration will support the use of advanced manufacturing technologies and other innovative manufacturing approaches for drugs.

(2) Program guidance

(A) In general

The Secretary shall—

(i) not later than 180 days after the public meeting under paragraph (1), issue draft guidance regarding the goals and implementation of the program under this section; and

(ii) not later than 2 years after December 29, 2022, issue final guidance regarding the implementation of such program.

(B) Content

The guidance described in subparagraph (A) shall address—

(i) the process by which a person may request a designation under subsection (b);

(ii) the data and information that a person requesting such a designation is required to submit under subsection (c), and how the Secretary intends to evaluate such submissions;

(iii) the process to expedite the development and review of applications under subsection (d); and

(iv) the criteria described in subsection (b) for eligibility for such a designation.

(3) Report

Not later than 3 years after December 29, 2022, and annually thereafter, the Secretary shall publish on the website of the Food and Drug Administration and submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives a report containing a description and evaluation of the program being conducted under this section, including the types of innovative manufacturing approaches supported under the program. Such report shall include the following:

(A) The number of persons that have requested designations and that have been granted designations.

(B) The number of methods of manufacturing that have been the subject of designation requests and that have been granted designations.

(C) The average number of calendar days for completion of evaluations under subsection (c)(2).

(D) An analysis of the factors in data submissions that result in determinations to designate and not to designate after evaluation under subsection (c)(2).

(E) The number of applications received under section 355 of this title or section 262

of title 42, including supplemental applications, that have included an advanced manufacturing technology designated under this section, and the number of such applications approved.

(f) Sunset

The Secretary—

(1) may not consider any requests for designation submitted under subsection (c) after October 1, 2032; and

(2) may continue all activities under this section with respect to advanced manufacturing technologies that were designated pursuant to subsection (b) prior to such date, if the Secretary determines such activities are in the interest of the public health.

(June 25, 1938, ch. 675, § 506L, as added Pub. L. 117–328, div. FF, title III, § 3213, Dec. 29, 2022, 136 Stat. 5826.)

§ 357. Qualification of drug development tools

(a) Process for qualification

(1) In general

The Secretary shall establish a process for the qualification of drug development tools for a proposed context of use under which—

(A)(i) a requestor initiates such process by submitting a letter of intent to the Secretary; and

(ii) the Secretary accepts or declines to accept such letter of intent;

(B)(i) if the Secretary accepts the letter of intent, a requestor submits a qualification plan to the Secretary; and

(ii) the Secretary accepts or declines to accept the qualification plan; and

(C)(i) if the Secretary accepts the qualification plan, the requestor submits to the Secretary a full qualification package;

(ii) the Secretary determines whether to accept such qualification package for review; and

(iii) if the Secretary accepts such qualification package for review, the Secretary conducts such review in accordance with this section.

(2) Acceptance and review of submissions

(A) In general

Subparagraphs (B), (C), and (D) shall apply with respect to the treatment of a letter of intent, a qualification plan, or a full qualification package submitted under paragraph (1) (referred to in this paragraph as ''qualification submissions'').

(B) Acceptance factors; nonacceptance

The Secretary shall determine whether to accept a qualification submission based on factors which may include the scientific merit of the qualification submission. A determination not to accept a submission under paragraph (1) shall not be construed as a final determination by the Secretary under this section regarding the qualification of a drug development tool for its proposed context of use.

(C) Prioritization of qualification review

The Secretary may prioritize the review of a full qualification package submitted under paragraph (1) with respect to a drug development tool, based on factors determined appropriate by the Secretary, including—

(i) as applicable, the severity, rarity, or prevalence of the disease or condition targeted by the drug development tool and the availability or lack of alternative treatments for such disease or condition; and

(ii) the identification, by the Secretary or by biomedical research consortia and other expert stakeholders, of such a drug development tool and its proposed context of use as a public health priority.

(D) Engagement of external experts

The Secretary may, for purposes of the review of qualification submissions, through the use of cooperative agreements, grants, or other appropriate mechanisms, consult with biomedical research consortia and may consider the recommendations of such consortia with respect to the review of any qualification plan submitted under paragraph (1) or the review of any full qualification package under paragraph (3).

(3) Review of full qualification package

The Secretary shall—

(A) conduct a comprehensive review of a full qualification package accepted under paragraph (1)(C); and

(B) determine whether the drug development tool at issue is qualified for its proposed context of use.

(4) Qualification

The Secretary shall determine whether a drug development tool is qualified for a proposed context of use based on the scientific merit of a full qualification package reviewed under paragraph (3).

(b) Effect of qualification

(1) In general

A drug development tool determined to be qualified under subsection (a)(4) for a proposed context of use specified by the requestor may be used by any person in such context of use for the purposes described in paragraph (2).

(2) Use of a drug development tool

Subject to paragraph (3), a drug development tool qualified under this section may be used for—

(A) supporting or obtaining approval or licensure (as applicable) of a drug or biological product (including in accordance with section 356(c) of this title) under section 355 of this title or section 351 of the Public Health Service Act [42 U.S.C. 262]; or

(B) supporting the investigational use of a drug or biological product under section 355(i) of this title or section 351(a)(3) of the Public Health Service Act [42 U.S.C. 262(a)(3)].

(3) Rescission or modification

(A) In general

The Secretary may rescind or modify a determination under this section to qualify a drug development tool if the Secretary de-

termines that the drug development tool is not appropriate for the proposed context of use specified by the requestor. Such a determination may be based on new information that calls into question the basis for such qualification.

(B) Meeting for review

If the Secretary rescinds or modifies under subparagraph (A) a determination to qualify a drug development tool, the requestor involved shall, on request, be granted a meeting with the Secretary to discuss the basis of the Secretary's decision to rescind or modify the determination before the effective date of the rescission or modification.

(c) Transparency

(1) In general

Subject to paragraph (3), the Secretary shall make publicly available, and update on at least a biannual basis, on the Internet website of the Food and Drug Administration the following:

(A) Information with respect to each qualification submission under the qualification process under subsection (a), including—

(i) the stage of the review process applicable to the submission;

(ii) the date of the most recent change in stage status;

(iii) whether external scientific experts were utilized in the development of a qualification plan or the review of a full qualification package; and

(iv) submissions from requestors under the qualification process under subsection (a), including any data and evidence contained in such submissions, and any updates to such submissions.

(B) The Secretary's formal written determinations in response to such qualification submissions.

(C) Any rescissions or modifications under subsection (b)(3) of a determination to qualify a drug development tool.

(D) Summary reviews that document conclusions and recommendations for determinations to qualify drug development tools under subsection (a).

(E) A comprehensive list of—

(i) all drug development tools qualified under subsection (a); and

(ii) all surrogate endpoints which were the basis of approval or licensure (as applicable) of a drug or biological product (including in accordance with section 356(c) of this title) under section 355 of this title or section 351 of the Public Health Service Act [42 U.S.C. 262].

(2) Relation to Trade Secrets Act

Information made publicly available by the Secretary under paragraph (1) shall be considered a disclosure authorized by law for purposes of section 1905 of title 18.

(3) Applicability

(A) In general

Nothing in this section shall be construed as authorizing or directing the Secretary to disclose—

(i) any information contained in an application submitted under section 355 of this title or section 351 of the Public Health Service Act [42 U.S.C. 262] that is confidential commercial or trade secret information subject to section 552(b)(4) of title 5 or section 1905 of title 18; or

(ii) in the case of a drug development tool that may be used to support the development of a qualified countermeasure, security countermeasure, or qualified pandemic or epidemic product, as defined in sections 319F–1, 319F–2, and 319F–3, respectively, of the Public Health Service Act [42 U.S.C. 247d–6a, 247d–6b, 247d–6d], any information that the Secretary determines has a significant potential to affect national security.

(B) Public acknowledgment

In the case that the Secretary, pursuant to subparagraph (A)(ii), does not make information publicly available, the Secretary shall provide on the internet website of the Food and Drug Administration an acknowledgment of the information that has not been disclosed, pursuant to subparagraph (A)(ii).

(d) Rule of construction

Nothing in this section shall be construed—

(1) to alter the standards of evidence under subsection (c) or (d) of section 355 of this title, including the substantial evidence standard in such subsection (d), or under section 351 of the Public Health Service Act [42 U.S.C. 262] (as applicable); or

(2) to limit the authority of the Secretary to approve or license products under this chapter or the Public Health Service Act [42 U.S.C. 201 et seq.], as applicable (as in effect before December 13, 2016).

(e) Definitions

In this section:

(1) Biomarker

The term ''biomarker''—

(A) means a characteristic (such as a physiologic, pathologic, or anatomic characteristic or measurement) that is objectively measured and evaluated as an indicator of normal biologic processes, pathologic processes, or biological responses to a therapeutic intervention; and

(B) includes a surrogate endpoint.

(2) Biomedical research consortia

The term ''biomedical research consortia'' means collaborative groups that may take the form of public-private partnerships and may include government agencies, institutions of higher education (as defined in section 1001(a) of title 20), patient advocacy groups, industry representatives, clinical and scientific experts, and other relevant entities and individuals.

(3) Clinical outcome assessment

The term ''clinical outcome assessment'' means—

(A) a measurement of a patient's symptoms, overall mental state, or the effects of a disease or condition on how the patient functions; and

(B) includes a patient-reported outcome.

(4) Context of use

The term ''context of use'' means, with respect to a drug development tool, the circumstances under which the drug development tool is to be used in drug development and regulatory review.

(5) Drug development tool

The term ''drug development tool'' includes—

(A) a biomarker;

(B) a clinical outcome assessment; and

(C) any other method, material, or measure that the Secretary determines aids drug development and regulatory review for purposes of this section.

(6) Patient-reported outcome

The term ''patient-reported outcome'' means a measurement based on a report from a patient regarding the status of the patient's health condition without amendment or interpretation of the patient's report by a clinician or any other person.

(7) Qualification

The terms ''qualification'' and ''qualified'' mean a determination by the Secretary that a drug development tool and its proposed context of use can be relied upon to have a specific interpretation and application in drug development and regulatory review under this chapter.

(8) Requestor

The term ''requestor'' means an entity or entities, including a drug sponsor or a biomedical research consortia, seeking to qualify a drug development tool for a proposed context of use under this section.

(9) Surrogate endpoint

The term ''surrogate endpoint'' means a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure, that is not itself a direct measurement of clinical benefit, and—

(A) is known to predict clinical benefit and could be used to support traditional approval of a drug or biological product; or

(B) is reasonably likely to predict clinical benefit and could be used to support the accelerated approval of a drug or biological product in accordance with section 356(c) of this title.

(June 25, 1938, ch. 675, § 507, as added Pub. L. 114–255, div. A, title III, § 3011(a), Dec. 13, 2016, 130 Stat. 1086; amended Pub. L. 116–22, title VII, § 705(e), June 24, 2019, 133 Stat. 964.)

Editorial Notes

REFERENCES IN TEXT

The Public Health Service Act, referred to in subsec. (d)(2), is act July 1, 1944, ch. 373, 58 Stat. 682, which is classified generally to chapter 6A (§ 201 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 201 of Title 42 and Tables.

PRIOR PROVISIONS

A prior section 357, act June 25, 1938, ch. 675, § 507, as added July 6, 1945, ch. 281, § 3, 59 Stat. 463; amended Mar. 10, 1947, ch. 16, § 3, 61 Stat. 12; July 13, 1949, ch. 305, § 2, 63 Stat. 409; Aug. 5, 1953, ch. 334, § 2, 67 Stat. 389; Pub. L. 87–781, title I, §§ 105(a), (b), (d)–(f), 106(a), (b), Oct. 10, 1962, 76 Stat. 785, 786, 787; Pub. L. 90–399, § 105(b), July 13, 1968, 82 Stat. 352; Pub. L. 102–300, § 6(b)(2), June 16, 1992, 106 Stat. 240; Pub. L. 103–80, § 3(p), Aug. 13, 1993, 107 Stat. 777, related to certification of drugs containing penicillin, streptomycin, chlortetracycline, chloramphenicol, bacitracin, or any other antibiotic drug, prior to repeal by Pub. L. 105–115, title I, § 125(b)(1), Nov. 21, 1997, 111 Stat. 2325.

AMENDMENTS

2019—Subsec. (c)(3). Pub. L. 116–22 designated existing provisions as subpar. (A), inserted heading and ''or directing'' after ''authorizing'' in text, substituted ''disclose—'' for ''disclose'', designated remainder of existing provisions as cl. (i) of subpar. (A), substituted '';or'' for period at end, and added cl. (ii) of subpar. (A) and subpar. (B).

Statutory Notes and Related Subsidiaries

GUIDANCE

Pub. L. 114–255, div. A, title III, § 3011(b), Dec. 13, 2016, 130 Stat. 1089, provided that:

''(1) IN GENERAL.—The Secretary of Health and Human Services (referred to in this section [this note] as the 'Secretary') shall, in consultation with biomedical research consortia (as defined in subsection (e) of section 507 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 357] (as added by subsection (a)) and other interested parties through a collaborative public process, issue guidance to implement such section 507 that—

''(A) provides a conceptual framework describing appropriate standards and scientific approaches to support the development of biomarkers delineated under the taxonomy established under paragraph (3);

''(B) with respect to the qualification process under such section 507—

''(i) describes the requirements that entities seeking to qualify a drug development tool under such section shall observe when engaging in such process;

''(ii) outlines reasonable timeframes for the Secretary's review of letters, qualification plans, or full qualification packages submitted under such process; and

''(iii) establishes a process by which such entities or the Secretary may consult with biomedical research consortia and other individuals and entities with expert knowledge and insights that may assist the Secretary in the review of qualification plans and full qualification submissions under such section; and

''(C) includes such other information as the Secretary determines appropriate.

''(2) TIMING.—Not later than 3 years after the date of the enactment of this Act [Dec. 13, 2016], the Secretary shall issue draft guidance under paragraph (1) on the implementation of section 507 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 357] (as added by subsection (a)). The Secretary shall issue final guidance on the implementation of such section not later than 6 months after the date on which the comment period for the draft guidance closes.

''(3) TAXONOMY.—

''(A) IN GENERAL.—For purposes of informing guidance under this subsection, the Secretary shall, in consultation with biomedical research consortia and other interested parties through a collaborative public process, establish a taxonomy for the classification of biomarkers (and related scientific concepts) for use in drug development.

''(B) PUBLIC AVAILABILITY.—Not later than 2 years after the date of the enactment of this Act, the Secretary shall make such taxonomy publicly available in draft form for public comment. The Secretary

shall finalize the taxonomy not later than 1 year after the close of the public comment period.''

§ 358. Authority to designate official names

(a) Necessity or desirability; use in official compendiums; infringement of trademarks

The Secretary may designate an official name for any drug or device if he determines that such action is necessary or desirable in the interest of usefulness and simplicity. Any official name designated under this section for any drug or device shall be the only official name of that drug or device used in any official compendium published after such name has been prescribed or for any other purpose of this chapter. In no event, however, shall the Secretary establish an official name so as to infringe a valid trademark.

(b) Review of names in official compendiums

Within a reasonable time after October 10, 1962, and at such other times as he may deem necessary, the Secretary shall cause a review to be made of the official names by which drugs are identified in the official United States Pharmacopoeia, the official Homoeopathic Pharmacopoeia of the United States, and the official National Formulary, and all supplements thereto, and at such times as he may deem necessary shall cause a review to be made of the official names by which devices are identified in any official compendium (and all supplements thereto) to determine whether revision of any of those names is necessary or desirable in the interest of usefulness and simplicity.

(c) Determinations of complexity, usefulness, multiplicity, or lack of name; designation by Secretary

Whenever he determines after any such review that (1) any such official name is unduly complex or is not useful for any other reason, (2) two or more official names have been applied to a single drug or device, or to two or more drugs which are identical in chemical structure and pharmacological action and which are substantially identical in strength, quality, and purity, or to two or more devices which are substantially equivalent in design and purpose or (3) no official name has been applied to a medically useful drug or device, he shall transmit in writing to the compiler of each official compendium in which that drug or drugs or device are identified and recognized his request for the recommendation of a single official name for such drug or drugs or device which will have usefulness and simplicity. Whenever such a single official name has not been recommended within one hundred and eighty days after such request, or the Secretary determines that any name so recommended is not useful for any reason, he shall designate a single official name for such drug or drugs or device. Whenever he determines that the name so recommended is useful, he shall designate that name as the official name of such drug or drugs or device. Such designation shall be made as a regulation upon public notice and in accordance with the procedure set forth in section 553 of title 5.

(d) Revised official names; compilation, publication, and public distribution of listings

After each such review, and at such other times as the Secretary may determine to be necessary or desirable, the Secretary shall cause to be compiled, published, and publicly distributed a list which shall list all revised official names of drugs or devices designated under this section and shall contain such descriptive and explanatory matter as the Secretary may determine to be required for the effective use of those names.

(e) Request by compiler of official compendium for designation of name

Upon a request in writing by any compiler of an official compendium that the Secretary exercise the authority granted to him under subsection (a), he shall upon public notice and in accordance with the procedure set forth in section 553 of title 5 designate the official name of the drug or device for which the request is made.

(June 25, 1938, ch. 675, § 508, as added Pub. L. 87–781, title I, § 111(a), Oct. 10, 1962, 76 Stat. 789; amended Pub. L. 94–295, § 5(b), May 28, 1976, 90 Stat. 581; Pub. L. 103–80, § 3(q), Aug. 13, 1993, 107 Stat. 777.)

Editorial Notes

AMENDMENTS

1993—Subsecs. (c), (e). Pub. L. 103–80 substituted reference to section 553 of title 5 for ''section 4 of the Administrative Procedure Act (5 U.S.C. 1003)''.

1976—Subsec. (a). Pub. L. 94–295 substituted ''drug or device'' for ''drug'' wherever appearing.

Subsec. (b). Pub. L. 94–295 substituted ''National Formulary, and all supplements thereto, and at such times as he may deem necessary shall cause a review to be made of the official names by which devices are identified in any official compendium (and all supplements thereto)'' for ''National Formulary, and all supplements thereto,''.

Subsec. (c)(2). Pub. L. 94–295 inserted ''or device'' after ''single drug'', and ''or to two or more devices which are substantially equivalent in design and purpose'' after ''purity,''.

Subsec. (c)(3). Pub. L. 94–295 inserted ''or device'' after ''useful drug'' and after ''drug or drugs'' wherever appearing.

Subsec. (d). Pub. L. 94–295 inserted ''or devices'' after ''drugs''.

Subsec. (e). Pub. L. 94–295 substituted ''drug or device'' for ''drug''.

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE

Pub. L. 87–781, title I, § 111(b), Oct. 10, 1962, 76 Stat. 790, provided that: ''This section [enacting this section] shall take effect on the date of its enactment [Oct. 10, 1962].''

§ 359. Nonapplicability of subchapter to cosmetics

This subchapter, as amended by the Drug Amendments of 1962, shall not apply to any cosmetic unless such cosmetic is also a drug or device or component thereof.

(June 25, 1938, ch. 675, § 509, as added Pub. L. 87–781, title I, § 113, Oct. 10, 1962, 76 Stat. 791.)

Editorial Notes

REFERENCES IN TEXT

This subchapter, as amended by the Drug Amendments of 1962, referred to in text, means the amendment of this subchapter by Pub. L. 87–781 which enacted

sections 358 to 360 of this title, amended sections 351 to 353, 355, and 357 of this title, and enacted provisions set out as notes under sections 352, 355, 358, and 360 of this title.

The Drug Amendments of 1962, referred to in text, is Pub. L. 87–781, Oct. 10, 1962, 76 Stat. 780, as amended. For complete classification of this Act to the Code, see Short Title of 1962 Amendment note set out under section 301 of this title and Tables.

§ 360. Registration of producers of drugs or devices

(a) Definitions

As used in this section—

(1) the term ''manufacture, preparation, propagation, compounding, or processing'' shall include repackaging or otherwise changing the container, wrapper, or labeling of any drug package or device package in furtherance of the distribution of the drug or device from the original place of manufacture to the person who makes final delivery or sale to the ultimate consumer or user; and

(2) the term ''name'' shall include in the case of a partnership the name of each partner and, in the case of a corporation, the name of each corporate officer and director, and the State of incorporation.

(b) Annual registration

(1) During the period beginning on October 1 and ending on December 31 of each year, every person who owns or operates any establishment in any State engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs shall register with the Secretary the name of such person, places of business of such person, all such establishments, the unique facility identifier of each such establishment, and a point of contact e-mail address.

(2) During the period beginning on October 1 and ending on December 31 of each year, every person who owns or operates any establishment in any State engaged in the manufacture, preparation, propagation, compounding, or processing of a device or devices shall register with the Secretary his name, places of business, and all such establishments.

(3) The Secretary shall specify the unique facility identifier system that shall be used by registrants under paragraph (1). The requirement to include a unique facility identifier in a registration under paragraph (1) shall not apply until the date that the identifier system is specified by the Secretary under the preceding sentence.

(c) New producers

Every person upon first engaging in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs or a device or devices in any establishment which he owns or operates in any State shall immediately register with the Secretary—

(1) with respect to drugs, the information described under subsection (b)(1); and

(2) with respect to devices, the information described under subsection (b)(2)..[1]

(d) Additional establishments

Every person duly registered in accordance with the foregoing subsections of this section shall immediately register with the Secretary any additional establishment which he owns or operates in any State and in which he begins the manufacture, preparation, propagation, compounding, or processing of a drug or drugs or a device or devices.

(e) Registration number; uniform system for identification of devices intended for human use

The Secretary may assign a registration number to any person or any establishment registered in accordance with this section. The Secretary may also assign a listing number to each drug or class of drugs listed under subsection (j). Any number assigned pursuant to the preceding sentence shall be the same as that assigned pursuant to the National Drug Code. The Secretary may by regulation prescribe a uniform system for the identification of devices intended for human use and may require that persons who are required to list such devices pursuant to subsection (j) shall list such devices in accordance with such system.

(f) Availability of registrations for inspection

The Secretary shall make available for inspection, to any person so requesting, any registration filed pursuant to this section; except that any list submitted pursuant to paragraph (3) of subsection (j) and the information accompanying any list or notice filed under paragraph (1) or (2) of that subsection shall be exempt from such inspection unless the Secretary finds that such an exemption would be inconsistent with protection of the public health.

(g) Exclusions from application of section

The foregoing subsections of this section shall not apply to—

(1) pharmacies which maintain establishments in conformance with any applicable local laws regulating the practice of pharmacy and medicine and which are regularly engaged in dispensing prescription drugs or devices, upon prescriptions of practitioners licensed to administer such drugs or devices to patients under the care of such practitioners in the course of their professional practice, and which do not manufacture, prepare, propagate, compound, or process drugs or devices for sale other than in the regular course of their business of dispensing or selling drugs or devices at retail;

(2) practitioners licensed by law to prescribe or administer drugs or devices and who manufacture, prepare, propagate, compound, or process drugs or devices solely for use in the course of their professional practice;

(3) persons who manufacture, prepare, propagate, compound, or process drugs or devices solely for use in research, teaching, or chemical analysis and not for sale;

(4) any distributor who acts as a wholesale distributor of devices, and who does not manufacture, repackage, process, or relabel a device; or

(5) such other classes of persons as the Secretary may by regulation exempt from the application of this section upon a finding that registration by such classes of persons in accordance with this section is not necessary for the protection of the public health.

[1] So in original.

In this subsection, the term ''wholesale distributor'' means any person (other than the manufacturer or the initial importer) who distributes a device from the original place of manufacture to the person who makes the final delivery or sale of the device to the ultimate consumer or user.

(h) Inspections

(1) In general

Every establishment that is required to be registered with the Secretary under this section shall be subject to inspection pursuant to section 374 of this title.

(2) Risk-based schedule for devices

(A) In general

The Secretary, acting through one or more officers or employees duly designated by the Secretary, shall inspect establishments described in paragraph (1) that are engaged in the manufacture, propagation, compounding, or processing of a device or devices (referred to in this subsection as ''device establishments'') in accordance with a risk-based schedule established by the Secretary.

(B) Factors and considerations

In establishing the risk-based schedule under subparagraph (A), the Secretary shall—

(i) apply, to the extent applicable for device establishments, the factors identified in paragraph (4); and

(ii) consider the participation of the device establishment, as applicable, in international device audit programs in which the United States participates or the United States recognizes for purposes of inspecting device establishments.

(3) Risk-based schedule for drugs

The Secretary, acting through one or more officers or employees duly designated by the Secretary, shall inspect establishments described in paragraph (1) that are engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs (referred to in this subsection as ''drug establishments'') in accordance with a risk-based schedule established by the Secretary.

(4) Risk factors

In establishing a risk-based schedule under paragraph (2) or (3), the Secretary shall inspect establishments according to the known safety risks of such establishments, which shall be based on the following factors:

(A) The compliance history of the establishment.

(B) The record, history, and nature of recalls linked to the establishment.

(C) The inherent risk of the drug or device manufactured, prepared, propagated, compounded, or processed at the establishment.

(D) The inspection frequency and history of the establishment, including whether the establishment has been inspected pursuant to section 374 of this title within the last 4 years.

(E) Whether the establishment has been inspected by a foreign government or an agency of a foreign government recognized under section 384e of this title.

(F) The compliance history of establishments in the country or region in which the establishment is located that are subject to regulation under this chapter, including the history of violations related to products exported from such country or region that are subject to such regulation.

(G) Any other criteria deemed necessary and appropriate by the Secretary for purposes of allocating inspection resources.

(5) Effect of status

In determining the risk associated with an establishment for purposes of establishing a risk-based schedule under paragraph (3), the Secretary shall not consider whether the drugs manufactured, prepared, propagated, compounded, or processed by such establishment are drugs described in section 353(b) of this title.

(6) Annual report on inspections of establishments

Not later than May 1 of each year, the Secretary shall make available on the Internet Web site of the Food and Drug Administration a report regarding—

(A)(i) the number of domestic and foreign establishments registered pursuant to this section in the previous fiscal year;

(ii) the number of such registered establishments in each region of interest;

(iii) the number of such domestic establishments and the number of such foreign establishments, including the number of establishments in each region of interest, that the Secretary inspected in the previous fiscal year;

(iv) the number of inspections to support actions by the Secretary on applications under section 355 of this title or section 262 of title 42, including the number of inspections to support actions by the Secretary on supplemental applications, including changes to manufacturing processes, the Secretary conducted in the previous fiscal year;

(v) the number of routine surveillance inspections the Secretary conducted in the previous fiscal year, including in each region of interest;

(vi) the number of for-cause inspections the Secretary conducted in the previous fiscal year, not including inspections described in clause (iv), including in each region of interest; and

(vii) the number of inspections the Secretary has recognized pursuant to an agreement entered into pursuant to section 384e of this title, or otherwise recognized, for each of the types of inspections described in clauses (v) and (vi), including for inspections of establishments in each region of interest.[2]

(B) with respect to establishments that manufacture, prepare, propagate, compound, or process an active ingredient of a drug or a finished drug product, the number of each such type of establishment;

[2] So in original. The period probably should be a semicolon.

(C) the percentage of the budget of the Food and Drug Administration used to fund the inspections described under subparagraph (A); and

(D) the status of the efforts of the Food and Drug Administration to expand its recognition of inspections conducted or recognized by foreign regulatory authorities under section 384e of this title, including any obstacles to expanding the use of such recognition.

(7) Region of interest

For purposes of paragraph (6)(A), the term ''region of interest'' means a foreign geographic region or country, including the People's Republic of China, India, the European Union, the United Kingdom, and any other country or geographic region, as the Secretary determines appropriate.

(i) Registration of foreign establishments

(1) Every person who owns or operates any establishment within any foreign country engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or device that is imported or offered for import into the United States shall, through electronic means in accordance with the criteria of the Secretary—

(A) upon first engaging in any such activity, immediately submit a registration to the Secretary that includes—

(i) with respect to drugs, the name and place of business of such person, all such establishments, the unique facility identifier of each such establishment, a point of contact e-mail address, the name of the United States agent of each such establishment, the name of each importer of such drug in the United States that is known to the establishment, and the name of each person who imports or offers for import such drug to the United States for purposes of importation; and

(ii) with respect to devices, the name and place of business of the establishment, the name of the United States agent for the establishment, the name of each importer of such device in the United States that is known to the establishment, and the name of each person who imports or offers for import such device to the United States for purposes of importation; and

(B) each establishment subject to the requirements of subparagraph (A) shall thereafter register with the Secretary during the period beginning on October 1 and ending on December 31 of each year.

(2) The establishment shall also provide the information required by subsection (j).

(3) The Secretary is authorized to enter into cooperative arrangements with officials of foreign countries to ensure that adequate and effective means are available for purposes of determining, from time to time, whether drugs or devices manufactured, prepared, propagated, compounded, or processed by an establishment described in paragraph (1), if imported or offered for import into the United States, shall be refused admission on any of the grounds set forth in section 381(a) of this title.

(4) The Secretary shall specify the unique facility identifier system that shall be used by registrants under paragraph (1) with respect to drugs. The requirement to include a unique facility identifier in a registration under paragraph (1) with respect to drugs shall not apply until the date that the identifier system is specified by the Secretary under the preceding sentence.

(5) The requirements of paragraphs (1) and (2) shall apply regardless of whether the drug or device undergoes further manufacture, preparation, propagation, compounding, or processing at a separate establishment outside the United States prior to being imported or offered for import into the United States.

(j) Filing of lists of drugs and devices manufactured, prepared, propagated and compounded by registrants; statements; accompanying disclosures

(1) Every person who registers with the Secretary under subsection (b), (c), (d), or (i) shall, at the time of registration under any such subsection, file with the Secretary a list of all drugs and a list of all devices and a brief statement of the basis for believing that each device included in the list is a device rather than a drug (with each drug and device in each list listed by its established name (as defined in section 352(e) of this title) and by any proprietary name) which are being manufactured, prepared, propagated, compounded, or processed by him for commercial distribution and which he has not included in any list of drugs or devices filed by him with the Secretary under this paragraph or paragraph (2) before such time of registration. Such list shall be prepared in such form and manner as the Secretary may prescribe and shall be accompanied by—

(A) in the case of a drug contained in the applicable list and subject to section 355 or 360b of this title, or a device intended for human use contained in the applicable list with respect to which a performance standard has been established under section 360d of this title or which is subject to section 360e of this title, a reference to the authority for the marketing of such drug or device and a copy of all labeling for such drug or device;

(B) in the case of any other drug or device contained in an applicable list—

(i) which drug is subject to section 353(b)(1) of this title, or which device is a restricted device, a copy of all labeling for such drug or device, a representative sampling of advertisements for such drug or device, and, upon request made by the Secretary for good cause, a copy of all advertisements for a particular drug product or device, or

(ii) which drug is not subject to section 353(b)(1) of this title or which device is not a restricted device, the label and package insert for such drug or device and a representative sampling of any other labeling for such drug or device;

(C) in the case of any drug contained in an applicable list which is described in subparagraph (B), a quantitative listing of its active ingredient or ingredients, except that with respect to a particular drug product the Sec-

retary may require the submission of a quantitative listing of all ingredients if he finds that such submission is necessary to carry out the purposes of this chapter;

(D) if the registrant filing a list has determined that a particular drug product or device contained in such list is not subject to section 355 or 360b of this title, or the particular device contained in such list is not subject to a performance standard established under section 360d of this title or to section 360e of this title or is not a restricted device a brief statement of the basis upon which the registrant made such determination if the Secretary requests such a statement with respect to that particular drug product or device; and

(E) in the case of a drug contained in the applicable list, the name and place of business of each manufacturer of an excipient of the listed drug with which the person listing the drug conducts business, including all establishments used in the production of such excipient, the unique facility identifier of each such establishment, and a point of contact e-mail address for each such excipient manufacturer.

(2) Each person who registers with the Secretary under this section shall report to the Secretary, with regard to drugs once during the month of June of each year and once during the month of December of each year, and with regard to devices once each year during the period beginning on October 1 and ending on December 31, the following information:

(A) A list of each drug or device introduced by the registrant for commercial distribution which has not been included in any list previously filed by him with the Secretary under this subparagraph or paragraph (1) of this subsection. A list under this subparagraph shall list a drug or device by its established name (as defined in section 352(e) of this title), and by any proprietary name it may have and shall be accompanied by the other information required by paragraph (1).

(B) If since the date the registrant last made a report under this paragraph (or if he has not made a report under this paragraph, since February 1, 1973) he has discontinued the manufacture, preparation, propagation, compounding, or processing for commercial distribution of a drug or device included in a list filed by him under subparagraph (A) or paragraph (1); notice of such discontinuance, the date of such discontinuance, and the identity (by established name (as defined in section 352(e) of this title) and by any proprietary name) of such drug or device.

(C) If since the date the registrant reported pursuant to subparagraph (B) a notice of discontinuance he has resumed the manufacture, preparation, propagation, compounding, or processing for commercial distribution of the drug or device with respect to which such notice of discontinuance was reported; notice of such resumption, the date of such resumption, the identity of such drug or device (each by established name (as defined in section 352(e) of this title) and by any proprietary name), and the other information required by paragraph (1), unless the registrant has previously reported such resumption to the Secretary pursuant to this subparagraph.

(D) Any material change in any information previously submitted pursuant to this paragraph or paragraph (1).

(3)(A) Each person who registers with the Secretary under this section with regard to a drug shall report annually to the Secretary on the amount of each drug listed under paragraph (1) that was manufactured, prepared, propagated, compounded, or processed by such person for commercial distribution. Such information may be required to be submitted in an electronic format as determined by the Secretary. The Secretary may require that information required to be reported under this paragraph be submitted at the time a public health emergency is declared by the Secretary under section 247d of title 42.

(B) By order of the Secretary, certain biological products or categories of biological products regulated under section 262 of title 42 may be exempt from some or all of the reporting requirements under subparagraph (A), if the Secretary determines that applying such reporting requirements to such biological products or categories of biological products is not necessary to protect the public health.

(4) The Secretary may also require each registrant under this section to submit a list of each drug product which (A) the registrant is manufacturing, preparing, propagating, compounding, or processing for commercial distribution, and (B) contains a particular ingredient. The Secretary may not require the submission of such a list unless he has made a finding that the submission of such a list is necessary to carry out the purposes of this chapter.

(5) The Secretary shall require persons subject to this subsection to use, for purposes of this subsection, the unique facility identifier systems specified under subsections (b)(3) and (i)(4) with respect to drugs. Such requirement shall not apply until the date that the identifier system under subsection (b)(3) or (i)(4), as applicable, is specified by the Secretary.

(k) Report preceding introduction of devices into interstate commerce

Each person who is required to register under this section and who proposes to begin the introduction or delivery for introduction into interstate commerce for commercial distribution of a device intended for human use shall, at least ninety days before making such introduction or delivery, report to the Secretary or person who is accredited under section 360m(a) of this title (in such form and manner as the Secretary shall by regulation prescribe)—

(1) the class in which the device is classified under section 360c of this title or if such person determines that the device is not classified under such section, a statement of that determination and the basis for such person's determination that the device is or is not so classified, and

(2) action taken by such person to comply with requirements under section 360d or 360e of this title which are applicable to the device.

A notification submitted under this subsection that contains clinical trial data for an applicable device clinical trial (as defined in section

282(j)(1) of title 42) shall be accompanied by the certification required under section 282(j)(5)(B) of such title. Such certification shall not be considered an element of such notification.

(*l*) Exemption from reporting requirements

(1) A report under subsection (k) is not required for a device intended for human use that is exempted from the requirements of this subsection under subsection (m) or is within a type that has been classified into class I under section 360c of this title, or with respect to a change that is consistent with a predetermined change control plan cleared under section 360e–4 of this title. The exception established in the preceding sentence does not apply to any class I device that is intended for a use which is of substantial importance in preventing impairment of human health, or to any class I device that presents a potential unreasonable risk of illness or injury.

(2) Not later than 120 calendar days after December 13, 2016, and at least once every 5 years thereafter, as the Secretary determines appropriate, the Secretary shall identify, through publication in the Federal Register, any type of class I device that the Secretary determines no longer requires a report under subsection (k) to provide reasonable assurance of safety and effectiveness. Upon such publication—

(A) each type of class I device so identified shall be exempt from the requirement for a report under subsection (k); and

(B) the classification regulation applicable to each such type of device shall be deemed amended to incorporate such exemption.

(m) List of exempt class II devices; initial and final determinations by Secretary; publication in Federal Register

(1) The Secretary shall—

(A) not later than 90 days after December 13, 2016, and at least once every 5 years thereafter, as the Secretary determines appropriate—

(i) publish in the Federal Register a notice that contains a list of each type of class II device that the Secretary determines no longer requires a report under subsection (k) to provide reasonable assurance of safety and effectiveness; and

(ii) provide for a period of not less than 60 calendar days for public comment beginning on the date of the publication of such notice; and

(B) not later than 210 calendar days after December 13, 2016, publish in the Federal Register a list representing the Secretary's final determination with respect to the devices contained in the list published under subparagraph (A).

(2) Beginning on the date that is 1 calendar day after the date of publication of the final list under paragraph (1)(B), the Secretary may exempt a class II device from the requirement to submit a report under subsection (k), upon the Secretary's own initiative or a petition of an interested person, if the Secretary determines that such report is not necessary to assure the safety and effectiveness of the device. The Secretary shall publish in the Federal Register notice of the intent of the Secretary to exempt the device, or of the petition, and provide a 60-calendar-day period for public comment. Within 120 days after the issuance of the notice in the Federal Register, the Secretary shall publish an order in the Federal Register that sets forth the final determination of the Secretary regarding the exemption of the device that was the subject of the notice. If the Secretary fails to respond to a petition within 180 days of receiving it, the petition shall be deemed to be granted.

(3) Upon the publication of the final list under paragraph (1)(B)—

(A) each type of class II device so listed shall be exempt from the requirement for a report under subsection (k); and

(B) the classification regulation applicable to each such type of device shall be deemed amended to incorporate such exemption.

(n) Review of report; time for determination by Secretary

(1) The Secretary shall review the report required in subsection (k) and make a determination under section 360c(f)(1) of this title not later than 90 days after receiving the report.

(2)(A) Not later than 18 months after July 9, 2012, the Secretary shall submit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate a report regarding when a premarket notification under subsection (k) should be submitted for a modification or change to a legally marketed device. The report shall include the Secretary's interpretation of the following terms: ''could significantly affect the safety or effectiveness of the device'', ''a significant change or modification in design, material, chemical composition, energy source, or manufacturing process'', and ''major change or modification in the intended use of the device''. The report also shall discuss possible processes for industry to use to determine whether a new submission under subsection (k) is required and shall analyze how to leverage existing quality system requirements to reduce premarket burden, facilitate continual device improvement, and provide reasonable assurance of safety and effectiveness of modified devices. In developing such report, the Secretary shall consider the input of interested stakeholders.

(B) The Secretary shall withdraw the Food and Drug Administration draft guidance entitled ''Guidance for Industry and FDA Staff—510(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device'', dated July 27, 2011, and shall not use this draft guidance as part of, or for the basis of, any premarket review or any compliance or enforcement decisions or actions. The Secretary shall not issue—

(i) any draft guidance or proposed regulation that addresses when to submit a premarket notification submission for changes and modifications made to a manufacturer's previously cleared device before the receipt by the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate of the report required in subparagraph (A); and

(ii) any final guidance or regulation on that topic for one year after date of receipt of such report by the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate.

(C) The Food and Drug Administration guidance entitled ''Deciding When to Submit a 510(k) for a Change to an Existing Device'', dated January 10, 1997, shall be in effect until the subsequent issuance of guidance or promulgation, if appropriate, of a regulation described in subparagraph (B), and the Secretary shall interpret such guidance in a manner that is consistent with the manner in which the Secretary has interpreted such guidance since 1997.

(*o*) Reprocessed single-use devices

(1) With respect to reprocessed single-use devices for which reports are required under subsection (k):

(A) The Secretary shall identify such devices or types of devices for which reports under such subsection must, in order to ensure that the device is substantially equivalent to a predicate device, include validation data, the types of which shall be specified by the Secretary, regarding cleaning and sterilization, and functional performance demonstrating that the single-use device will remain substantially equivalent to its predicate device after the maximum number of times the device is reprocessed as intended by the person submitting the premarket notification. Within six months after October 26, 2002, the Secretary shall publish in the Federal Register a list of the types so identified, and shall revise the list as appropriate. Reports under subsection (k) for devices or types of devices within a type included on the list are, upon publication of the list, required to include such validation data.

(B) In the case of each report under subsection (k) that was submitted to the Secretary before the publication of the initial list under subparagraph (A), or any revision thereof, and was for a device or type of device included on such list, the person who submitted the report under subsection (k) shall submit validation data as described in subparagraph (A) to the Secretary not later than nine months after the publication of the list. During such nine-month period, the Secretary may not take any action under this chapter against such device solely on the basis that the validation data for the device have not been submitted to the Secretary. After the submission of the validation data to the Secretary, the Secretary may not determine that the device is misbranded under section 352(*o*) of this title or adulterated under section 351(f)(1)(B) of this title, or take action against the device under section 331(p) of this title for failure to provide any information required by subsection (k) until (i) the review is terminated by withdrawal of the submission of the report under subsection (k); (ii) the Secretary finds the data to be acceptable and issues a letter; or (iii) the Secretary determines that the device is not substantially equivalent to a predicate device. Upon a determination that a device is not substantially equivalent to a predicate device, or if such submission is withdrawn, the device can no longer be legally marketed.

(C) In the case of a report under subsection (k) for a device identified under subparagraph (A) that is of a type for which the Secretary has not previously received a report under such subsection, the Secretary may, in advance of revising the list under subparagraph (A) to include such type, require that the report include the validation data specified in subparagraph (A).

(D) Section 352(*o*) of this title applies with respect to the failure of a report under subsection (k) to include validation data required under subparagraph (A).

(2) With respect to critical or semi-critical reprocessed single-use devices that, under subsection (*l*) or (m), are exempt from the requirement of submitting reports under subsection (k):

(A) The Secretary shall identify such devices or types of devices for which such exemptions should be terminated in order to provide a reasonable assurance of the safety and effectiveness of the devices. The Secretary shall publish in the Federal Register a list of the devices or types of devices so identified, and shall revise the list as appropriate. The exemption for each device or type included on the list is terminated upon the publication of the list. For each report under subsection (k) submitted pursuant to this subparagraph the Secretary shall require the validation data described in paragraph (1)(A).

(B) For each device or type of device included on the list under subparagraph (A), a report under subsection (k) shall be submitted to the Secretary not later than 15 months after the publication of the initial list, or a revision of the list, whichever terminates the exemption for the device. During such 15-month period, the Secretary may not take any action under this chapter against such device solely on the basis that such report has not been submitted to the Secretary. After the submission of the report to the Secretary the Secretary may not determine that the device is misbranded under section 352(*o*) of this title or adulterated under section 351(f)(1)(B) of this title, or take action against the device under section 331(p) of this title for failure to provide any information required by subsection (k) until (i) the review is terminated by withdrawal of the submission; (ii) the Secretary determines by order that the device is substantially equivalent to a predicate device; or (iii) the Secretary determines by order that the device is not substantially equivalent to a predicate device. Upon a determination that a device is not substantially equivalent to a predicate device, the device can no longer be legally marketed.

(C) In the case of semi-critical devices, the initial list under subparagraph (A) shall be published not later than 18 months after the effective date of this subsection. In the case of critical devices, the initial list under such subparagraph shall be published not later than six months after such effective date.

(D) Section 352(*o*) of this title applies with respect to the failure to submit a report under

subsection (k) that is required pursuant to subparagraph (A), including a failure of the report to include validation data required in such subparagraph.

(E) The termination under subparagraph (A) of an exemption under subsection (*l*) or (m) for a critical or semi-critical reprocessed single-use device does not terminate the exemption under subsection (*l*) or (m) for the original device.

(p) Electronic registration and listing

(1) In general

Registrations and listings under this section (including the submission of updated information) shall be submitted to the Secretary by electronic means unless the Secretary grants a request for waiver of such requirement because use of electronic means is not reasonable for the person requesting such waiver.

(2) Electronic database

Not later than 2 years after the Secretary specifies a unique facility identifier system under subsections (b) and (i), the Secretary shall maintain an electronic database, which shall not be subject to inspection under subsection (f), populated with the information submitted as described under paragraph (1) that—

(A) enables personnel of the Food and Drug Administration to search the database by any field of information submitted in a registration described under paragraph (1), or combination of such fields; and

(B) uses the unique facility identifier system to link with other relevant databases within the Food and Drug Administration, including the database for submission of information under section 381(r) of this title.

(3) Risk-based information and coordination

The Secretary shall ensure the accuracy and coordination of relevant Food and Drug Administration databases in order to identify and inform risk-based inspections under subsection (h).

(q) Reusable medical devices

(1) In general

Not later than 180 days after December 13, 2016, the Secretary shall identify and publish a list of reusable device types for which reports under subsection (k) are required to include—

(A) instructions for use, which have been validated in a manner specified by the Secretary; and

(B) validation data, the types of which shall be specified by the Secretary;

regarding cleaning, disinfection, and sterilization, and for which a substantial equivalence determination may be based.

(2) Revision of list

The Secretary shall revise the list under paragraph (2),[3] as the Secretary determines appropriate, with notice in the Federal Register.

(3) Content of reports

Reports under subsection (k) that are submitted after the publication of the list described in paragraph (1), for devices or types of devices included on such list, shall include such instructions for use and validation data.

(June 25, 1938, ch. 675, § 510, as added Pub. L. 87–781, title III, § 302, Oct. 10, 1962, 76 Stat. 794; amended Pub. L. 89–74, § 4, July 15, 1965, 79 Stat. 231; Pub. L. 91–513, title II, § 701(e), Oct. 27, 1970, 84 Stat. 1282; Pub. L. 92–387, §§ 3, 4(a)–(c), Aug. 16, 1972, 86 Stat. 560–562; Pub. L. 94–295, § 4(a), May 28, 1976, 90 Stat. 579; Pub. L. 105–115, title I, § 125(a)(2)(C), title II, §§ 206(a), 209(a), 213(b), title IV, § 417, Nov. 21, 1997, 111 Stat. 2325, 2338, 2341, 2347, 2379; Pub. L. 107–188, title III, § 321(a), June 12, 2002, 116 Stat. 675; Pub. L. 107–250, title II, §§ 201(e), 207, 211, title III, § 302(b), Oct. 26, 2002, 116 Stat. 1609, 1613, 1614, 1616; Pub. L. 108–214, § 2(c)(2), Apr. 1, 2004, 118 Stat. 576; Pub. L. 110–85, title II, §§ 222–224, title VIII, § 801(b)(3)(C), Sept. 27, 2007, 121 Stat. 853, 921; Pub. L. 112–144, title VI, § 604, title VII, §§ 701, 702(b)–705, July 9, 2012, 126 Stat. 1052, 1064–1066; Pub. L. 114–255, div. A, title III, §§ 3054, 3059(a), 3101(a)(2)(H), Dec. 13, 2016, 130 Stat. 1126, 1130, 1154; Pub. L. 115–52, title VII, § 701(a), title IX, § 901(e), Aug. 18, 2017, 131 Stat. 1054, 1076; Pub. L. 116–136, div. A, title III, § 3112(e), Mar. 27, 2020, 134 Stat. 363; Pub. L. 117–328, div. FF, title II, §§ 2511(a), 2515(a)(3), title III, §§ 3308(b)(1), 3613(a), 3616(c), Dec. 29, 2022, 136 Stat. 5803, 5806, 5836, 5872, 5875.)

Editorial Notes

REFERENCES IN TEXT

The effective date of this subsection, referred to in subsec. (*o*)(2)(C), probably means the date of the enactment of Pub. L. 107–250, which enacted subsec. (*o*) of this section and was approved Oct. 26, 2002.

AMENDMENTS

2022—Subsec. (h)(4)(F), (G). Pub. L. 117–328, § 3613(a), added subpar. (F) and redesignated former subpar. (F) as (G).

Subsec. (h)(6). Pub. L. 117–328, § 3616(c)(1)(A), substituted ''Not'' for ''Beginning in 2014, not'' in introductory provisions.

Subsec. (h)(6)(A). Pub. L. 117–328, § 3616(c)(1)(B), amended subpar. (A) generally. Prior to amendment, subpar. (A) read as follows:

''(A)(i) the number of domestic and foreign establishments registered pursuant to this section in the previous calendar year; and

''(ii) the number of such domestic establishments and the number of such foreign establishments that the Secretary inspected in the previous calendar year;''.

Subsec. (h)(6)(D). Pub. L. 117–328, § 3616(c)(1)(C)–(E), added subpar. (D).

Subsec. (h)(7). Pub. L. 117–328, § 3616(c)(2), added par. (7).

Subsec. (i)(5). Pub. L. 117–328, § 2511(a), added par. (5).

Subsec. (j)(3) to (5). Pub. L. 117–328, § 2515(a)(3), made technical amendment to directory language of Pub. L. 116–136, § 3112(e). See 2020 Amendment note below.

Subsec. (*l*)(1). Pub. L. 117–328, § 3308(b)(1), inserted '', or with respect to a change that is consistent with a predetermined change control plan cleared under section 360e–4 of this title'' after ''section 360c of this title''.

2020—Subsec. (j)(3) to (5). Pub. L. 116–136, § 3112(e), as amended by Pub. L. 117–328, § 2515(a)(3), added par. (3) and redesignated former pars. (3) and (4) as (4) and (5), respectively.

2017—Subsec. (h)(2). Pub. L. 115–52, § 701(a)(1), added par. (2) and struck out former par. (2). Prior to amendment, text read as follows: ''Every establishment described in paragraph (1), in any State, that is engaged

[3] So in original. Probably should be ''paragraph (1),''.

in the manufacture, propagation, compounding, or processing of a device or devices classified in class II or III shall be so inspected by one or more officers or employees duly designated by the Secretary, or by persons accredited to conduct inspections under section 374(g) of this title, at least once in the 2-year period beginning with the date of registration of such establishment pursuant to this section and at least once in every successive 2-year period thereafter.''

Subsec. (h)(4). Pub. L. 115–52, § 701(a)(2)(A), substituted ''paragraph (2) or (3)'' for ''paragraph (3)'' in introductory provisions.

Subsec. (h)(4)(C). Pub. L. 115–52, § 701(a)(2)(B), inserted ''or device'' after ''drug''.

Subsec. (h)(6). Pub. L. 115–52, § 901(e), substituted ''May 1'' for ''February 1'' in introductory provisions.

2016—Subsec. (h)(4). Pub. L. 114–255, § 3101(a)(2)(H)(i), substituted ''establishing a risk-based schedule'' for ''establishing the risk-based scheduled'' in introductory provisions.

Subsec. (h)(6)(A). Pub. L. 114–255, § 3101(a)(2)(H)(ii)(I), substituted ''calendar'' for ''fiscal'' in cls. (i) and (ii).

Subsec. (h)(6)(B). Pub. L. 114–255, § 3101(a)(2)(H)(ii)(II), substituted ''an active ingredient of a drug or a finished drug product'' for ''an active ingredient of a drug, a finished drug product, or an excipient of a drug''.

Subsec. (*l*). Pub. L. 114–255, § 3054(a), designated existing provisions as par. (1) and added par. (2).

Subsec. (m)(1). Pub. L. 114–255, § 3054(b)(1), added par. (1) and struck out former par. (1) which read as follows: ''Not later than 60 days after November 21, 1997, the Secretary shall publish in the Federal Register a list of each type of class II device that does not require a report under subsection (k) to provide reasonable assurance of safety and effectiveness. Each type of class II device identified by the Secretary as not requiring the report shall be exempt from the requirement to provide a report under subsection (k) as of the date of the publication of the list in the Federal Register. The Secretary shall publish such list on the Internet site of the Food and Drug Administration. The list so published shall be updated not later than 30 days after each revision of the list by the Secretary.''

Subsec. (m)(2). Pub. L. 114–255, § 3054(b)(2)(B), substituted ''60-calendar-day period'' for ''30-day period''.

Pub. L. 114–255, § 3054(b)(2)(A), which directed the substitution of ''1 calendar day after the date of publication of the final list under paragraph (1)(B),'' for ''1 day after the date of publication of a list under this subsection,'', was executed by making the substitution for ''1 day after the date of the publication of a list under this subsection,'' to reflect the probable intent of Congress.

Subsec. (m)(3). Pub. L. 114–255, § 3054(b)(2)(C), added par. (3).

Subsec. (q). Pub. L. 114–255, § 3059(a), added subsec. (q).

2012—Subsec. (b)(1). Pub. L. 112–144, § 701(1)(A), which directed amendment of par. (1) by ''striking 'On or before' and all that follows through the period at the end and inserting the following: 'During the period beginning on October 1 and ending on December 31 of each year, every person who owns or operates any establishment in any State engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs shall register with the Secretary the name of such person, places of business of such person, all such establishments, the unique facility identifier of each such establishment, and a point of contact e-mail address.; and'', was executed as if an end quotation mark for the inserted material followed ''address.'', to reflect the probable intent of Congress. Prior to amendment, stricken text read as follows: ''On or before December 31 of each year every person who owns or operates any establishment in any State engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs shall register with the Secretary his name, places of business, and all such establishments.''

Subsec. (b)(3). Pub. L. 112–144, § 701(1)(B), added par. (3).

Subsec. (c). Pub. L. 112–144, § 701(2), substituted ''with the Secretary—'' and pars. (1) and (2) for ''with the Secretary his name, place of business, and such establishment''.

Subsec. (h). Pub. L. 112–144, § 705, amended subsec. (h) generally. Prior to amendment, text read as follows: ''Every establishment in any State registered with the Secretary pursuant to this section shall be subject to inspection pursuant to section 374 of this title and every such establishment engaged in the manufacture, propagation, compounding, or processing of a drug or drugs or of a device or devices classified in class II or III shall be so inspected by one or more officers or employees duly designated by the Secretary, or by persons accredited to conduct inspections under section 374(g) of this title, at least once in the two-year period beginning with the date of registration of such establishment pursuant to this section and at least once in every successive two-year period thereafter.''

Subsec. (i)(1). Pub. L. 112–144, § 702(b)(1)(A), amended introductory provisions generally. Prior to amendment, text read as follows: ''Any establishment within any foreign country engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or device that is imported or offered for import into the United States shall, through electronic means in accordance with the criteria of the Secretary—''.

Subsec. (i)(1)(A). Pub. L. 112–144, § 702(b)(1)(B), amended subpar. (A) generally. Prior to amendment, subpar. (A) read as follows: ''upon first engaging in any such activity, immediately register with the Secretary the name and place of business of the establishment, the name of the United States agent for the establishment, the name of each importer of such drug or device in the United States that is known to the establishment, and the name of each person who imports or offers for import such drug or device to the United States for purposes of importation; and''.

Subsec. (i)(1)(B). Pub. L. 112–144, § 702(b)(1)(C), amended subpar. (B) generally. Prior to amendment, subpar. (B) read as follows: ''each establishment subject to the requirements of subparagraph (A) shall thereafter—

''(i) with respect to drugs, register with the Secretary on or before December 31 of each year; and

''(ii) with respect to devices, register with the Secretary during the period beginning on October 1 and ending on December 31 of each year.''

Subsec. (i)(4). Pub. L. 112–144, § 702(b)(2), added par. (4).

Subsec. (j)(1)(E). Pub. L. 112–144, § 703(1), added subpar. (E).

Subsec. (j)(4). Pub. L. 112–144, § 703(2), added par. (4).

Subsec. (n). Pub. L. 112–144, § 604, designated existing provisions as par. (1) and added par. (2).

Subsec. (p). Pub. L. 112–144, § 704, inserted subsec. heading, designated existing provisions as par. (1) and inserted par. heading, and added pars. (2) and (3).

2007—Subsec. (b). Pub. L. 110–85, § 222(a), designated existing provisions as par. (1), struck out ''or a device or devices'' after ''drug or drugs'', and added par. (2).

Subsec. (i)(1). Pub. L. 110–85, § 222(b), inserted text of par. (1) and struck out former text of par. (1) which related to registration requirement for foreign establishments engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or device to be imported or offered for import into the United States.

Subsec. (j)(2). Pub. L. 110–85, § 223, in introductory provisions, substituted ''Each person who registers with the Secretary under this section shall report to the Secretary, with regard to drugs once during the month of June of each year and once during the month of December of each year, and with regard to devices once each year during the period beginning on October 1 and ending on December 31, the following information:'' for ''Each person who registers with the Secretary under this section shall report to the Secretary once during the month of June of each year and once during the month of December of each year the following information:''.

Subsec. (k). Pub. L. 110–85, §801(b)(3)(C), inserted concluding provisions.

Subsec. (p). Pub. L. 110–85, §224, amended subsec. (p) generally. Prior to amendment, subsec. (p) read as follows: ''Registrations under subsections (b), (c), (d), and (i) of this section (including the submission of updated information) shall be submitted to the Secretary by electronic means, upon a finding by the Secretary that the electronic receipt of such registrations is feasible, unless the Secretary grants a request for waiver of such requirement because use of electronic means is not reasonable for the person requesting such waiver.''

2004—Subsec. (*o*)(1)(B), (2)(B). Pub. L. 108–214, §2(c)(2)(A), (B)(i), substituted ''or adulterated'' for '', adulterated''.

Subsec. (*o*)(2)(E). Pub. L. 108–214, §2(c)(2)(B)(ii), substituted ''semi-critical'' for ''semicritical''.

2002—Subsec. (h). Pub. L. 107–250, §201(e), inserted '', or by persons accredited to conduct inspections under section 374(g) of this title,'' after ''duly designated by the Secretary''.

Subsec. (i)(1). Pub. L. 107–188, §321(a)(1), substituted ''On or before December 31 of each year, any establishment'' for ''Any establishment'' and ''shall, through electronic means in accordance with the criteria of the Secretary, register with the Secretary the name and place of business of the establishment, the name of the United States agent for the establishment, the name of each importer of such drug or device in the United States that is known to the establishment, and the name of each person who imports or offers for import such drug or device to the United States for purposes of importation'' for ''shall register with the Secretary the name and place of business of the establishment and the name of the United States agent for the establishment''.

Subsec. (j)(1). Pub. L. 107–188, §321(a)(2), substituted ''subsection (b), (c), (d), or (i)'' for ''subsection (b), (c), or (d)'' in first sentence.

Subsec. (m)(1). Pub. L. 107–250, §211, inserted at end ''The Secretary shall publish such list on the Internet site of the Food and Drug Administration. The list so published shall be updated not later than 30 days after each revision of the list by the Secretary.''

Subsec. (*o*). Pub. L. 107–250, §302(b), added subsec. (*o*).

Subsec. (p). Pub. L. 107–250, §207, added subsec. (p).

1997—Subsec. (g). Pub. L. 105–115, §213(b)(3), inserted at end ''In this subsection, the term 'wholesale distributor' means any person (other than the manufacturer or the initial importer) who distributes a device from the original place of manufacture to the person who makes the final delivery or sale of the device to the ultimate consumer or user.''

Subsec. (g)(4), (5). Pub. L. 105–115, §213(b)(1), (2), added par. (4) and redesignated former par. (4) as (5).

Subsec. (i). Pub. L. 105–115, §417, amended subsec. (i) generally. Prior to amendment, subsec. (i) read as follows: ''Any establishment within any foreign country engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs, or a device or devices, shall be permitted to register under this section pursuant to regulations promulgated by the Secretary. Such regulations shall require such establishment to provide the information required by subsection (j) of this section and shall require such establishment to provide the information required by subsection (j) of this section in the case of a device or devices and shall include provisions for registration of any such establishment upon condition that adequate and effective means are available, by arrangement with the government of such foreign country or otherwise, to enable the Secretary to determine from time to time whether drugs or devices manufactured, prepared, propagated, compounded, or processed in such establishment, if imported or offered for import into the United States, shall be refused admission on any of the grounds set forth in section 381(a) of this title.''

Subsec. (j)(1)(A), (D). Pub. L. 105–115, §125(a)(2)(C), struck out '', 356, 357,'' before ''or 360b of this title''.

Subsec. (k). Pub. L. 105–115, §206(a)(1), inserted ''or person who is accredited under section 360m(a) of this title'' after ''report to the Secretary''.

Subsecs. (*l*), (m). Pub. L. 105–115, §206(a)(2), added subsecs. (*l*) and (m).

Subsec. (n). Pub. L. 105–115, §209(a), added subsec. (n).

1976—Subsec. (a)(1). Pub. L. 94–295, §4(a)(2), substituted ''drug package or device package'' for ''drug package'', ''distribution of the drug or device'' for ''distribution of the drug'', and ''ultimate consumer or user'' for ''ultimate consumer''.

Subsecs. (b) to (d). Pub. L. 94–295, §4(a)(3), inserted ''or a device or devices'' after ''drug or drugs''.

Subsec. (e). Pub. L. 94–295, §4(a)(4), authorized the Secretary to prescribe by regulation a uniform system for the identification of devices intended for human use and authorized him, in addition, to require that persons who are required to list devices pursuant to subsec. (j) also list such devices in accordance with the system.

Subsec. (g)(1) to (3). Pub. L. 94–295, §4(a)(5), substituted ''drugs or devices'' for ''drugs''.

Subsec. (h). Pub. L. 94–295, §4(a)(6), inserted reference to establishments engaged in the manufacture, propagation, compounding, or processing of a drug or drugs or of a device or devices classified in class II or III.

Subsec. (i). Pub. L. 94–295, §4(a)(7), inserted reference to devices and inserted requirement that regulations require establishments to provide the information required by subsection (j) of this section in the case of a device or devices.

Subsec. (j)(1). Pub. L. 94–295, §4(a)(8)(A), in introductory provisions substituted ''a list of all drugs and a list of all devices and a brief statement of the basis for believing that each device included in the list is a device rather than a drug (with each drug and device in each list listed by its established name'' for ''a list of all drugs (by established name'' and ''drugs or devices filed'' for ''drugs filed''.

Subsec. (j)(1)(A). Pub. L. 94–295, §4(a)(8)(B), substituted ''the applicable list'' for ''such list'', inserted ''or a device intended for human use contained in the applicable list with respect to which a performance standard has been established under section 360d of this title or which is subject to section 360e of this title,'' after ''360b of this title,'', and substituted ''such drug or device'' for ''such drug'' wherever appearing.

Subsec. (j)(1)(B). Pub. L. 94–295, §4(a)(8)(C), in introductory provisions substituted ''drug or device contained in an applicable list'' for ''drug contained in such list''.

Subsec. (j)(1)(B)(i). Pub. L. 94–295, §4(a)(8)(D), substituted ''which drug is subject to section 353(b)(1) of this title, or which device is a restricted device, a copy of all labeling for such drug or device, a representative sampling of advertisements for such drug or device, and, upon request made by the Secretary for good cause, a copy of all advertisements for a particular drug product or device, or'' for ''which is subject to section 353(b)(1) of this title, a copy of all labeling for such drug, a representative sampling of advertisements for such drug, and, upon request made by the Secretary for good cause, a copy of all advertisements for a particular drug product, or''.

Subsec. (j)(1)(B)(ii). Pub. L. 94–295, §4(a)(8)(E), substituted ''which drug is not subject to section 353(b)(1) of this title or which device is not a restricted device, the label and package insert for such drug or device and a representative sampling of any other labeling for such drug or device'' for ''which is not subject to section 353(b)(1) of this title, the label and package insert for such drug and a representative sampling of any other labeling for such drug''.

Subsec. (j)(1)(C). Pub. L. 94–295, §4(a)(8)(F), substituted ''an applicable list'' for ''such list''.

Subsec. (j)(1)(D). Pub. L. 94–295, §4(a)(8)(G), substituted ''a list'' for ''the list'', inserted ''or the particular device contained in such list is not subject to a performance standard established under section 360d of this title or to section 360e of this title or is not a restricted device'' after ''or 360b of this title,'', and substituted ''particular drug product or device'' for ''particular drug product'' wherever appearing.

Subsec. (j)(2). Pub. L. 94–295, §4(a)(8)(H), substituted ''drug or device'' for ''drug'' in subpars. (A), (B), and

(C), and substituted ''(each by established name'' for ''(by established name'' in subpar. (C).

Subsec. (k). Pub. L. 94–295, § 4(a)(9), added subsec. (k).

1972—Subsec. (e). Pub. L. 92–387, § 4(a), inserted provision that the Secretary may assign a listing number to each drug or class of drugs listed under subsec. (j).

Subsec. (f). Pub. L. 92–387, § 4(b), inserted exception that the list submitted under subsec. (j)(3) and information submitted under subsec. (j)(1), (2) shall be exempt from inspection unless the Secretary determines otherwise.

Subsec. (i). Pub. L. 92–387, § 4(c), inserted provision that the regulations shall require such establishment to provide the information required by subsec. (j).

Subsec. (j). Pub. L. 92–387, § 3, added subsec. (j).

1970—Subsec. (a). Pub. L. 91–513 struck out provisions defining the wholesaling, jobbing, or distributing of depressant or stimulant drugs.

Subsec. (b). Pub. L. 91–513 struck out provisions covering establishments engaged in the wholesaling, jobbing, or distributing of depressant or stimulant drugs and the inclusion of the fact of such activity in the annual registration.

Subsec. (c). Pub. L. 91–513 struck out provisions covering new registrations of persons first engaging in the wholesaling, jobbing, or distributing of depressant or stimulant drugs and the inclusion of the fact of such activity in the registration.

Subsec. (d). Pub. L. 91–513 struck out number designation ''(1)'' preceding first sentence, struck out portion of such redesignated provisions covering the wholesaling, jobbing, or distributing of depressant or stimulant drugs, and struck out par. (2) covering the filing of supplemental registration whenever a person not previously engaged or involved with depressant or stimulant drugs goes into the manufacturing, preparation, or processing thereof.

1965—Pub. L. 89–74, § 4(e), included certain wholesalers in section catchline.

Subsec. (a)(2), (3). Pub. L. 89–74, § 4(a), added par. (2) and redesignated former par. (2) as (3).

Subsecs. (b), (c). Pub. L. 89–74, § 4(b), (c), inserted ''or in the wholesaling, jobbing, or distributing of any depressant or stimulant drug'' after ''drug or drugs'' and inserted requirement that establishment indicate activity in depressant or stimulant drugs at time of registration.

Subsec. (d). Pub. L. 89–74 § 4(d), designated existing provisions as par. (1), inserted ''or the wholesaling, jobbing, or distributing of any depressant or stimulant drug'' and the requirement that the additional establishment indicate activity in depressant or stimulant drugs at time of registration, and added par. (2).

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 2020 AMENDMENT

Amendment by Pub. L. 116–136 effective 180 days after Mar. 27, 2020, see section 3112(g) of Pub. L. 116–136, set out as a note under section 356c of this title.

EFFECTIVE DATE OF 2002 AMENDMENT

Amendment by Pub. L. 107–188 effective upon the expiration of the 180-day period beginning June 12, 2002, see section 321(c) of Pub. L. 107–188, set out as a note under section 331 of this title.

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by sections 206(a), 209(a), 213(b), and 417 of Pub. L. 105–115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as a note under section 321 of this title.

EFFECTIVE DATE OF 1972 AMENDMENT

Pub. L. 92–387, § 5, Aug. 16, 1972, 86 Stat. 562, provided that: ''The amendments made by this Act [amending this section and sections 331 and 335 of this title and enacting provisions set out below] shall take effect on the first day of the sixth month beginning after the date of enactment of this Act [Aug. 16, 1972].''

EFFECTIVE DATE OF 1970 AMENDMENT

Amendment by Pub. L. 91–513 effective on first day of seventh calendar month that begins after Oct. 26, 1970, see section 704 of Pub. L. 91–513, set out as an Effective Date note under section 801 of this title.

EFFECTIVE DATE OF 1965 AMENDMENT

Amendment by Pub. L. 89–74 effective Feb. 1, 1966, subject to registration with Secretary of names, places of business, establishments, and other prescribed information prior to Feb. 1, 1966, see section 11 of Pub. L. 89–74, set out as a note under section 321 of this title.

UPDATING REGULATIONS

Pub. L. 117–328, div. FF, title II, § 2511(b), Dec. 29, 2022, 136 Stat. 5804, provided that: ''Not later than 2 years after the date of enactment of this Act [Dec. 29, 2022], the Secretary of Health and Human Services shall update regulations, as appropriate, to implement the amendment made by subsection (a) [amending this section].''

SAVINGS PROVISION

Amendment by Pub. L. 91–513 not to affect or abate any prosecutions for any violation of law or any civil seizures or forfeitures and injunctive proceedings commenced prior to the effective date of such amendment, and all administrative proceedings pending before the Bureau of Narcotics and Dangerous Drugs [now the Drug Enforcement Administration] on Oct. 27, 1970, to be continued and brought to final determination in accord with laws and regulations in effect prior to Oct. 27, 1970, see section 702 of Pub. L. 91–513, set out as a note under section 321 of this title.

DEVICE MODIFICATIONS

Pub. L. 114–255, div. A, title III, § 3059(b), Dec. 13, 2016, 130 Stat. 1130, provided that: ''The Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs, shall issue final guidance regarding when a premarket notification under section 510(k) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360(k)) is required to be submitted for a modification or change to a legally marketed device. Such final guidance shall be issued not later than 1 year after the date on which the comment period closes for the draft guidance on such subject.''

DECLARATION OF POLICY OF DRUG LISTING ACT OF 1972

Pub. L. 92–387, § 2, Aug. 16, 1972, 86 Stat. 559, provided that: ''The Federal Government which is responsible for regulating drugs has no ready means of determining what drugs are actually being manufactured or packed by establishments registered under the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 301 et seq.] except by periodic inspection of such registered establishments. Knowledge of which particular drugs are being manufactured or packed by each registered establishment would substantially assist in the enforcement of Federal laws requiring that such drugs be pure, safe, effective, and properly labeled. Information on the discontinuance of a particular drug could serve to alleviate the burden of reviewing and implementing enforcement actions against drugs which, although commercially discontinued, remain active for regulatory purposes. Information on the type and number of different drugs being manufactured or packed by drug establishments could permit more effective and timely regulation by the agencies of the Federal Government responsible for regulating drugs, including identification of which drugs in interstate commerce are subject to section 505 or 507 [21 U.S.C. 355, 357], or to other provisions of the Federal Food, Drug, and Cosmetic Act.''

CONGRESSIONAL DECLARATION OF NEED FOR REGISTRATION AND INSPECTION OF DRUG ESTABLISHMENTS

Pub. L. 87–781, title III, § 301, Oct. 10, 1962, 76 Stat. 793, provided that: ''The Congress hereby finds and declares

that in order to make regulation of interstate commerce in drugs effective, it is necessary to provide for registration and inspection of all establishments in which drugs are manufactured, prepared, propagated, compounded, or processed; that the products of all such establishments are likely to enter the channels of interstate commerce and directly affect such commerce; and that the regulation of interstate commerce in drugs without provision for registration and inspection of establishments that may be engaged only in intrastate commerce in such drugs would discriminate against and depress interstate commerce in such drugs, and adversely burden, obstruct, and affect such interstate commerce.''

REGISTRATION OF CERTAIN PERSONS OWNING OR OPERATING DRUG ESTABLISHMENTS PRIOR TO OCT. 10, 1962

Pub. L. 87–781, title III, § 303, Oct. 10, 1962, 76 Stat. 795, provided that any person who, on the day immediately preceding Oct. 10, 1962, owned or operated an establishment which manufactured or processed drugs, registered before the first day of the seventh month following October, 1962, would be deemed to be registered in accordance with subsec. (b) of this section for the calendar year 1962 and if registered within this period and effected in 1963, be deemed in compliance for that calendar year.

§ 360a. Clinical trial guidance for antibiotic drugs

(a) In general

Not later than 1 year after September 27, 2007, the Secretary shall issue guidance for the conduct of clinical trials with respect to antibiotic drugs, including antimicrobials to treat acute bacterial sinusitis, acute bacterial otitis media, and acute bacterial exacerbation of chronic bronchitis. Such guidance shall indicate the appropriate models and valid surrogate markers.

(b) Review

Not later than 5 years after September 27, 2007, the Secretary shall review and update the guidance described under subsection (a) to reflect developments in scientific and medical information and technology.

(June 25, 1938, ch. 675, § 511, as added Pub. L. 110–85, title IX, § 911, Sept. 27, 2007, 121 Stat. 951.)

Editorial Notes

PRIOR PROVISIONS

A prior section 360a, act June 25, 1938, ch. 675, § 511, as added July 15, 1965, Pub. L. 89–74, § 3(b), 79 Stat. 227; amended Oct. 24, 1968, Pub. L. 90–639, § 2(a), 82 Stat. 1361, regulated the manufacture, compounding, and processing of depressant and stimulant drugs and their sale, delivery, disposal, possession, and recordkeeping activities connected therewith, prior to repeal by Pub. L. 91–513, title II, §§ 701(a), 704, Oct. 27, 1970, 84 Stat. 1281, 1284, effective on the first day of the seventh calendar month that began after Oct. 26, 1970.

§ 360a–1. Clinical trials

(a) Review and revision of guidance documents

(1) In general

The Secretary of Health and Human Services (referred to in this section as the ''Secretary'') shall review and, as appropriate, revise not fewer than 3 guidance documents per year, which shall include—

(A) reviewing the guidance documents of the Food and Drug Administration for the conduct of clinical trials with respect to antibacterial and antifungal drugs; and

(B) as appropriate, revising such guidance documents to reflect developments in scientific and medical information and technology and to ensure clarity regarding the procedures and requirements for approval of antibacterial and antifungal drugs under chapter V of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351 et seq.).

(2) Issues for review

At a minimum, the review under paragraph (1) shall address the appropriate animal models of infection, in vitro techniques, valid microbiological surrogate markers, the use of noninferiority versus superiority trials, trial enrollment, data requirements, and appropriate delta values for noninferiority trials.

(3) Rule of construction

Except to the extent to which the Secretary makes revisions under paragraph (1)(B), nothing in this section shall be construed to repeal or otherwise effect the guidance documents of the Food and Drug Administration.

(b) Recommendations for investigations

(1) Request

The sponsor of a drug intended to be designated as a qualified infectious disease product may request that the Secretary provide written recommendations for nonclinical and clinical investigations which the Secretary believes may be necessary to be conducted with the drug before such drug may be approved under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) for use in treating, detecting, preventing, or identifying a qualifying pathogen, as defined in section 505E of such Act [21 U.S.C. 355f].

(2) Recommendations

If the Secretary has reason to believe that a drug for which a request is made under this subsection is a qualified infectious disease product, the Secretary shall provide the person making the request written recommendations for the nonclinical and clinical investigations which the Secretary believes, on the basis of information available to the Secretary at the time of the request, would be necessary for approval under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) of such drug for the use described in paragraph (1).

(c) Qualified infectious disease product

For purposes of this section, the term ''qualified infectious disease product'' has the meaning given such term in section 505E(g) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355f(g)], as added by section 801 of this Act.

(Pub. L. 112–144, title VIII, § 804, July 9, 2012, 126 Stat. 1080.)

Editorial Notes

REFERENCES IN TEXT

The Federal Food, Drug, and Cosmetic Act, referred to in subsec. (a)(1)(B), is act June 25, 1938, ch. 675, 52 Stat. 1040, which is classified generally to this chapter.

Chapter V of the Act is classified generally to this subchapter. For complete classification of this Act to the Code, see section 301 of this title and Tables.

This Act, referred to in subsec. (c), is Pub. L. 112–144, July 9, 2012, 126 Stat. 993, known as the Food and Drug Administration Safety and Innovation Act. For complete classification of this Act to the Code, see Tables.

CODIFICATION

Section was enacted as part of the Food and Drug Administration Safety and Innovation Act, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

Statutory Notes and Related Subsidiaries

DECENTRALIZED CLINICAL STUDIES

Pub. L. 117–328, div. FF, title III, §3606, Dec. 29, 2022, 136 Stat. 5865, provided that:

''(a) GUIDANCE.—The Secretary [of Health and Human Services] shall—

''(1) not later than 1 year after the date of enactment of this Act [Dec. 29, 2022], issue or revise draft guidance that includes recommendations to clarify and advance the use of decentralized clinical studies to support the development of drugs and devices, including recommendations for how to advance the use of flexible and novel clinical trial designs and to help improve trial participant engagement, recruitment, enrollment, and retention of a meaningfully diverse clinical population, including with respect to race, ethnicity, age, sex, and geographic location, when appropriate; and

''(2) not later than 1 year after closing the comment period on such draft guidance, finalize such guidance.

''(b) CONTENT OF GUIDANCE.—The guidance under subsection (a) shall address the following:

''(1) Recommendations related to digital health technology or other assessment options, such as telehealth, local laboratories, local health care providers, or other options for remote data collection, could support decentralized clinical studies, including guidance on considerations for selecting technological platforms and mediums, data collection and use, data integrity and security, and communication to study participants through digital technology.

''(2) Recommendations for subject recruitment, retention, and engagement, including considerations for sponsors to minimize or reduce burdens for clinical study participants through the use of digital health technology, telehealth, local health care providers and laboratories, health care provider home visits, direct-to-participant engagement, electronic informed consent, or other means, as appropriate.

''(3) Recommendations with respect to the evaluation of data collected within a decentralized clinical study setting.

''(4) Recommendations for methods of remote data collection, including clinical trial participant experience data, through the use of digital health technologies, telemedicine, local laboratories, local health care providers, or other options for data collection.

''(5) Considerations for sponsors to minimize or reduce burdens for clinical trial participants associated with participating in a clinical trial, such as the use of digital technologies, telemedicine, local laboratories, local health care providers, or other data collection or assessment options, health care provider home visits, direct-to-participant shipping of investigational drugs and devices, and electronic informed consent, as appropriate.

''(6) Recommendations regarding conducting decentralized clinical trials to facilitate and encourage meaningful diversity among clinical trial participants, including with respect to race, ethnicity, age, sex, and geographic location, as appropriate.

''(7) Recommendations for strategies and methods for recruiting, retaining, and engaging with clinical trial participants, including communication regarding the role of clinical trial participants and community partners to facilitate clinical trial recruitment and engagement, including with respect to diverse and underrepresented populations, as appropriate.

''(8) Considerations for review and oversight by sponsors and institutional review boards, including remote trial oversight.

''(9) Recommendations for decentralized clinical trial protocol designs and processes for evaluating such proposed clinical trial designs.

''(10) Recommendations related to digital health technology and other remote assessment tools that may support decentralized clinical trials, including guidance on appropriate technological platforms and tools, data collection and use, data integrity, and communication to clinical trial participants through such technology.

''(11) A description of the manner in which the Secretary will assess or evaluate data collected within a decentralized clinical trial to support the development of the drug or device, if the manner is different from that used for a nondecentralized trial.

''(12) Considerations for sponsors to validate digital technologies and establish appropriate clinical endpoints for use in decentralized trials.

''(13) Considerations for privacy and security of personally identifiable information of trial participants.

''(14) Considerations for conducting clinical trials using centralized approaches in conjunction with decentralized approaches.

''(c) DEFINITION.—In this section, the term 'decentralized clinical study' means a clinical study in which some or all of the study-related activities occur at a location separate from the investigator's location.''

MODERNIZING CLINICAL TRIALS

Pub. L. 117–328, div. FF, title III, §3607, Dec. 29, 2022, 136 Stat. 5866, provided that:

''(a) CLARIFYING THE USE OF DIGITAL HEALTH TECHNOLOGIES IN CLINICAL TRIALS.—

''(1) IN GENERAL.—Not later than 1 year after the date of enactment of this Act [Dec. 29, 2022], the Secretary [of Health and Human Services] shall issue or revise draft guidance regarding the appropriate use of digital health technologies in clinical trials to help improve recruitment for, retention in, participation in, and data collection during, clinical trials, and provide for novel clinical trial designs utilizing such technology for purposes of supporting the development of, and review of applications for, drugs and devices. Not later than 18 months after the public comment period on such draft guidance ends, the Secretary shall issue a revised draft guidance or final guidance.

''(2) CONTENT.—The guidance described in paragraph (1) shall include—

''(A) recommendations for data collection methodologies by which sponsors may incorporate the use of digital health technologies in clinical trials to collect data remotely from trial participants;

''(B) considerations for privacy and security protections for data collected during a clinical trial, including—

''(i) recommendations for the protection of trial participant data that are collected or used in research using digital health technologies;

''(ii) compliance with the regulations promulgated under section 264(c) of the Health Insurance Portability and Accountability Act of 1996 ([Pub. L. 104–191;] 42 U.S.C. 1320d–2 note), subpart B of part 50 of title 21, Code of Federal Regulations, subpart C of part 56 of title 21, Code of Federal Regulations, the Federal policy for the protection of human subjects under subpart A of part 46 of title 45, Code of Federal Regulations (commonly known as the 'Common Rule'), and part 2 of title 42, Code of Federal Regulations (or any successor regulations); and

''(iii) recommendations for the protection of clinical trial participant data against cybersecurity threats, as applicable;

''(C) considerations on data collection methods to help increase recruitment of clinical trial participants and the level of participation of such participants, reduce burden on clinical trial participants, and optimize data quality;

''(D) recommendations for the use of electronic methods to obtain informed consent from clinical trial participants, taking into consideration applicable Federal law, including subpart B of part 50 of title 21, Code of Federal Regulations (or successor regulations), and, as appropriate, State law;

''(E) best practices for communication between sponsors and the Secretary on the development of data collection methods;

''(F) the appropriate format to submit such data to the Secretary;

''(G) a description of the manner in which the Secretary may assess or evaluate data collected through digital health technologies to support the development of the drug or device;

''(H) recommendations regarding the data and information needed to demonstrate that a digital health technology is fit-for-purpose for a clinical trial, and a description of how the Secretary will evaluate such data and information; and

''(I) recommendations for increasing access to, and the use of, digital health technologies in clinical trials to facilitate the inclusion of diverse and underrepresented populations, as appropriate, including considerations for access to, and the use of, digital health technologies in clinical trials by people with disabilities and pediatric populations.

''(b) SEAMLESS AND CONCURRENT CLINICAL TRIALS.—

''(1) IN GENERAL.—Not later than 1 year after the date of enactment of this Act, the Secretary shall issue or revise draft guidance on the use of seamless, concurrent, and other innovative clinical trial designs to support the expedited development and review of applications for drugs, as appropriate. Not later than 18 months after the public comment period on such draft guidance ends, the Secretary shall issue a revised draft guidance or final guidance.

''(2) CONTENT.—The guidance described in paragraph (1) shall include—

''(A) recommendations on the use of expansion cohorts and other seamless clinical trial designs to assess different aspects of product candidates in one continuous trial, including how such clinical trial designs can be used as part of meeting the substantial evidence standard under section 505(d) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(d));

''(B) recommendations on the use of clinical trial designs that involve the concurrent conduct of different or multiple clinical trial phases, and the concurrent conduct of preclinical testing, to expedite the development of new drugs and facilitate the timely collection of data;

''(C) recommendations for how to streamline trial logistics and facilitate the efficient collection and analysis of clinical trial data, including any planned interim analyses and how such analyses could be used to streamline the product development and review processes;

''(D) considerations to assist sponsors in ensuring the rights, safety, and welfare of clinical trial participants, maintaining compliance with good clinical practice regulations, minimizing risks to clinical trial data integrity, and ensuring the reliability of clinical trial results;

''(E) recommendations for communication between sponsors and the Food and Drug Administration on the development of seamless, concurrent, or other adaptive clinical trial designs, including review of, and feedback on, clinical trial protocols; and

''(F) a description of the manner in which the Secretary will assess or evaluate data collected through seamless, concurrent, or other adaptive clinical trial designs to support the development of drugs.

''(c) INTERNATIONAL HARMONIZATION.—The Secretary shall, as appropriate, work with foreign regulators pursuant to memoranda of understanding or other arrangements governing the exchange of information to facilitate international harmonization of the regulation and use of decentralized clinical trials, digital technology in clinical trials, and seamless, concurrent, and other adaptive or innovative clinical trial designs.''

§ 360a–2. Susceptibility test interpretive criteria for microorganisms

(a) Purpose; identification of criteria

(1) Purpose

The purpose of this section is to clarify the Secretary's authority to—

(A) efficiently update susceptibility test interpretive criteria for antimicrobial drugs when necessary for public health, due to, among other things, the constant evolution of microorganisms that leads to the development of resistance to drugs that have been effective in decreasing morbidity and mortality for patients, which warrants unique management of antimicrobial drugs that is inappropriate for most other drugs in order to delay or prevent the development of further resistance to existing therapies;

(B) provide for public notice of the availability of recognized interpretive criteria and interpretive criteria standards; and

(C) clear under section 360(k) of this title, classify under section 360c(f)(2) of this title, or approve under section 360e of this title, antimicrobial susceptibility testing devices utilizing updated, recognized susceptibility test interpretive criteria to characterize the in vitro susceptibility of particular bacteria, fungi, or other microorganisms, as applicable, to antimicrobial drugs.

(2) Identification of criteria

The Secretary shall identify appropriate susceptibility test interpretive criteria with respect to antimicrobial drugs—

(A) if such criteria are available on the date of approval of the drug under section 355 of this title or licensure of the drug under section 262 of title 42 (as applicable), upon such approval or licensure; or

(B) if such criteria are unavailable on such date, on the date on which such criteria are available for such drug.

(3) Bases for initial identification

The Secretary shall identify appropriate susceptibility test interpretive criteria under paragraph (2), based on the Secretary's review of, to the extent available and relevant—

(A) preclinical and clinical data, including pharmacokinetic, pharmacodynamic, and epidemiological data;

(B) the relationship of susceptibility test interpretive criteria to morbidity and mortality associated with the disease or condition for which such drug is used; and

(C) such other evidence and information as the Secretary considers appropriate.

(b) Susceptibility test Interpretive Criteria Website

(1) In general

Not later than 1 year after December 13, 2016, the Secretary shall establish, and main-

tain thereafter, on the website of the Food and Drug Administration, a dedicated website that contains a list of any appropriate new or updated susceptibility test interpretive criteria standards and interpretive criteria in accordance with paragraph (2) (referred to in this section as the ''Interpretive Criteria Website'').

(2) Listing of susceptibility test interpretive criteria standards and interpretive criteria

(A) In general

The list described in paragraph (1) shall consist of any new or updated susceptibility test interpretive criteria standards that are—

(i) established by a nationally or internationally recognized standard development organization that—

(I) establishes and maintains procedures to address potential conflicts of interest and ensure transparent decisionmaking;

(II) holds open meetings to ensure that there is an opportunity for public input by interested parties, and establishes and maintains processes to ensure that such input is considered in decisionmaking; and

(III) permits its standards to be made publicly available, through the National Library of Medicine or another similar source acceptable to the Secretary; and

(ii) recognized in whole, or in part, by the Secretary under subsection (c).

(B) Other list

The Interpretive Criteria Website shall, in addition to the list described in subparagraph (A), include a list of interpretive criteria, if any, that the Secretary has determined to be appropriate with respect to legally marketed antimicrobial drugs, where—

(i) the Secretary does not recognize, in whole or in part, an interpretive criteria standard described under subparagraph (A) otherwise applicable to such a drug;

(ii) the Secretary withdraws under subsection (c)(1)(A) recognition of a standard, in whole or in part, otherwise applicable to such a drug;

(iii) the Secretary approves an application under section 355 of this title or section 262 of title 42, as applicable, with respect to marketing of such a drug for which there are no relevant interpretive criteria included in a standard recognized by the Secretary under subsection (c); or

(iv) because the characteristics of such a drug differ from other drugs with the same active ingredient, the interpretive criteria with respect to such drug—

(I) differ from otherwise applicable interpretive criteria included in a standard listed under subparagraph (A) or interpretive criteria otherwise listed under this subparagraph; and

(II) are determined by the Secretary to be appropriate for the drug.

(C) Required statements

The Interpretive Criteria Website shall include statements conveying—

(i) that the website provides information about the in vitro susceptibility of bacteria, fungi, or other microorganisms, as applicable to a certain drug (or drugs);

(ii) that—

(I) the safety and efficacy of such drugs in treating clinical infections due to such bacteria, fungi, or other microorganisms, as applicable, may or may not have been established in adequate and well-controlled clinical trials in order for the susceptibility information described in clause (i) to be included on the website; and

(II) the clinical significance of such susceptibility information in such instances is unknown;

(iii) that the approved product labeling for specific drugs provides the uses for which the Secretary has approved the product; and

(iv) any other information that the Secretary determines appropriate to adequately convey the meaning of the data supporting the recognition or listing of susceptibility test interpretive criteria standards or susceptibility test interpretive criteria included on the website.

(3) Notice

Not later than the date on which the Interpretive Criteria Website is established, the Secretary shall publish a notice of that establishment in the Federal Register.

(4) Inapplicability of misbranding provision

The inclusion in the approved labeling of an antimicrobial drug of a reference or hyperlink to the Interpretive Criteria Website, in and of itself, shall not cause the drug to be misbranded in violation of section 352 of this title.

(5) Trade secrets and confidential information

Nothing in this section shall be construed as authorizing the Secretary to disclose any information that is a trade secret or confidential information subject to section 552(b)(4) of title 5.

(c) Recognition of susceptibility test interpretive criteria

(1) Evaluation and publication

(A) In general

Beginning on the date of the establishment of the Interpretive Criteria Website, and at least every 6 months thereafter, the Secretary shall—

(i) evaluate any appropriate new or updated susceptibility test interpretive criteria standards established by a nationally or internationally recognized standard development organization described in subsection (b)(2)(A)(i); and

(ii) publish on the public website of the Food and Drug Administration a notice—

(I) withdrawing recognition of any different susceptibility test interpretive criteria standard, in whole or in part;

(II) recognizing the new or updated standards;

(III) recognizing one or more parts of the new or updated interpretive criteria

specified in such a standard and declining to recognize the remainder of such standard; and

(IV) making any necessary updates to the lists under subsection (b)(2).

(B) Upon approval of a drug

Upon the approval of an initial or supplemental application for an antimicrobial drug under section 355 of this title or section 262 of title 42, as applicable, where such approval is based on susceptibility test interpretive criteria which differ from those contained in a standard recognized, or from those otherwise listed, by the Secretary pursuant to this subsection, or for which there are no relevant interpretive criteria standards recognized, or interpretive criteria otherwise listed, by the Secretary pursuant to this subsection, the Secretary shall update the lists under subparagraphs (A) and (B) of subsection (b)(2) to include the susceptibility test interpretive criteria upon which such approval was based.

(2) Bases for updating interpretive criteria standards

In evaluating new or updated susceptibility test interpretive criteria standards under paragraph (1)(A), the Secretary may consider—

(A) the Secretary's determination that such a standard is not applicable to a particular drug because the characteristics of the drug differ from other drugs with the same active ingredient;

(B) information provided by interested third parties, including public comment on the annual compilation of notices published under paragraph (3);

(C) any bases used to identify susceptibility test interpretive criteria under subsection (a)(2); and

(D) such other information or factors as the Secretary determines appropriate.

(3) Annual compilation of notices

Each year, the Secretary shall compile the notices published under paragraph (1)(A) and publish such compilation in the Federal Register and provide for public comment. If the Secretary receives comments, the Secretary shall review such comments and, if the Secretary determines appropriate, update pursuant to this subsection susceptibility test interpretive criteria standards or criteria—

(A) recognized by the Secretary under this subsection; or

(B) otherwise listed on the Interpretive Criteria Website under subsection (b)(2).

(4) Relation to section 360d(c) of this title

Any susceptibility test interpretive standard recognized under this subsection or any criteria otherwise listed under subsection (b)(2)(B) shall be deemed to be recognized as a standard by the Secretary under section 360d(c)(1) of this title.

(5) Voluntary use of interpretive criteria

Nothing in this section prohibits a person from seeking approval or clearance of a drug or device, or changes to the drug or the device, on the basis of susceptibility test interpretive criteria which differ from those contained in a standard recognized, or from those otherwise listed, by the Secretary pursuant to subsection (b)(2).

(d) Antimicrobial drug labeling

(1) Drugs marketed prior to establishment of Interpretive Criteria Website

(A) In general

With respect to an antimicrobial drug lawfully introduced or delivered for introduction into interstate commerce for commercial distribution before the establishment of the Interpretive Criteria Website, a holder of an approved application under section 355 of this title or section 262 of title 42, as applicable, for each such drug, not later than 1 year after establishment of the Interpretive Criteria Website described in subsection (b)(1), shall remove susceptibility test interpretive criteria, if any, and related information from the approved drug labeling and replace it with a reference to the Interpretive Criteria Website.

(B) Labeling changes

The labeling changes required by this section shall be considered a minor change under section 314.70 of title 21, Code of Federal Regulations (or any successor regulations) that may be implemented through documentation in the next applicable annual report.

(2) Drugs marketed subsequent to establishment of Interpretive Criteria Website

With respect to antimicrobial drugs approved on or after the date of the establishment of the Interpretive Criteria Website described in subsection (b)(1), the labeling for such a drug shall include, in lieu of susceptibility test interpretive criteria and related information, a reference to such Website.

(e) Special condition for marketing of antimicrobial susceptibility testing devices

(1) In general

Notwithstanding sections 351, 352, 355, 360, 360c, and 360e of this title, if the conditions specified in paragraph (2) are met (in addition to other applicable provisions under this subchapter) with respect to an antimicrobial susceptibility testing device described in subsection (f)(1), the Secretary may authorize the marketing of such device for a use described in such subsection.

(2) Conditions applicable to antimicrobial susceptibility testing devices

The conditions specified in this paragraph are the following:

(A) The device is used to make a determination of susceptibility using susceptibility test interpretive criteria that are—

(i) included in a standard recognized by the Secretary under subsection (c); or

(ii) otherwise listed on the Interpretive Criteria Website under subsection (b)(2).

(B) The labeling of such device includes statements conveying—

(i) that the device provides information about the in vitro susceptibility of bacteria, fungi, or other microorganisms, as applicable to antimicrobial drugs;

(ii) that—

(I) the safety and efficacy of such drugs in treating clinical infections due to such bacteria, fungi, or other microorganisms, as applicable, may or may not have been established in adequate and well-controlled clinical trials in order for the device to report the susceptibility of such bacteria, fungi, or other microorganisms, as applicable, to such drugs; and

(II) the clinical significance of such susceptibility information in those instances is unknown;

(iii) that the approved labeling for drugs tested using such a device provides the uses for which the Secretary has approved such drugs; and

(iv) any other information the Secretary determines appropriate to adequately convey the meaning of the data supporting the recognition or listing of susceptibility test interpretive criteria standards or susceptibility test interpretive criteria described in subparagraph (A).

(C) The antimicrobial susceptibility testing device meets all other requirements to be cleared under section 360(k) of this title, classified under section 360c(f)(2) of this title, or approved under section 360e of this title.

(f) Definitions

In this section:

(1) The term ''antimicrobial susceptibility testing device'' means a device that utilizes susceptibility test interpretive criteria to determine and report the in vitro susceptibility of certain microorganisms to a drug (or drugs).

(2) The term ''qualified infectious disease product'' means a qualified infectious disease product designated under section 355f(d) of this title.

(3) The term ''susceptibility test interpretive criteria'' means—

(A) one or more specific numerical values which characterize the susceptibility of bacteria or other microorganisms to the drug tested; and

(B) related categorizations of such susceptibility, including categorization of the drug as susceptible, intermediate, resistant, or such other term as the Secretary determines appropriate.

(4)(A) The term ''antimicrobial drug'' means, subject to subparagraph (B), a systemic antibacterial or antifungal drug that—

(i) is intended for human use in the treatment of a disease or condition caused by a bacterium or fungus;

(ii) may include a qualified infectious disease product designated under section 355f(d) of this title; and

(iii) is subject to section 353(b)(1) of this title.

(B) If provided by the Secretary through regulations, such term may include—

(i) drugs other than systemic antibacterial and antifungal drugs; and

(ii) biological products (as such term is defined in section 262 of title 42) to the extent such products exhibit antimicrobial activity.

(5) The term ''interpretive criteria standard'' means a compilation of susceptibility test interpretive criteria developed by a standard development organization that meets the criteria set forth in subsection (b)(2)(A)(i).

(g) Rule of construction

Nothing in this section shall be construed to—

(1) alter the standards of evidence under subsection (c) or (d) of section 355 of this title (including the substantial evidence standard under section 355(d) of this title) or under section 262 of title 42 (as applicable); or

(2) with respect to clearing devices under section 360(k) of this title, classifying devices under section 360c(f)(2) of this title, or approving devices under section 360e of this title—

(A) apply with respect to any drug, device, or biological product, in any context other than an antimicrobial drug and an antimicrobial susceptibility testing device that uses susceptibility test interpretive criteria to characterize and report the susceptibility of certain bacteria, fungi, or other microorganisms, as applicable, to such drug to reflect patient morbidity and mortality in accordance with this section; or

(B) unless specifically stated, have any effect on authorities provided under other sections of this chapter, including any regulations issued under such sections.

(June 25, 1938, ch. 675, §511A, as added Pub. L. 114–255, div. A, title III, §3044(a), Dec. 13, 2016, 130 Stat. 1114.)

Statutory Notes and Related Subsidiaries

CONSTRUCTION

Nothing in this section to be construed to restrict the prescribing of antimicrobial drugs or other products, including drugs approved under section 356(h) of this title, by health care professionals, or to limit the practice of health care, see section 3043 of Pub. L. 114–255, set out as a Construction of 2016 Amendments note under section 356 of this title.

REQUESTS FOR UPDATES TO INTERPRETIVE CRITERIA WEBSITE

Pub. L. 114–255, div. A, title III, §3044(d), Dec. 13, 2016, 130 Stat. 1121, provided that: ''Chapter 35 of title 44, United States Code, shall not apply to the collection of information from interested parties regarding updating the lists established under section 511A(b) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360a–2(b)] and posted on the Interpretive Criteria Website established under section 511A(c) [probably means section 511A(b)] of such Act.''

§ 360b. New animal drugs

(a) Unsafe new animal drugs and animal feed containing such drugs; conditions of safety; exemption of drugs for research; import tolerances

(1) A new animal drug shall, with respect to any particular use or intended use of such drug,

be deemed unsafe for purposes of section 351(a)(5) of this title and section 342(a)(2)(C)(ii) of this title unless—

(A) there is in effect an approval of an application filed pursuant to subsection (b) with respect to such use or intended use of such drug, and such drug, its labeling, and such use conform to such approved application;

(B) there is in effect a conditional approval of an application filed pursuant to section 360ccc of this title with respect to such use or intended use of such drug, and such drug, its labeling, and such use conform to such conditionally approved application;

(C) there is in effect an index listing pursuant to section 360ccc–1 of this title with respect to such use or intended use of such drug in a minor species, and such drug, its labeling, and such use conform to such index listing; or

(D) there is in effect an authorization pursuant to section 360bbb–3 of this title with respect to such use or intended use of such drug, and such drug, its labeling, and such use conform to any conditions of such authorization.

A new animal drug shall also be deemed unsafe for such purposes in the event of removal from the establishment of a manufacturer, packer, or distributor of such drug for use in the manufacture of animal feed in any State unless at the time of such removal such manufacturer, packer, or distributor has an unrevoked written statement from the consignee of such drug, or notice from the Secretary, to the effect that, with respect to the use of such drug in animal feed, such consignee (i) holds a license issued under subsection (m) and has in its possession current approved labeling for such drug in animal feed; or (ii) will, if the consignee is not a user of the drug, ship such drug only to a holder of a license issued under subsection (m).

(2) An animal feed bearing or containing a new animal drug shall, with respect to any particular use or intended use of such animal feed be deemed unsafe for purposes of section 351(a)(6) of this title unless—

(A) there is in effect—

(i) an approval of an application filed pursuant to subsection (b) with respect to such drug, as used in such animal feed, and such animal feed and its labeling, distribution, holding, and use conform to such approved application;

(ii) a conditional approval of an application filed pursuant to section 360ccc of this title with respect to such drug, as used in such animal feed, and such animal feed and its labeling, distribution, holding, and use conform to such conditionally approved application; or

(iii) an index listing pursuant to section 360ccc–1 of this title with respect to such drug, as used in such animal feed, and such animal feed and its labeling, distribution, holding, and use conform to such index listing; and

(B) such animal feed is manufactured at a site for which there is in effect a license issued pursuant to subsection (m)(1) to manufacture such animal feed.

(3) A new animal drug or an animal feed bearing or containing a new animal drug shall not be deemed unsafe for the purposes of section 351(a)(5) or (6) of this title if such article is for investigational use and conforms to the terms of an exemption in effect with respect thereto under subsection (j).

(4)(A) Except as provided in subparagraph (B), if an approval of an application filed under subsection (b) is in effect with respect to a particular use or intended use of a new animal drug, the drug shall not be deemed unsafe for the purposes of paragraph (1) and shall be exempt from the requirements of section 352(f) of this title with respect to a different use or intended use of the drug, other than a use in or on animal feed, if such use or intended use—

(i) is by or on the lawful written or oral order of a licensed veterinarian within the context of a veterinarian-client-patient relationship, as defined by the Secretary; and

(ii) is in compliance with regulations promulgated by the Secretary that establish the conditions for such different use or intended use.

The regulations promulgated by the Secretary under clause (ii) may prohibit particular uses of an animal drug and shall not permit such different use of an animal drug if the labeling of another animal drug that contains the same active ingredient and which is in the same dosage form and concentration provides for such different use.

(B) If the Secretary finds that there is a reasonable probability that a use of an animal drug authorized under subparagraph (A) may present a risk to the public health, the Secretary may—

(i) establish a safe level for a residue of an animal drug when it is used for such different use authorized by subparagraph (A); and

(ii) require the development of a practical, analytical method for the detection of residues of such drug above the safe level established under clause (i).

The use of an animal drug that results in residues exceeding a safe level established under clause (i) shall be considered an unsafe use of such drug under paragraph (1). Safe levels may be established under clause (i) either by regulation or order.

(C) The Secretary may by general regulation provide access to the records of veterinarians to ascertain any use or intended use authorized under subparagraph (A) that the Secretary has determined may present a risk to the public health.

(D) If the Secretary finds, after affording an opportunity for public comment, that a use of an animal drug authorized under subparagraph (A) presents a risk to the public health or that an analytical method required under subparagraph (B) has not been developed and submitted to the Secretary, the Secretary may, by order, prohibit any such use.

(5) If the approval of an application filed under section 355 of this title is in effect, the drug under such application shall not be deemed unsafe for purposes of paragraph (1) and shall be exempt from the requirements of section 352(f) of this title with respect to a use or intended use of the drug in animals if such use or intended use—

(A) is by or on the lawful written or oral order of a licensed veterinarian within the context of a veterinarian-client-patient relationship, as defined by the Secretary; and

(B) is in compliance with regulations promulgated by the Secretary that establish the conditions for the use or intended use of the drug in animals.

(6) For purposes of section 342(a)(2)(D)[1] of this title, a use or intended use of a new animal drug shall not be deemed unsafe under this section if the Secretary establishes a tolerance for such drug and any edible portion of any animal imported into the United States does not contain residues exceeding such tolerance. In establishing such tolerance, the Secretary shall rely on data sufficient to demonstrate that a proposed tolerance is safe based on similar food safety criteria used by the Secretary to establish tolerances for applications for new animal drugs filed under subsection (b)(1). The Secretary may consider and rely on data submitted by the drug manufacturer, including data submitted to appropriate regulatory authorities in any country where the new animal drug is lawfully used or data available from a relevant international organization, to the extent such data are not inconsistent with the criteria used by the Secretary to establish a tolerance for applications for new animal drugs filed under subsection (b)(1). For purposes of this paragraph, ''relevant international organization'' means the Codex Alimenterius[2] Commission or other international organization deemed appropriate by the Secretary. The Secretary may, under procedures specified by regulation, revoke a tolerance established under this paragraph if information demonstrates that the use of the new animal drug under actual use conditions results in food being imported into the United States with residues exceeding the tolerance or if scientific evidence shows the tolerance to be unsafe.

(b) Filing application for uses of new animal drug; contents; patent information; abbreviated application; presubmission conference

(1) Any person may file with the Secretary an application with respect to any intended use or uses of a new animal drug. Such person shall submit to the Secretary as a part of the application (A) full reports of investigations which have been made to show whether or not such drug is safe and effective for use; (B) a full list of the articles used as components of such drug; (C) a full statement of the composition of such drug; (D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (E) such samples of such drug and of the articles used as components thereof, of any animal feed for use in or on which such drug is intended, and of the edible portions or products (before or after slaughter) of animals to which such drug (directly or in or on animal feed) is intended to be administered, as the Secretary may require; (F) specimens of the labeling proposed to be used for such drug, or in case such drug is intended for use in animal feed, proposed labeling appropriate for such use, and specimens of the labeling for the drug to be manufactured, packed, or distributed by the applicant; (G) a description of practicable methods for determining the quantity, if any, of such drug in or on food, and any substance formed in or on food, because of its use; and (H) the proposed tolerance or withdrawal period or other use restrictions for such drug if any tolerance or withdrawal period or other use restrictions are required in order to assure that the proposed use of such drug will be safe. The applicant shall file with the application the patent number and the expiration date of any patent which claims the new animal drug for which the applicant filed the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If an application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, the applicant shall amend the application to include the information required by the preceding sentence. Upon approval of the application, the Secretary shall publish information submitted under the two preceding sentences.

(2) Any person may file with the Secretary an abbreviated application for the approval of a new animal drug. An abbreviated application shall contain the information required by subsection (n).

(3) Any person intending to file an application under paragraph (1), section 360ccc of this title, or a request for an investigational exemption under subsection (j) shall be entitled to one or more conferences prior to such submission to reach an agreement acceptable to the Secretary establishing a submission or an investigational requirement, which may include a requirement for a field investigation. A decision establishing a submission or an investigational requirement shall bind the Secretary and the applicant or requestor unless (A) the Secretary and the applicant or requestor mutually agree to modify the requirement, or (B) the Secretary by written order determines that a substantiated scientific requirement essential to the determination of safety or effectiveness of the animal drug involved has appeared after the conference. No later than 25 calendar days after each such conference, the Secretary shall provide a written order setting forth a scientific justification specific to the animal drug and intended uses under consideration if the agreement referred to in the first sentence requires more than one field investigation as being essential to provide substantial evidence of effectiveness for the intended uses of the drug. Nothing in this paragraph shall be construed as compelling the Secretary to require a field investigation.

(4) Beginning on October 1, 2018, all applications or submissions pursuant to this subsection shall be submitted by electronic means in such format as the Secretary may require.

[1] See References in Text note below.

[2] So in original. Probably should be ''Alimentarius''.

(c) Period for submission and approval of application; period for notice and expedition of hearing; period for issuance of order; abbreviated applications; withdrawal periods; effective date of approval; relationship to other applications; withdrawal or suspension of approval; bioequivalence; filing of additional patent information

(1) Within one hundred and eighty days after the filing of an application pursuant to subsection (b), or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either (A) issue an order approving the application if he then finds that none of the grounds for denying approval specified in subsection (d) applies, or (B) give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) on the question whether such application is approvable. If the applicant elects to accept the opportunity for a hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(2)(A) Subject to subparagraph (C), the Secretary shall approve an abbreviated application for a drug unless the Secretary finds—

(i) the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are inadequate to assure and preserve its identity, strength, quality, and purity;

(ii) the conditions of use prescribed, recommended, or suggested in the proposed labeling are not reasonably certain to be followed in practice or, except as provided in subparagraph (B), information submitted with the application is insufficient to show that each of the proposed conditions of use or similar limitations (whether in the labeling or published pursuant to subsection (i)) have been previously approved for the approved new animal drug referred to in the application;

(iii) information submitted with the application is insufficient to show that the active ingredients are the same as those of the approved new animal drug referred to in the application;

(iv)(I) if the application is for a drug whose active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed is the same as the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed of the approved new animal drug referred to in the application, information submitted in the application is insufficient to show that the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed is the same as that of the approved new animal drug, or

(II) if the application is for a drug whose active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed is different from that of the approved new animal drug referred to in the application, no petition to file an application for the drug with the different active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed was approved under subsection (n)(3);

(v) if the application was filed pursuant to the approval of a petition under subsection (n)(3), the application did not contain the information required by the Secretary respecting the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed which is not the same;

(vi) information submitted in the application is insufficient to show that the drug is bioequivalent to the approved new animal drug referred to in the application, or if the application is filed under a petition approved pursuant to subsection (n)(3), information submitted in the application is insufficient to show that the active ingredients of the new animal drug are of the same pharmacological or therapeutic class as the pharmacological or therapeutic class of the approved new animal drug and that the new animal drug can be expected to have the same therapeutic effect as the approved new animal drug when used in accordance with the labeling;

(vii) information submitted in the application is insufficient to show that the labeling proposed for the drug is the same as the labeling approved for the approved new animal drug referred to in the application except for changes required because of differences approved under a petition filed under subsection (n)(3), because of a different withdrawal period, or because the drug and the approved new animal drug are produced or distributed by different manufacturers;

(viii) information submitted in the application or any other information available to the Secretary shows that (I) the inactive ingredients of the drug are unsafe for use under the conditions prescribed, recommended, or suggested in the labeling proposed for the drug, (II) the composition of the drug is unsafe under such conditions because of the type or quantity of inactive ingredients included or the manner in which the inactive ingredients are included, or (III) in the case of a drug for food producing animals, the inactive ingredients of the drug or its composition may be unsafe with respect to human food safety;

(ix) the approval under subsection (b)(1) of the approved new animal drug referred to in the application filed under subsection (b)(2) has been withdrawn or suspended for grounds described in paragraph (1) of subsection (e), the Secretary has published a notice of a hearing to withdraw approval of the approved new animal drug for such grounds, the approval under this paragraph of the new animal drug for which the application under subsection (b)(2) was filed has been withdrawn or suspended under subparagraph (G) for such grounds, or the Secretary has determined that the approved new animal drug has been withdrawn from sale for safety or effectiveness reasons;

(x) the application does not meet any other requirement of subsection (n); or

(xi) the application contains an untrue statement of material fact.

(B) If the Secretary finds that a new animal drug for which an application is submitted under subsection (b)(2) is bioequivalent to the approved new animal drug referred to in such application and that residues of the new animal drug are consistent with the tolerances established for such approved new animal drug but at a withdrawal period which is different than the withdrawal period approved for such approved new animal drug, the Secretary may establish, on the basis of information submitted, such different withdrawal period as the withdrawal period for the new animal drug for purposes of the approval of such application for such drug.

(C) Within 180 days of the initial receipt of an application under subsection (b)(2) or within such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall approve or disapprove the application.

(D) The approval of an application filed under subsection (b)(2) shall be made effective on the last applicable date determined under the following:

(i) If the applicant only made a certification described in clause (i) or (ii) of subsection (n)(1)(G) or in both such clauses, the approval may be made effective immediately.

(ii) If the applicant made a certification described in clause (iii) of subsection (n)(1)(G), the approval may be made effective on the date certified under clause (iii).

(iii) If the applicant made a certification described in clause (iv) of subsection (n)(1)(G), the approval shall be made effective immediately unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of 45 days from the date the notice provided under subsection (n)(2)(B)(i) is received. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the 30 month period beginning on the date of the receipt of the notice provided under subsection (n)(2)(B) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that if before the expiration of such period—

(I) the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of the court decision,

(II) the court decides that such patent has been infringed, the approval shall be made effective on such date as the court orders under section 271(e)(4)(A) of title 35, or

(III) the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of such court decision.

In such an action, each of the parties shall reasonably cooperate in expediting the action. Until the expiration of 45 days from the date the notice made under subsection (n)(2)(B) is received, no action may be brought under section 2201 of title 28 for a declaratory judgment with respect to the patent. Any action brought under section 2201 of title 28 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(iv) If the application contains a certification described in clause (iv) of subsection (n)(1)(G) and is for a drug for which a previous application has been filed under this subsection containing such a certification, the application shall be made effective not earlier than 180 days after—

(I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or

(II) the date of a decision of a court in an action described in subclause (III)[3] holding the patent which is the subject of the certification to be invalid or not infringed,

whichever is earlier.

(E) If the Secretary decides to disapprove an application, the Secretary shall give the applicant notice of an opportunity for a hearing before the Secretary on the question of whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within 30 days after such notice, such hearing shall commence not more than 90 days after the expiration of such 30 days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within 90 days after the date fixed by the Secretary for filing final briefs.

(F)(i) If an application submitted under subsection (b)(1) for a drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under subsection (b)(1), is approved after November 16, 1988, no application may be submitted under subsection (b)(2) which refers to the drug for which the subsection (b)(1) application was submitted before the expiration of 5 years from the date of the approval of the application under subsection (b)(1), except that such an application may be submitted under subsection (b)(2) after the expiration of 4 years from the date of the approval of the subsection (b)(1) application if it contains a certification of patent invalidity or noninfringement described in clause (iv) of subsection (n)(1)(G). The approval of such an application shall be made effective in accordance with subparagraph (B) except that, if an action for patent infringement is commenced during the one-year period beginning 48 months after the date of the approval of the subsection (b) application, the 30 month period referred to in subparagraph (D)(iii) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

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[3] So in original. Probably should be ''clause (iii)(III)''.

(ii) If an application submitted under subsection (b)(1) for a drug, which includes an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) that has been approved in another application approved under such subsection, is approved after November 16, 1988, and if such application contains substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or, in the case of food producing animals, human food safety studies (other than bioequivalence studies or residue depletion studies, except residue depletion studies for minor uses or minor species) required for the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b)(2) for the conditions of approval of such drug in the subsection (b)(1) application effective before the expiration of 3 years from the date of the approval of the application under subsection (b)(1) for such drug.

(iii) If a supplement to an application approved under subsection (b)(1) is approved after November 16, 1988, and the supplement contains substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or, in the case of food producing animals, human food safety studies (other than bioequivalence studies or residue depletion studies, except residue depletion studies for minor uses or minor species) required for the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under subsection (b)(2) for a change approved in the supplement effective before the expiration of 3 years from the date of the approval of the supplement.

(iv) An applicant under subsection (b)(1) who comes within the provisions of clause (i) of this subparagraph as a result of an application which seeks approval for a use solely in non-food producing animals, may elect, within 10 days of receiving such approval, to waive clause (i) of this subparagraph, in which event the limitation on approval of applications submitted under subsection (b)(2) set forth in clause (ii) of this subparagraph shall be applicable to the subsection (b)(1) application.

(v) If an application (including any supplement to a new animal drug application) submitted under subsection (b)(1) for a new animal drug for a food-producing animal use, which includes an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) which has been the subject of a waiver under clause (iv) is approved after November 16, 1988, and if the application contains substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or human food safety studies (other than bioequivalence studies or residue depletion studies, except residue depletion studies for minor uses or minor species) required for the new approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application (including any supplement to such application) submitted under subsection (b)(2) for the new conditions of approval of such drug in the subsection (b)(1) application effective before the expiration of five years from the date of approval of the application under subsection (b)(1) for such drug. The provisions of this paragraph shall apply only to the first approval for a food-producing animal use for the same applicant after the waiver under clause (iv).

(G) If an approved application submitted under subsection (b)(2) for a new animal drug refers to a drug the approval of which was withdrawn or suspended for grounds described in paragraph (1) or (2) of subsection (e) or was withdrawn or suspended under this subparagraph or which, as determined by the Secretary, has been withdrawn from sale for safety or effectiveness reasons, the approval of the drug under this paragraph shall be withdrawn or suspended—

(i) for the same period as the withdrawal or suspension under subsection (e) or this subparagraph, or

(ii) if the approved new animal drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

(H) For purposes of this paragraph:

(i) The term ''bioequivalence'' means the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a new animal drug and becomes available at the site of drug action.

(ii) A new animal drug shall be considered to be bioequivalent to the approved new animal drug referred to in its application under subsection (n) if—

(I) the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the approved new animal drug referred to in the application when administered at the same dose of the active ingredient under similar experimental conditions in either a single dose or multiple doses;

(II) the extent of absorption of the drug does not show a significant difference from the extent of absorption of the approved new animal drug referred to in the application when administered at the same dose of the active ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the approved new animal drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective drug concentrations in use, and is considered scientifically insignificant for the drug in attaining the intended purposes of its use and preserving human food safety; or

(III) in any case in which the Secretary determines that the measurement of the rate and extent of absorption or excretion of the new animal drug in biological fluids is inappropriate or impractical, an appropriate acute pharmacological effects test or other test of the new animal drug and, when deemed scientifically necessary, of the approved new animal drug referred to in the

application in the species to be tested or in an appropriate animal model does not show a significant difference between the new animal drug and such approved new animal drug when administered at the same dose under similar experimental conditions.

If the approved new animal drug referred to in the application for a new animal drug under subsection (n) is approved for use in more than one animal species, the bioequivalency information described in subclauses (I), (II), and (III) shall be obtained for one species, or if the Secretary deems appropriate based on scientific principles, shall be obtained for more than one species. The Secretary may prescribe the dose to be used in determining bioequivalency under subclause (I), (II), or (III). To assure that the residues of the new animal drug will be consistent with the established tolerances for the approved new animal drug referred to in the application under subsection (b)(2) upon the expiration of the withdrawal period contained in the application for the new animal drug, the Secretary shall require bioequivalency data or residue depletion studies of the new animal drug or such other data or studies as the Secretary considers appropriate based on scientific principles. If the Secretary requires one or more residue studies under the preceding sentence, the Secretary may not require that the assay methodology used to determine the withdrawal period of the new animal drug be more rigorous than the methodology used to determine the withdrawal period for the approved new animal drug referred to in the application. If such studies are required and if the approved new animal drug, referred to in the application for the new animal drug for which such studies are required, is approved for use in more than one animal species, such studies shall be conducted for one species, or if the Secretary deems appropriate based on scientific principles, shall be conducted for more than one species.

(3) If the patent information described in subsection (b)(1) could not be filed with the submission of an application under subsection (b)(1) because the application was filed before the patent information was required under subsection (b)(1) or a patent was issued after the application was approved under such subsection, the holder of an approved application shall file with the Secretary the patent number and the expiration date of any patent which claims the new animal drug for which the application was filed or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If the holder of an approved application could not file patent information under subsection (b)(1) because it was not required at the time the application was approved, the holder shall file such information under this subsection not later than 30 days after November 16, 1988, and if the holder of an approved application could not file patent information under subsection (b)(1) because no patent had been issued when an application was filed or approved, the holder shall file such information under this subsection not later than 30 days after the date the patent involved is issued. Upon the submission of patent information under this subsection, the Secretary shall publish it.

(4) A drug manufactured in a pilot or other small facility may be used to demonstrate the safety and effectiveness of the drug and to obtain approval for the drug prior to manufacture of the drug in a larger facility, unless the Secretary makes a determination that a full scale production facility is necessary to ensure the safety or effectiveness of the drug.

(d) Grounds for refusing application; approval of application; factors; "substantial evidence" defined; combination drugs

(1) If the Secretary finds, after due notice to the applicant in accordance with subsection (c) and giving him an opportunity for a hearing, in accordance with said subsection, that—

(A) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b), do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof;

(B) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions;

(C) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity;

(D) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions;

(E) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof;

(F) upon the basis of information submitted to the Secretary as part of the application or any other information before the Secretary with respect to such drug, any use prescribed, recommended, or suggested in labeling proposed for such drug will result in a residue of such drug in excess of a tolerance found by the Secretary to be safe for such drug;

(G) the application failed to contain the patent information prescribed by subsection (b)(1);

(H) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; or

(I) such drug induces cancer when ingested by man or animal or, after tests which are appropriate for the evaluation of the safety of such drug, induces cancer in man or animal,

except that the foregoing provisions of this subparagraph shall not apply with respect to such drug if the Secretary finds that, under the conditions of use specified in proposed labeling and reasonably certain to be followed in practice (i) such drug will not adversely affect the animals for which it is intended, and (ii) no residue of such drug will be found (by methods of examination prescribed or approved by the Secretary by regulations, which regulations shall not be subject to subsections (c), (d), and (h)), in any edible portion of such animals after slaughter or in any food yielded by or derived from the living animals;

he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearings, the Secretary finds that subparagraphs (A) through (I) do not apply, he shall issue an order approving the application.

(2) In determining whether such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof, the Secretary shall consider, among other relevant factors, (A) the probable consumption of such drug and of any substance formed in or on food because of the use of such drug, (B) the cumulative effect on man or animal of such drug, taking into account any chemically or pharmacologically related substance, (C) safety factors which in the opinion of experts, qualified by scientific training and experience to evaluate the safety of such drugs, are appropriate for the use of animal experimentation data, and (D) whether the conditions of use prescribed, recommended, or suggested in the proposed labeling are reasonably certain to be followed in practice. Any order issued under this subsection refusing to approve an application shall state the findings upon which it is based.

(3) As used in this section, the term ''substantial evidence'' means evidence consisting of one or more adequate and well controlled investigations, such as—

(A) a study in a target species;

(B) a study in laboratory animals;

(C) any field investigation that may be required under this section and that meets the requirements of subsection (b)(3) if a presubmission conference is requested by the applicant;

(D) a bioequivalence study; or

(E) an in vitro study;

by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and reasonably be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.

(4) In a case in which an animal drug contains more than one active ingredient, or the labeling of the drug prescribes, recommends, or suggests use of the drug in combination with one or more other animal drugs, and the active ingredients or drugs intended for use in the combination have previously been separately approved pursuant to an application submitted under subsection (b)(1) for particular uses and conditions of use for which they are intended for use in the combination—

(A) the Secretary shall not issue an order under paragraph (1)(A), (1)(B), or (1)(D) refusing to approve the application for such combination on human food safety grounds unless the Secretary finds that the application fails to establish that—

(i) none of the active ingredients or drugs intended for use in the combination, respectively, at the longest withdrawal time of any of the active ingredients or drugs in the combination, respectively, exceeds its established tolerance; or

(ii) none of the active ingredients or drugs in the combination interferes with the methods of analysis for another of the active ingredients or drugs in the combination, respectively;

(B) the Secretary shall not issue an order under paragraph (1)(A), (1)(B), or (1)(D) refusing to approve the application for such combination on target animal safety grounds unless the Secretary finds that—

(i)(I) there is a substantiated scientific issue, specific to one or more of the active ingredients or animal drugs in the combination, that cannot adequately be evaluated based on information contained in the application for the combination (including any investigations, studies, or tests for which the applicant has a right of reference or use from the person by or for whom the investigations, studies, or tests were conducted); or

(II) there is a scientific issue raised by target animal observations contained in studies submitted to the Secretary as part of the application; and

(ii) based on the Secretary's evaluation of the information contained in the application with respect to the issues identified in clauses (i)(I) and (II), paragraph (1)(A), (B), or (D) apply;

(C) except in the case of a combination that contains a nontopical antibacterial ingredient or animal drug, the Secretary shall not issue an order under paragraph (1)(E) refusing to approve an application for a combination animal drug intended for use other than in animal feed or drinking water unless the Secretary finds that the application fails to demonstrate that—

(i) there is substantial evidence that any active ingredient or animal drug intended only for the same use as another active ingredient or animal drug in the combination makes a contribution to labeled effectiveness;

(ii) each active ingredient or animal drug intended for at least one use that is different from all other active ingredients or animal drugs used in the combination provides appropriate concurrent use for the intended target population; or

(iii) where based on scientific information the Secretary has reason to believe the active ingredients or animal drugs may be physically incompatible or have disparate

dosing regimens, such active ingredients or animal drugs are physically compatible or do not have disparate dosing regimens; and

(D) the Secretary shall not issue an order under paragraph (1)(E) refusing to approve an application for a combination animal drug intended for use in animal feed or drinking water unless the Secretary finds that the application fails to demonstrate that—

(i) there is substantial evidence that any active ingredient or animal drug intended only for the same use as another active ingredient or animal drug in the combination makes a contribution to the labeled effectiveness;

(ii) each of the active ingredients or animal drugs intended for at least one use that is different from all other active ingredients or animal drugs used in the combination provides appropriate concurrent use for the intended target population;

(iii) where a combination contains more than one nontopical antibacterial ingredient or animal drug, there is substantial evidence that each of the nontopical antibacterial ingredients or animal drugs makes a contribution to the labeled effectiveness, except that for purposes of this clause, antibacterial ingredient or animal drug does not include the ionophore or arsenical classes of animal drugs; or

(iv) where based on scientific information the Secretary has reason to believe the active ingredients or animal drugs intended for use in drinking water may be physically incompatible, such active ingredients or animal drugs intended for use in drinking water are physically compatible.

(5) In reviewing an application that proposes a change to add an intended use for a minor use or a minor species to an approved new animal drug application, the Secretary shall reevaluate only the relevant information in the approved application to determine whether the application for the minor use or minor species can be approved. A decision to approve the application for the minor use or minor species is not, implicitly or explicitly, a reaffirmation of the approval of the original application.

(e) Withdrawal of approval; grounds; immediate suspension upon finding imminent hazard to health of man or animals

(1) The Secretary shall, after due notice and opportunity for hearing to the applicant, issue an order withdrawing approval of an application filed pursuant to subsection (b) with respect to any new animal drug if the Secretary finds—

(A) that experience or scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved or the condition of use authorized under subsection (a)(4)(A);

(B) that new evidence not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved or that subparagraph (I) of paragraph (1) of subsection (d) applies to such drug;

(C) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that such drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof;

(D) the patent information prescribed by subsection (c)(3) was not filed within 30 days after the receipt of written notice from the Secretary specifying the failure to file such information;

(E) that the application contains any untrue statement of a material fact; or

(F) that the applicant has made any changes from the standpoint of safety or effectiveness beyond the variations provided for in the application unless he has supplemented the application by filing with the Secretary adequate information respecting all such changes and unless there is in effect an approval of the supplemental application. The supplemental application shall be treated in the same manner as the original application.

If the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the health of man or of the animals for which such drug is intended, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this sentence to suspend the approval of an application shall not be delegated.

(2) The Secretary may also, after due notice and opportunity for hearing to the applicant, issue an order withdrawing the approval of an application with respect to any new animal drug under this section if the Secretary finds—

(A) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports in accordance with a regulation or order under subsection (*l*), or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection;

(B) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or

(C) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved,

the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of.

(3) Any order under this subsection shall state the findings upon which it is based.

(f) Revocation of order refusing, withdrawing or suspending approval of application

Whenever the Secretary finds that the facts so require, he shall revoke any previous order under subsection (d), (e), or (m), or section 360ccc(c), (d), or (e) of this title refusing, withdrawing, or suspending approval of an application and shall approve such application or reinstate such approval, as may be appropriate.

(g) Service of orders

Orders of the Secretary issued under this section, or section 360ccc of this title (other than orders issuing, amending, or repealing regulations) shall be served (1) in person by any officer or employee of the department designated by the Secretary or (2) by mailing the order by registered mail or by certified mail addressed to the applicant or respondent at his last known address in the records of the Secretary.

(h) Appeal from order

An appeal may be taken by the applicant from an order of the Secretary refusing or withdrawing approval of an application filed under subsection (b) or (m) of this section. The provisions of subsection (h) of section 355 of this title shall govern any such appeal.

(i) Publication in Federal Register; effective date and revocation or suspension of regulation

When a new animal drug application filed pursuant to subsection (b) or section 360ccc of this title is approved, the Secretary shall by notice, which upon publication shall be effective as a regulation, publish in the Federal Register the name and address of the applicant and the conditions and indications of use of the new animal drug covered by such application, including any tolerance and withdrawal period or other use restrictions and, if such new animal drug is intended for use in animal feed, appropriate purposes and conditions of use (including special labeling requirements and any requirement that an animal feed bearing or containing the new animal drug be limited to use under the professional supervision of a licensed veterinarian) applicable to any animal feed for use in which such drug is approved, and such other information, upon the basis of which such application was approved, as the Secretary deems necessary to assure the safe and effective use of such drug. Upon withdrawal of approval of such new animal drug application or upon its suspension or upon failure to renew a conditional approval under section 360ccc of this title, the Secretary shall forthwith revoke or suspend, as the case may be, the regulation published pursuant to this subsection (i) insofar as it is based on the approval of such application.

(j) Exemption of drugs for research; discretionary and mandatory conditions

To the extent consistent with the public health, the Secretary shall promulgate regulations for exempting from the operation of this section new animal drugs, and animal feeds bearing or containing new animal drugs, intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of animal drugs. Such regulations may, in the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such article, of data (including but not limited to analytical reports by investigators) obtained as a result of such investigational use of such article, as the Secretary finds will enable him to evaluate the safety and effectiveness of such article in the event of the filing of an application pursuant to this section. Such regulations, among other things, shall set forth the conditions (if any) upon which animals treated with such articles, and any products of such animals (before or after slaughter), may be marketed for food use.

(k) Food containing new animal drug considered unadulterated while approval of application for such drug is effective

While approval of an application for a new animal drug is effective, a food shall not, by reason of bearing or containing such drug or any substance formed in or on the food because of its use in accordance with such application (including the conditions and indications of use prescribed pursuant to subsection (i)), be considered adulterated within the meaning of clause (1) of section 342(a) of this title.

***(l)* Records and reports; required information; regulations and orders; examination of data; access to records**

(1) In the case of any new animal drug for which an approval of an application filed pursuant to subsection (b) or section 360ccc of this title is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to experience, including experience with uses authorized under subsection (a)(4)(A), and other data or information, received or otherwise obtained by such applicant with respect to such drug, or with respect to animal feeds bearing or containing such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) or subsection (m)(4) of this section. Such regulation or order shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulation or order is applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this subsection to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all

reasonable times to have access to and copy and verify such records.

(3)(A) In the case of each new animal drug described in paragraph (1) that contains an antimicrobial active ingredient, the sponsor of the drug shall submit an annual report to the Secretary on the amount of each antimicrobial active ingredient in the drug that is sold or distributed for use in food-producing animals, including information on any distributor-labeled product.

(B) Each report under this paragraph shall specify the amount of each antimicrobial active ingredient—

(i) by container size, strength, and dosage form;

(ii) by quantities distributed domestically and quantities exported; and

(iii) by dosage form, including, for each such dosage form, a listing of the target animals, indications, and production classes that are specified on the approved label of the product.

(C) Each report under this paragraph shall—

(i) be submitted not later than March 31 each year;

(ii) cover the period of the preceding calendar year; and

(iii) include separate information for each month of such calendar year.

(D) The Secretary may share information reported under this paragraph with the Antimicrobial Resistance Task Force established under section 247d–5 of title 42.

(E) The Secretary shall make summaries of the information reported under this paragraph publicly available, except that—

(i) the summary data shall be reported by antimicrobial class, and no class with fewer than 3 distinct sponsors of approved applications shall be independently reported; and

(ii) the data shall be reported in a manner consistent with protecting both national security and confidential business information.

(m) Feed mill licenses

(1) Any person may file with the Secretary an application for a license to manufacture animal feeds bearing or containing new animal drugs. Such person shall submit to the Secretary as part of the application (A) a full statement of the business name and address of the specific facility at which the manufacturing is to take place and the facility's registration number, (B) the name and signature of the responsible individual or individuals for that facility, (C) a certification that the animal feeds bearing or containing new animal drugs are manufactured and labeled in accordance with the applicable regulations published pursuant to subsection (i) or for indexed new animal drugs in accordance with the index listing published pursuant to section 360ccc–1(e)(2) of this title and the labeling requirements set forth in section 360ccc–1(h) of this title, and (D) a certification that the methods used in, and the facilities and controls used for, manufacturing, processing, packaging, and holding such animal feeds are in conformity with current good manufacturing practice as described in section 351(a)(2)(B) of this title.

(2) Within 90 days after the filing of an application pursuant to paragraph (1), or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall (A) issue an order approving the application if the Secretary then finds that none of the grounds for denying approval specified in paragraph (3) applies, or (B) give the applicant notice of an opportunity for a hearing before the Secretary under paragraph (3) on the question whether such application is approvable. The procedure governing such a hearing shall be the procedure set forth in the last two sentences of subsection (c)(1).

(3) If the Secretary, after due notice to the applicant in accordance with paragraph (2) and giving the applicant an opportunity for a hearing in accordance with such paragraph, finds, on the basis of information submitted to the Secretary as part of the application, on the basis of a preapproval inspection, or on the basis of any other information before the Secretary—

(A) that the application is incomplete, false, or misleading in any particular;

(B) that the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such animal feed are inadequate to preserve the identity, strength, quality, and purity of the new animal drug therein; or

(C) that the facility manufactures animal feeds bearing or containing new animal drugs in a manner that does not accord with the specifications for manufacture or labels animal feeds bearing or containing new animal drugs in a manner that does not accord with the conditions or indications of use that are published pursuant to subsection (i) or an index listing pursuant to section 360ccc–1(e) of this title,

the Secretary shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that subparagraphs (A) through (C) do not apply, the Secretary shall issue an order approving the application. An order under this subsection approving an application for a license to manufacture animal feeds bearing or containing new animal drugs shall permit a facility to manufacture only those animal feeds bearing or containing new animal drugs for which there are in effect regulations pursuant to subsection (i) or an index listing pursuant to section 360ccc–1(e) of this title relating to the use of such drugs in or on such animal feed.

(4)(A) The Secretary shall, after due notice and opportunity for hearing to the applicant, revoke a license to manufacture animal feeds bearing or containing new animal drugs under this subsection if the Secretary finds—

(i) that the application for such license contains any untrue statement of a material fact; or

(ii) that the applicant has made changes that would cause the application to contain any untrue statements of material fact or that would affect the safety or effectiveness of the animal feeds manufactured at the facility unless the applicant has supplemented the application by filing with the Secretary adequate information respecting all such changes and unless there is in effect an approval of the supplemental application.

If the Secretary (or in the Secretary's absence the officer acting as the Secretary) finds that there is an imminent hazard to the health of humans or of the animals for which such animal feed is intended, the Secretary may suspend the license immediately, and give the applicant prompt notice of the action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this sentence shall not be delegated.

(B) The Secretary may also, after due notice and opportunity for hearing to the applicant, revoke a license to manufacture animal feed under this subsection if the Secretary finds—

(i) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports in accordance with a regulation or order under paragraph (5)(A) of this subsection or section 354(a)(3)(A) of this title, or the applicant has refused to permit access to, or copying or verification of, such records as required by subparagraph (B) of such paragraph or section 354(a)(3)(B) of this title;

(ii) that on the basis of new information before the Secretary, evaluated together with the evidence before the Secretary when such license was issued, the methods used in, or the facilities and controls used for, the manufacture, processing, packing, and holding of such animal feed are inadequate to assure and preserve the identity, strength, quality, and purity of the new animal drug therein, and were not made adequate within a reasonable time after receipt of written notice from the Secretary, specifying the matter complained of;

(iii) that on the basis of new information before the Secretary, evaluated together with the evidence before the Secretary when such license was issued, the labeling of any animal feeds, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or

(iv) that on the basis of new information before the Secretary, evaluated together with the evidence before the Secretary when such license was issued, the facility has manufactured, processed, packed, or held animal feed bearing or containing a new animal drug adulterated under section 351(a)(6) of this title and the facility did not discontinue the manufacture, processing, packing, or holding of such animal feed within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of.

(C) The Secretary may also revoke a license to manufacture animal feeds under this subsection if an applicant gives notice to the Secretary of intention to discontinue the manufacture of all animal feed covered under this subsection and waives an opportunity for a hearing on the matter.

(D) Any order under this paragraph shall state the findings upon which it is based.

(5) When a license to manufacture animal feeds bearing or containing new animal drugs has been issued—

(A) the applicant shall establish and maintain such records, and make such reports to the Secretary, or (at the option of the Secretary) to the appropriate person or persons holding an approved application filed under subsection (b), as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) or paragraph (4); and

(B) every person required under this subsection to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

(6) To the extent consistent with the public health, the Secretary may promulgate regulations for exempting from the operation of this subsection facilities that manufacture, process, pack, or hold animal feeds bearing or containing new animal drugs.

(n) Abbreviated applications for new animal drugs; contents, filing, etc.; lists of approved drugs

(1) An abbreviated application for a new animal drug shall contain—

(A)(i) except as provided in clause (ii), information to show that the conditions of use or similar limitations (whether in the labeling or published pursuant to subsection (i)) prescribed, recommended, or suggested in the labeling proposed for the new animal drug have been previously approved for a new animal drug listed under paragraph (4) (hereinafter in this subsection referred to as an ''approved new animal drug''), and

(ii) information to show that the withdrawal period at which residues of the new animal drug will be consistent with the tolerances established for the approved new animal drug is the same as the withdrawal period previously established for the approved new animal drug or, if the withdrawal period is proposed to be different, information showing that the residues of the new animal drug at the proposed different withdrawal period will be consistent with the tolerances established for the approved new animal drug;

(B)(i) information to show that the active ingredients of the new animal drug are the same as those of the approved new animal drug, and

(ii) if the approved new animal drug has more than one active ingredient, and if one of the active ingredients of the new animal drug is different from one of the active ingredients of the approved new animal drug and the application is filed pursuant to the approval of a petition filed under paragraph (3)—

(I) information to show that the other active ingredients of the new animal drug are the same as the active ingredients of the approved new animal drug,

(II) information to show either that the different active ingredient is an active ingre-

dient of another approved new animal drug or of an animal drug which does not meet the requirements of section 321(v) of this title, and

(III) such other information respecting the different active ingredients as the Secretary may require;

(C)(i) if the approved new animal drug is permitted to be used with one or more animal drugs in animal feed, information to show that the proposed uses of the new animal drug with other animal drugs in animal feed are the same as the uses of the approved new animal drug, and

(ii) if the approved new animal drug is permitted to be used with one or more other animal drugs in animal feed, and one of the other animal drugs proposed for use with the new animal drug in animal feed is different from one of the other animal drugs permitted to be used in animal feed with the approved new animal drug, and the application is filed pursuant to the approval of a petition filed under paragraph (3)—

(I) information to show either that the different animal drug proposed for use with the approved new animal drug in animal feed is an approved new animal drug permitted to be used in animal feed or does not meet the requirements of section 321(v) of this title when used with another animal drug in animal feed,

(II) information to show that other animal drugs proposed for use with the new animal drug in animal feed are the same as the other animal drugs permitted to be used with the approved new animal drug, and

(III) such other information respecting the different animal drug or combination with respect to which the petition was filed as the Secretary may require,

(D) information to show that the route of administration, the dosage form, and the strength of the new animal drug are the same as those of the approved new animal drug or, if the route of administration, the dosage form, or the strength of the new animal drug is different and the application is filed pursuant to the approval of a petition filed under paragraph (3), such information respecting the route of administration, dosage form, or strength with respect to which the petition was filed as the Secretary may require;

(E) information to show that the new animal drug is bioequivalent to the approved new animal drug, except that if the application is filed pursuant to the approval of a petition filed under paragraph (3) for the purposes described in subparagraph (B) or (C), information to show that the active ingredients of the new animal drug are of the same pharmacological or therapeutic class as the pharmacological or therapeutic class of the approved new animal drug and that the new animal drug can be expected to have the same therapeutic effect as the approved new animal drug when used in accordance with the labeling;

(F) information to show that the labeling proposed for the new animal drug is the same as the labeling approved for the approved new animal drug except for changes required because of differences approved under a petition filed under paragraph (3), because of a different withdrawal period, or because the new animal drug and the approved new animal drug are produced or distributed by different manufacturers;

(G) the items specified in clauses (B) through (F) of subsection (b)(1);

(H) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the approved new animal drug or which claims a use for such approved new animal drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b)(1) or (c)(3)—

(i) that such patent information has not been filed,

(ii) that such patent has expired,

(iii) of the date on which such patent will expire, or

(iv) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new animal drug for which the application is filed; and

(I) if with respect to the approved new animal drug information was filed under subsection (b)(1) or (c)(3) for a method of use patent which does not claim a use for which the applicant is seeking approval of an application under subsection (c)(2), a statement that the method of use patent does not claim such a use.

The Secretary may not require that an abbreviated application contain information in addition to that required by subparagraphs (A) through (I).

(2)(A) An applicant who makes a certification described in paragraph (1)(G)(iv) shall include in the application a statement that the applicant will give the notice required by subparagraph (B) to—

(i) each owner of the patent which is the subject of the certification or the representative of such owner designated to receive such notice, and

(ii) the holder of the approved application under subsection (c)(1) for the drug which is claimed by the patent or a use of which is claimed by the patent or the representative of such holder designated to receive such notice.

(B) The notice referred to in subparagraph (A) shall state that an application, which contains data from bioequivalence studies, has been filed under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of such drug before the expiration of the patent referred to in the certification. Such notice shall include a detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid or will not be infringed.

(C) If an application is amended to include a certification described in paragraph (1)(G)(iv), the notice required by subparagraph (B) shall be given when the amended application is filed.

(3) If a person wants to submit an abbreviated application for a new animal drug—

(A) whose active ingredients, route of administration, dosage form, or strength differ from that of an approved new animal drug, or

(B) whose use with other animal drugs in animal feed differs from that of an approved new animal drug,

such person shall submit a petition to the Secretary seeking permission to file such an application. The Secretary shall approve a petition for a new animal drug unless the Secretary finds that—

(C) investigations must be conducted to show the safety and effectiveness, in animals to be treated with the drug, of the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed which differ from the approved new animal drug, or

(D) investigations must be conducted to show the safety for human consumption of any residues in food resulting from the proposed active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed for the new animal drug which is different from the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed of the approved new animal drug.

The Secretary shall approve or disapprove a petition submitted under this paragraph within 90 days of the date the petition is submitted.

(4)(A)(i) Within 60 days of November 16, 1988, the Secretary shall publish and make available to the public a list in alphabetical order of the official and proprietary name of each new animal drug which has been approved for safety and effectiveness before November 16, 1988.

(ii) Every 30 days after the publication of the first list under clause (i) the Secretary shall revise the list to include each new animal drug which has been approved for safety and effectiveness under subsection (c) during the 30 day period.

(iii) When patent information submitted under subsection (b)(1) or (c)(3) respecting a new animal drug included on the list is to be published by the Secretary, the Secretary shall, in revisions made under clause (ii), include such information for such drug.

(B) A new animal drug approved for safety and effectiveness before November 16, 1988, or approved for safety and effectiveness under subsection (c) shall, for purposes of this subsection, be considered to have been published under subparagraph (A) on the date of its approval or November 16, 1988, whichever is later.

(C) If the approval of a new animal drug was withdrawn or suspended under subsection (c)(2)(G) or for grounds described in subsection (e) or if the Secretary determines that a drug has been withdrawn from sale for safety or effectiveness reasons, it may not be published in the list under subparagraph (A) or, if the withdrawal or suspension occurred after its publication in such list, it shall be immediately removed from such list—

(i) for the same period as the withdrawal or suspension under subsection (c)(2)(G) or (e), or

(ii) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

A notice of the removal shall be published in the Federal Register.

(5) If an application contains the information required by clauses (A), (G), and (H) of subsection (b)(1) and such information—

(A) is relied on by the applicant for the approval of the application, and

(B) is not information derived either from investigations, studies, or tests conducted by or for the applicant or for which the applicant had obtained a right of reference or use from the person by or for whom the investigations, studies, or tests were conducted,

such application shall be considered to be an application filed under subsection (b)(2).

(*o*) "Patent" defined

For purposes of this section, the term ''patent'' means a patent issued by the United States Patent and Trademark Office.

(p) Safety and effectiveness data

(1) Safety and effectiveness data and information which has been submitted in an application filed under subsection (b)(1) or section 360ccc(a) of this title for a drug and which has not previously been disclosed to the public shall be made available to the public, upon request, unless extraordinary circumstances are shown—

(A) if no work is being or will be undertaken to have the application approved,

(B) if the Secretary has determined that the application is not approvable and all legal appeals have been exhausted,

(C) if approval of the application under subsection (c) is withdrawn and all legal appeals have been exhausted,

(D) if the Secretary has determined that such drug is not a new drug, or

(E) upon the effective date of the approval of the first application filed under subsection (b)(2) which refers to such drug or upon the date upon which the approval of an application filed under subsection (b)(2) which refers to such drug could be made effective if such an application had been filed.

(2) Any request for data and information pursuant to paragraph (1) shall include a verified statement by the person making the request that any data or information received under such paragraph shall not be disclosed by such person to any other person—

(A) for the purpose of, or as part of a plan, scheme, or device for, obtaining the right to make, use, or market, or making, using, or marketing, outside the United States, the drug identified in the application filed under subsection (b)(1) or section 360ccc(a) of this title, and

(B) without obtaining from any person to whom the data and information are disclosed an identical verified statement, a copy of which is to be provided by such person to the Secretary, which meets the requirements of this paragraph.

(q) Date of approval in the case of recommended controls under the CSA

(1) In general

In the case of an application under subsection (b) with respect to a drug for which the Secretary provides notice to the sponsor that the Secretary intends to issue a scientific and medical evaluation and recommend controls under the Controlled Substances Act [21 U.S.C. 801 et seq.], approval of such application shall not take effect until the interim final rule controlling the drug is issued in accordance with section 201(j) of the Controlled Substances Act [21 U.S.C. 811(j)].

(2) Date of approval

For purposes of this section, with respect to an application described in paragraph (1), the term ''date of approval'' shall mean the later of—

(A) the date an application under subsection (b) is approved under subsection (c); or

(B) the date of issuance of the interim final rule controlling the drug.

(June 25, 1938, ch. 675, §512, as added Pub. L. 90–399, §101(b), July 13, 1968, 82 Stat. 343; amended Pub. L. 100–670, title I, §§101, 102, 104, 107(a)(2), Nov. 16, 1988, 102 Stat. 3971, 3981, 3982, 3984; Pub. L. 102–108, §2(e), Aug. 17, 1991, 105 Stat. 550; Pub. L. 103–80, §3(r), Aug. 13, 1993, 107 Stat. 777; Pub. L. 103–396, §2(a), (b)(2), (3), Oct. 22, 1994, 108 Stat. 4153, 4154; Pub. L. 104–250, §§2(a)–(d), 3, 4, 5(c), 6(a), (b), Oct. 9, 1996, 110 Stat. 3151–3153, 3155–3157; Pub. L. 105–115, title I, §124(b), Nov. 21, 1997, 111 Stat. 2325; Pub. L. 105–277, div. A, §101(a) [title VII, §737], Oct. 21, 1998, 112 Stat. 2681, 2681–30; Pub. L. 106–113, div. B, §1000(a)(9) [title IV, §4732(b)(11)], Nov. 29, 1999, 113 Stat. 1536, 1501A–584; Pub. L. 108–282, title I, §102(b)(2), (3), (5)(I)–(S), Aug. 2, 2004, 118 Stat. 892, 903, 904; Pub. L. 110–316, title I, §105(a), Aug. 14, 2008, 122 Stat. 3513; Pub. L. 114–89, §2(a)(3)(A), Nov. 25, 2015, 129 Stat. 699; Pub. L. 114–255, div. A, title III, §3088(b), Dec. 13, 2016, 130 Stat. 1149; Pub. L. 115–234, title III, §301(a), Aug. 14, 2018, 132 Stat. 2436; Pub. L. 117–9, §1(a)(2), Apr. 23, 2021, 135 Stat. 257.)

Editorial Notes

REFERENCES IN TEXT

Section 342(a)(2) of this title, referred to in subsec. (a)(6), was amended by Pub. L. 104–170, title IV, §404, Aug. 3, 1996, 110 Stat. 1514, and, as so amended, no longer contains a subcl. (D). See section 342(a)(2)(C)(ii) of this title.

The Controlled Substances Act, referred to in subsec. (q)(1), is title II of Pub. L. 91–513, Oct. 27, 1970, 84 Stat. 1242, which is classified principally to subchapter I (§801 et seq.) of chapter 13 of this title. For complete classification of this Act to the Code, see Short Title note set out under section 801 of this title and Tables.

AMENDMENTS

2021—Subsec. (c)(2)(F). Pub. L. 117–9 substituted ''active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations))'' for ''active ingredient (including any ester or salt of the active ingredient)'' in cls. (i), (ii), and (v).

2018—Subsec. (b)(4). Pub. L. 115–234 added par. (4).

2016—Subsec. (a)(1)(D). Pub. L. 114–255 added subpar. (D).

2015—Subsec. (q). Pub. L. 114–89 added subsec. (q).

2008—Subsec. (*l*)(3). Pub. L. 110–316 added par. (3).

2004—Subsec. (a)(1), (2). Pub. L. 108–282, §102(b)(5)(I), added pars. (1) and (2) and struck out former pars. (1) and (2) which deemed as unsafe new animal drugs and animal feed bearing or containing a new animal drug which did not have in effect certain approvals.

Subsec. (b)(3). Pub. L. 108–282, §102(b)(5)(J), substituted ''under paragraph (1), section 360ccc of this title, or a request for an investigational exemption under subsection (j)'' for ''under paragraph (1) or a request for an investigational exemption under subsection (j)''.

Subsec. (c)(2)(F)(ii), (iii), (v). Pub. L. 108–282, §102(b)(2), substituted ''(other than bioequivalence studies or residue depletion studies, except residue depletion studies for minor uses or minor species)'' for ''(other than bioequivalence or residue studies)''.

Subsec. (d)(4). Pub. L. 108–282, §102(b)(5)(K), substituted ''have previously been separately approved pursuant to an application submitted under subsection (b)(1)'' for ''have previously been separately approved'' in introductory provisions.

Subsec. (d)(5). Pub. L. 108–282, §102(b)(3), added par. (5).

Subsec. (f). Pub. L. 108–282, §102(b)(5)(L), substituted ''subsection (d), (e), or (m), or section 360ccc(c), (d), or (e) of this title'' for ''subsection (d), (e), or (m)''.

Subsec. (g). Pub. L. 108–282, §102(b)(5)(M), substituted ''this section, or section 360ccc of this title'' for ''this section''.

Subsec. (i). Pub. L. 108–282, §102(b)(5)(N), substituted ''subsection (b) or section 360ccc of this title'' for ''subsection (b)'' and inserted ''or upon failure to renew a conditional approval under section 360ccc of this title'' after ''or upon its suspension''.

Subsec. (*l*)(1). Pub. L. 108–282, §102(b)(5)(O), substituted ''subsection (b) or section 360ccc of this title'' for ''subsection (b)''.

Subsec. (m)(1)(C). Pub. L. 108–282, §102(b)(5)(P), substituted ''applicable regulations published pursuant to subsection (i) or for indexed new animal drugs in accordance with the index listing published pursuant to section 360ccc–1(e)(2) of this title and the labeling requirements set forth in section 360ccc–1(h) of this title'' for ''applicable regulations published pursuant to subsection (i)''.

Subsec. (m)(3). Pub. L. 108–282, §102(b)(5)(Q), inserted ''or an index listing pursuant to section 360ccc–1(e) of this title'' after ''subsection (i)'' in subpar. (C) and concluding provisions.

Subsec. (p)(1), (2)(A). Pub. L. 108–282, §102(b)(5)(R), (S), substituted ''subsection (b)(1) or section 360ccc(a) of this title'' for ''subsection (b)(1)''.

1999—Subsec. (*o*). Pub. L. 106–113 substituted ''United States Patent and Trademark Office'' for ''Patent and Trademark Office of the Department of Commerce''.

1998—Subsec. (d)(4)(D)(iii). Pub. L. 105–277 inserted before semicolon '', except that for purposes of this clause, antibacterial ingredient or animal drug does not include the ionophore or arsenical classes of animal drugs''.

1997—Subsec. (c)(4). Pub. L. 105–115 added par. (4).

1996—Subsec. (a)(1). Pub. L. 104–250, §6(a), amended par. (1) generally. Prior to amendment, par. (1) read as follows: ''A new animal drug shall, with respect to any particular use or intended use of such drug, be deemed unsafe for the purposes of section 351(a)(5) and section 342(a)(2)(D) of this title unless—

''(A) there is in effect an approval of an application filed pursuant to subsection (b) of this section with respect to such use or intended use of such drug, and

''(B) such drug, its labeling, and such use conform to such approved application.

A new animal drug shall also be deemed unsafe for such purposes in the event of removal from the establishment of a manufacturer, packer, or distributor of such drug for use in the manufacture of animal feed in any

State unless at the time of such removal such manufacturer, packer, or distributor has an unrevoked written statement from the consignee of such drug, or notice from the Secretary, to the effect that, with respect to the use of such drug in animal feed, such consignee—

''(i) is the holder of an approved application under subsection (m) of this section; or

''(ii) will, if the consignee is not a user of the drug, ship such drug only to a holder of an approved application under subsection (m) of this section.''

Subsec. (a)(2). Pub. L. 104–250, §6(a), amended par. (2) generally. Prior to amendment, par. (2) read as follows: ''An animal feed bearing or containing a new animal drug shall, with respect to any particular use or intended use of such animal feed, be deemed unsafe for the purposes of section 351(a)(6) of this title unless—

''(A) there is in effect an approval of an application filed pursuant to subsection (b) of this section with respect to such drugs, as used in such animal feed,

''(B) there is in effect an approval of an application pursuant to subsection (m)(1) of this section with respect to such animal feed, and

''(C) such animal feed, its labeling, and such use conform to the conditions and indications of use published pursuant to subsection (i) of this section and to the application with respect thereto approved under subsection (m) of this section.''

Subsec. (a)(6). Pub. L. 104–250, §4, added par. (6).

Subsec. (b)(3). Pub. L. 104–250, §2(d), added par. (3).

Subsec. (c)(2)(F)(ii), (iii). Pub. L. 104–250, §2(b)(1), substituted ''substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or,'' for ''reports of new clinical or field investigations (other than bioequivalence or residue studies) and,'' and ''required for the approval'' for ''essential to the approval''.

Subsec. (c)(2)(F)(v). Pub. L. 104–250, §2(b)(2), substituted ''clause (iv)'' for ''subparagraph (B)(iv)'' in two places, ''substantial evidence of the effectiveness of the drug involved, any studies of animal safety,'' for ''reports of clinical or field investigations'' and ''required for the new approval'' for ''essential to the new approval''.

Subsec. (d)(1)(F). Pub. L. 104–250, §3, amended subpar. (F) generally. Prior to amendment, subpar. (F) read as follows: ''upon the basis of the information submitted to him as part of the application or any other information before him with respect to such drug, the tolerance limitation proposed, if any, exceeds that reasonably required to accomplish the physical or other technical effect for which the drug is intended;''.

Subsec. (d)(3). Pub. L. 104–250, §2(a), amended par. (3) generally. Prior to amendment, par. (3) read as follows: ''As used in this subsection and subsection (e) of this section, the term 'substantial evidence' means evidence consisting of adequate and well-controlled investigations, including field investigation, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and reasonably be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.''

Subsec. (d)(4). Pub. L. 104–250, §2(c), added par. (4).

Subsec. (i). Pub. L. 104–250, §5(c), inserted ''and any requirement that an animal feed bearing or containing the new animal drug be limited to use under the professional supervision of a licensed veterinarian'' after ''(including special labeling requirements''.

Subsec. (m). Pub. L. 104–250, §6(b), amended subsec. (m) generally, substituting provisions relating to application for feed mill licenses, including approval, refusal, revocation, and suspension of such licenses, and provisions for record and reporting requirements for, as well as exemption from, such licenses, for provisions relating to application for uses of animal feed containing new animal drug, including required contents, approval, refusal, and withdrawal of approval or suspension of such usage applications, and provisions for record and reporting requirements of such usage applications.

1994—Subsec. (a)(4), (5). Pub. L. 103–396, §2(a), added pars. (4) and (5).

Subsec. (e)(1)(A). Pub. L. 103–396, §2(b)(2), inserted before semicolon at end ''or the condition of use authorized under subsection (a)(4)(A)''.

Subsec. (*l*)(1). Pub. L. 103–396, §2(b)(3), substituted ''relating to experience, including experience with uses authorized under subsection (a)(4)(A),'' for ''relating to experience''.

1993—Subsec. (c)(2)(A)(ii). Pub. L. 103–80, §3(r)(1), inserted ''in'' after ''except as provided''.

Subsec. (c)(2)(F)(i). Pub. L. 103–80, §3(r)(2), substituted ''subparagraph (D)(iii)'' for ''subparagraph (C)(iii)''.

Subsec. (c)(2)(H)(ii). Pub. L. 103–80, §3(r)(3), substituted ''subclauses'' for ''subclause'' after ''bioequivalency information described in'' in concluding provisions.

Subsec. (d)(1). Pub. L. 103–80, §3(r)(4), substituted ''subparagraphs (A) through (I)'' for ''subparagraphs (A) through (G)'' in concluding provisions.

Subsec. (n)(1). Pub. L. 103–80, §3(r)(5), substituted ''section 321(v) of this title'' for ''section 321(w) of this title'' in subpars. (B)(ii)(II) and (C)(ii)(I) and substituted ''through (I)'' for ''through (H)'' in concluding provisions.

1991—Subsec. (e)(1)(B). Pub. L. 102–108 substituted ''(I)'' for ''(H)''.

1988—Subsec. (a)(1)(C). Pub. L. 100–670, §107(a)(2), struck out subpar. (C) which read as follows: ''in the case of a new animal drug subject to subsection (n) of this section and not exempted therefrom by regulations it is from a batch with respect to which a certificate or release issued pursuant to subsection (n) of this section is in effect with respect to such drug.''

Subsec. (b). Pub. L. 100–670, §§101(a), 102(a), designated existing provisions as par. (1), redesignated cls. (1) to (8) as cls. (A) to (H), respectively, added par. (2), and inserted provisions at end of par. (1) which require applicant to file with application, patent number and expiration date of any patent which claims new animal drug, to amend application to include such information if patent which claims such drug or method of using such drug is issued after filing date but before approval of application, and to publish such information upon approval.

Subsec. (c). Pub. L. 100–670, §§101(c), 102(b)(1), designated existing provisions as par. (1), redesignated cls. (1) and (2) as cls. (A) and (B), respectively, and added pars. (2) and (3).

Subsec. (d)(1). Pub. L. 100–670, §102(b)(3), substituted ''(G)'' for ''(H)'' in last sentence.

Subsec. (d)(1)(G) to (I). Pub. L. 100–670, §102(b)(2), added subpar. (G) and redesignated former subpars. (G) and (H) as (H) and (I), respectively.

Subsec. (e)(1)(D) to (F). Pub. L. 100–670, §102(b)(4), added subpar. (D) and redesignated former subpars. (D) and (E) as (E) and (F), respectively.

Subsecs. (n), (*o*). Pub. L. 100–670, §101(b), added subsecs. (n) and (*o*) and struck out former subsec. (n) which related to certification of new drugs containing penicillin, streptomycin, chlortetracycline, chloramphenicol, or bacitracin, and release prior to certification.

Subsec. (p). Pub. L. 100–670, §104, added subsec. (p).

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 1999 AMENDMENT

Amendment by Pub. L. 106–113 effective 4 months after Nov. 29, 1999, see section 1000(a)(9) [title IV, §4731] of Pub. L. 106–113, set out as a note under section 1 of Title 35, Patents.

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by Pub. L. 105–115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as a note under section 321 of this title.

EFFECTIVE DATE OF 1994 AMENDMENT

Pub. L. 103–396, §2(d), Oct. 22, 1994, 108 Stat. 4154, provided that: ''The amendments made by this section [amending this section and section 331 of this title] shall take effect upon the adoption of the final regulations under subsection (c) [set out below].'' [Final regulations were dated Oct. 22, 1996, filed Nov. 6, 1996, published Nov. 7, 1996, 61 F.R. 57732, and effective Dec. 9, 1996.]

EFFECTIVE DATE OF 1988 AMENDMENT

Pub. L. 100–670, title I, §108, Nov. 16, 1988, 102 Stat. 3984, provided that: ''The Secretary of Health and Human Services may not make an approval of an application submitted under section 512(b)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360b(b)(2)) effective before January 1, 1991.''

EFFECTIVE DATE AND TRANSITIONAL PROVISIONS

Pub. L. 90–399, §108, July 13, 1968, 82 Stat. 353, as amended by Pub. L. 108–282, title I, §102(b)(5)(T), Aug. 2, 2004, 118 Stat. 905, provided that:

''(a) Except as otherwise provided in this section, the amendments made by the foregoing sections [see Short Title of 1968 Amendment note set out under section 301 of this title] shall take effect on the first day of the thirteenth calendar month which begins after the date of enactment of this Act [July 13, 1968].

''(b)(1) As used in this subsection, the term 'effective date' means the effective date specified in subsection (a) of this section; the term 'basic Act' means the Federal Food, Drug, and Cosmetic Act [this chapter]; and other terms used both in this section and the basic Act shall have the same meaning as they have, or had, at the time referred to in the context, under the basic Act.

''(2) Any approval, prior to the effective date, of a new animal drug or of an animal feed bearing or containing a new animal drug, whether granted by approval of a new-drug application, master file, antibiotic regulation, or food additive regulations, shall continue in effect, and shall be subject to change in accordance with the provisions of the basic Act as amended by this Act [see Short Title of 1968 Amendment note set out under section 301 of this title].

''(3) In the case of any drug (other than a drug subject to section 512(n) of the basic Act as amended by this Act) [subsection (n) of this section] intended for use in animals other than man which, on October 9, 1962, (A) was commercially used or sold in the United States, (B) was not a new drug as defined by section 201(p) of the basic Act [section 321(p) of this title] as then in force, and (C) was not covered by an effective application under section 505 of that Act [section 355 of this title], the words 'effectiveness' and 'effective' contained in section 201(v) to the basic Act [sic] [section 321(v) of this title] shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day.

''(4) Regulations providing for fees (and advance deposits to cover fees) which on the day preceding the effective date applicable under subsection (a) of this section were in effect pursuant to section 507 of the basic Act [section 357 of this title] shall, except as the Secretary may otherwise prescribe, be deemed to apply also under section 512(n) of the basic Act [subsection (n) of this section], and appropriations of fees (and of advance deposits to cover fees) available for the purposes specified in such section 507 [section 357 of this title] as in effect prior to the effective date shall also be available for the purposes specified in section 512(n) [subsection (n) of this section], including preparatory work or proceedings prior to that date.''

REGULATIONS

Pub. L. 104–250, §2(e), Oct. 9, 1996, 110 Stat. 3154, provided that:

''(1) IN GENERAL.—Not later than 6 months after the date of enactment of this Act [Oct. 9, 1996], the Secretary of Health and Human Services shall issue proposed regulations implementing the amendments made by this Act as described in paragraph (2)(A) of this subsection, and not later than 18 months after the date of enactment of this Act, the Secretary shall issue final regulations implementing such amendments. Not later than 12 months after the date of enactment of this Act, the Secretary shall issue proposed regulations implementing the other amendments made by this Act as described in paragraphs (2)(B) and (2)(C) of this subsection, and not later than 24 months after the date of enactment of this Act, the Secretary shall issue final regulations implementing such amendments.

''(2) CONTENTS.—In issuing regulations implementing the amendments made by this Act [see Short Title of 1996 Amendments note set out under section 301 of this title], and in taking an action to review an application for approval of a new animal drug under section 512 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360b), or a request for an investigational exemption for a new animal drug under subsection (j) of such section, that is pending or has been submitted prior to the effective date of the regulations, the Secretary shall—

''(A) further define the term 'adequate and well controlled', as used in subsection (d)(3) of section 512 of such Act, to require that field investigations be designed and conducted in a scientifically sound manner, taking into account practical conditions in the field and differences between field conditions and laboratory conditions;

''(B) further define the term 'substantial evidence', as defined in subsection (d)(3) of such section, in a manner that encourages the submission of applications and supplemental applications; and

''(C) take into account the proposals contained in the citizen petition (FDA Docket No. 91P–0434/CP) jointly submitted by the American Veterinary Medical Association and the Animal Health Institute, dated October 21, 1991.

Until the regulations required by subparagraph (A) are issued, nothing in the regulations published at 21 C.F.R. 514.111(a)(5) (April 1, 1996) shall be construed to compel the Secretary of Health and Human Services to require a field investigation under section 512(d)(1)(E) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360b(d)(1)(E)) or to apply any of its provisions in a manner inconsistent with the considerations for scientifically sound field investigations set forth in subparagraph (A).''

Pub. L. 103–396, §2(c), Oct. 22, 1994, 108 Stat. 4154, provided that: ''Not later than 2 years after the date of the enactment of this Act [Oct. 22, 1994], the Secretary of Health and Human Services shall promulgate regulations to implement paragraphs (4)(A) and (5) of section 512(a) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b(a)(4)(A), (5)] (as amended by subsection (a)).''

Pub. L. 100–670, title I, §103, Nov. 16, 1988, 102 Stat. 3982, provided that:

''(a) GENERAL RULE.—The Secretary of Health and Human Services shall promulgate, in accordance with the notice and comment requirements of section 553 of title 5, United States Code, such regulations as may be necessary for the administration of section 512 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b], as amended by sections 101 through 103 of this title, within one year of the date of enactment of this Act [Nov. 16, 1988].

''(b) TRANSITION.—During the period beginning 60 days after the date of enactment of this Act [Nov. 16, 1988] and ending on the date regulations promulgated under subsection (a) take effect, abbreviated new animal drug applications may be submitted in accordance with the provisions of section 314.55 and part 320 of title 21 of the Code of Federal Regulations and shall be considered as suitable for any drug which has been approved for safety and effectiveness under section 512(c) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b(c)] before the date of enactment of this Act. If any such provision of section 314.55 or part 320 is incon-

sistent with the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act (as amended by this title), the Secretary shall consider the application under the applicable requirements of section 512 (as so amended).''

GUIDANCE ADDRESSING INVESTIGATION DESIGNS

Pub. L. 115–234, title III, § 305, Aug. 14, 2018, 132 Stat. 2440, provided that:

''(a) IN GENERAL.—For purposes of assisting sponsors in incorporating complex adaptive and other novel investigation designs, data from foreign countries, real world evidence (including ongoing surveillance activities, observational studies, and registry data), biomarkers, and surrogate endpoints (referred to in this section as 'elements of investigations') into proposed clinical investigation protocols and applications for new animal drugs under sections 512 and 571 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360b; 360ccc), the Secretary of Health and Human Services (referred to in this section as the 'Secretary') shall issue guidance addressing the use of such elements of investigations in the development and regulatory review of such new animal drugs.

''(b) CONTENTS.—The guidance under subsection (a) shall address how the Secretary will evaluate the elements of investigations proposed or submitted pursuant to section 512(b)(1)(A) of the Federal Food, Drug, and Cosmetic Act or to meet the commitment under section 571(a)(2)(F) of such Act, and how sponsors of such applications may obtain feedback from the Secretary on technical issues related to such investigations prior to the submission of an application to the Secretary.

''(c) MEETING.—Prior to issuing the guidance under subsection (a), the Secretary shall consult with stakeholders, including representatives of regulated industry, consumer groups, academia, veterinarians, and food producers, through a public meeting to be held not later than 1 year after the date of enactment of this Act [Aug. 14, 2018].

''(d) TIMING.—The Secretary shall issue a draft guidance under subsection (a) not later than 1 year after the date of the public meeting under subsection (c), and shall finalize such guidance not later than 1 year after the date on which the public comment period on such draft guidance ends.''

ANTIMICROBIAL ANIMAL DRUG DISTRIBUTION REPORTS

Pub. L. 110–316, title I, § 105(b), (c), Aug. 14, 2008, 122 Stat. 3514, provided that:

''(b) FIRST REPORT.—For each new animal drug that is subject to the reporting requirement under section 512(*l*)(3) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b(*l*)(3)], as added by subsection (a), and for which an approval of an application filed pursuant to section 512(b) or 571 of such Act [21 U.S.C. 360b(b), 360ccc] is in effect on the date of the enactment of this title [Aug. 14, 2008], the Secretary of Health and Human Services shall require the sponsor of the drug to submit the first report under such section 512(*l*)(3) for the drug not later than March 31, 2010.

''(c) SEPARATE REPORT.—The reports required under section 512(*l*)(3) of the Federal Food, Drug, and Cosmetic Act, as added by subsection (a), shall be separate from periodic drug experience reports that are required under section 514.80(b)(4) of title 21, Code of Federal Regulations (as in effect on the date of the enactment of this title).''

DRUGS INTENDED FOR MINOR SPECIES AND MINOR USES

Pub. L. 104–250, § 2(f), Oct. 9, 1996, 110 Stat. 3154, provided that: ''The Secretary of Health and Human Services shall consider legislative and regulatory options for facilitating the approval under section 512 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b] of animal drugs intended for minor species and for minor uses and, within 18 months after the date of enactment of this Act [Oct. 9, 1996], announce proposals for legislative or regulatory change to the approval process under such section for animal drugs intended for use in minor species or for minor uses.''

TRANSITIONAL PROVISION REGARDING IMPLEMENTATION OF PUB. L. 104–250; APPROVED MEDICATED FEED APPLICATION DEEMED LICENSE

Pub. L. 104–250, § 6(c), Oct. 9, 1996, 110 Stat. 3160, provided that: ''A person engaged in the manufacture of animal feeds bearing or containing new animal drugs who holds at least one approved medicated feed application for an animal feed bearing or containing new animal drugs, the manufacture of which was not otherwise exempt from the requirement for an approved medicated feed application on the date of the enactment of this Act [Oct. 9, 1996], shall be deemed to hold a license for the manufacturing site identified in the approved medicated feed application. The revocation of license provisions of section 512(m)(4) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b(m)(4)], as amended by this Act, shall apply to such licenses. Such license shall expire within 18 months from the date of enactment of this Act unless the person submits to the Secretary a completed license application for the manufacturing site accompanied by a copy of an approved medicated feed application for such site, which license application shall be deemed to be approved upon receipt by the Secretary.''

DRUGS PRIMARILY MANUFACTURED USING BIOTECHNOLOGY

Pub. L. 100–670, title I, § 106, Nov. 16, 1988, 102 Stat. 3984, provided that: ''Notwithstanding section 512(b)(2) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b(b)(2)], the Secretary of Health and Human Services may not approve an abbreviated application submitted under such section for a new animal drug which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques.''

§ 360b–1. Priority zoonotic animal drugs

(a) In general

The Secretary shall, at the request of the sponsor intending to submit an application for approval of a new animal drug under section 360b(b)(1) of this title or an application for conditional approval of a new animal drug under section 360ccc of this title, expedite the development and review of such new animal drug if preliminary clinical evidence indicates that the new animal drug, alone or in combination with 1 or more other animal drugs, has the potential to prevent or treat a zoonotic disease in animals, including a vector borne-disease, that has the potential to cause serious adverse health consequences for, or serious or life-threatening diseases in, humans.

(b) Request for designation

The sponsor of a new animal drug may request the Secretary to designate a new animal drug described in subsection (a) as a priority zoonotic animal drug. A request for the designation may be made concurrently with, or at any time after, the opening of an investigational new animal drug file under section 360b(j) of this title or the filing of an application under section 360b(b)(1) or 360ccc of this title.

(c) Designation

(1) In general

Not later than 60 calendar days after the receipt of a request under subsection (b), the

Secretary shall determine whether the new animal drug that is the subject of the request meets the criteria described in subsection (a). If the Secretary determines that the new animal drug meets the criteria, the Secretary shall designate the new animal drug as a priority zoonotic animal drug and shall take such actions as are appropriate to expedite the development and review of the application for approval or conditional approval of such new animal drug.

(2) Actions

The actions to expedite the development and review of an application under paragraph (1) may include, as appropriate—

(A) taking steps to ensure that the design of clinical trials is as efficient as practicable, when scientifically appropriate, such as by utilizing novel trial designs or drug development tools (including biomarkers) that may reduce the number of animals needed for studies;

(B) providing timely advice to, and interactive communication with, the sponsor (which may include meetings with the sponsor and review team) regarding the development of the new animal drug to ensure that the development program to gather the nonclinical and clinical data necessary for approval is as efficient as practicable;

(C) involving senior managers and review staff with experience in zoonotic or vector-borne disease to facilitate collaborative, cross-disciplinary review, including, as appropriate, across agency centers; and

(D) implementing additional administrative or process enhancements, as necessary, to facilitate an efficient review and development program.

(June 25, 1938, ch. 675, § 512A, as added Pub. L. 116–136, div. A, title III, § 3302, Mar. 27, 2020, 134 Stat. 384.)

§ 360c. Classification of devices intended for human use

(a) Classes of devices

(1) There are established the following classes of devices intended for human use:

(A) CLASS I, GENERAL CONTROLS.—

(i) A device for which the controls authorized by or under section 351, 352, 360, 360f, 360h, 360i, or 360j of this title or any combination of such sections are sufficient to provide reasonable assurance of the safety and effectiveness of the device.

(ii) A device for which insufficient information exists to determine that the controls referred to in clause (i) are sufficient to provide reasonable assurance of the safety and effectiveness of the device or to establish special controls to provide such assurance, but because it—

(I) is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and

(II) does not present a potential unreasonable risk of illness or injury,

is to be regulated by the controls referred to in clause (i).

(B) CLASS II, SPECIAL CONTROLS.—A device which cannot be classified as a class I device because the general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device, and for which there is sufficient information to establish special controls to provide such assurance, including the promulgation of performance standards, postmarket surveillance, patient registries, development and dissemination of guidelines (including guidelines for the submission of clinical data in premarket notification submissions in accordance with section 360(k) of this title), recommendations, and other appropriate actions as the Secretary deems necessary to provide such assurance. For a device that is purported or represented to be for a use in supporting or sustaining human life, the Secretary shall examine and identify the special controls, if any, that are necessary to provide adequate assurance of safety and effectiveness and describe how such controls provide such assurance.

(C) CLASS III, PREMARKET APPROVAL.—A device which because—

(i) it (I) cannot be classified as a class I device because insufficient information exists to determine that the application of general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device, and (II) cannot be classified as a class II device because insufficient information exists to determine that the special controls described in subparagraph (B) would provide reasonable assurance of its safety and effectiveness, and

(ii)(I) is purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, or

(II) presents a potential unreasonable risk of illness or injury,

is to be subject, in accordance with section 360e of this title, to premarket approval to provide reasonable assurance of its safety and effectiveness.

If there is not sufficient information to establish a performance standard for a device to provide reasonable assurance of its safety and effectiveness, the Secretary may conduct such activities as may be necessary to develop or obtain such information.

(2) For purposes of this section and sections 360d and 360e of this title, the safety and effectiveness of a device are to be determined—

(A) with respect to the persons for whose use the device is represented or intended,

(B) with respect to the conditions of use prescribed, recommended, or suggested in the labeling of the device, and

(C) weighing any probable benefit to health from the use of the device against any probable risk of injury or illness from such use.

(3)(A) Except as authorized by subparagraph (B), the effectiveness of a device is, for purposes of this section and sections 360d and 360e of this

title, to be determined, in accordance with regulations promulgated by the Secretary, on the basis of well-controlled investigations, including 1 or more clinical investigations where appropriate, by experts qualified by training and experience to evaluate the effectiveness of the device, from which investigations it can fairly and responsibly be concluded by qualified experts that the device will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling of the device.

(B) If the Secretary determines that there exists valid scientific evidence (other than evidence derived from investigations described in subparagraph (A))—

(i) which is sufficient to determine the effectiveness of a device, and

(ii) from which it can fairly and responsibly be concluded by qualified experts that the device will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling of the device,

then, for purposes of this section and sections 360d and 360e of this title, the Secretary may authorize the effectiveness of the device to be determined on the basis of such evidence.

(C) In making a determination of a reasonable assurance of the effectiveness of a device for which an application under section 360e of this title has been submitted, the Secretary shall consider whether the extent of data that otherwise would be required for approval of the application with respect to effectiveness can be reduced through reliance on postmarket controls.

(D)(i) The Secretary, upon the written request of any person intending to submit an application under section 360e of this title, shall meet with such person to determine the type of valid scientific evidence (within the meaning of subparagraphs (A) and (B)) that will be necessary to demonstrate for purposes of approval of an application the effectiveness of a device for the conditions of use proposed by such person. The written request shall include a detailed description of the device, a detailed description of the proposed conditions of use of the device, a proposed plan for determining whether there is a reasonable assurance of effectiveness, and, if available, information regarding the expected performance from the device. Within 30 days after such meeting, the Secretary shall specify in writing the type of valid scientific evidence that will provide a reasonable assurance that a device is effective under the conditions of use proposed by such person.

(ii) Any clinical data, including one or more well-controlled investigations, specified in writing by the Secretary for demonstrating a reasonable assurance of device effectiveness shall be specified as result of a determination by the Secretary that such data are necessary to establish device effectiveness. The Secretary shall consider, in consultation with the applicant, the least burdensome appropriate means of evaluating device effectiveness that would have a reasonable likelihood of resulting in approval.

(iii) For purposes of clause (ii), the term ''necessary'' means the minimum required information that would support a determination by the Secretary that an application provides reasonable assurance of the effectiveness of the device.

(iv) Nothing in this subparagraph shall alter the criteria for evaluating an application for premarket approval of a device.

(v) The determination of the Secretary with respect to the specification of valid scientific evidence under clauses (i) and (ii) shall be binding upon the Secretary, unless such determination by the Secretary could be contrary to the public health.

(b) Classification panels

(1) For purposes of—

(A) determining which devices intended for human use should be subject to the requirements of general controls, performance standards, or premarket approval, and

(B) providing notice to the manufacturers and importers of such devices to enable them to prepare for the application of such requirements to devices manufactured or imported by them,

the Secretary shall classify all such devices (other than devices classified by subsection (f)) into the classes established by subsection (a). For the purpose of securing recommendations with respect to the classification of devices, the Secretary shall establish panels of experts or use panels of experts established before May 28, 1976, or both. Section 1013 of title 5 shall not apply to the duration of a panel established under this paragraph.

(2) The Secretary shall appoint to each panel established under paragraph (1) persons who are qualified by training and experience to evaluate the safety and effectiveness of the devices to be referred to the panel and who, to the extent feasible, possess skill in the use of, or experience in the development, manufacture, or utilization of, such devices. The Secretary shall make appointments to each panel so that each panel shall consist of members with adequately diversified expertise in such fields as clinical and administrative medicine, engineering, biological and physical sciences, and other related professions. In addition, each panel shall include as nonvoting members a representative of consumer interests and a representative of interests of the device manufacturing industry. Scientific, trade, and consumer organizations shall be afforded an opportunity to nominate individuals for appointment to the panels. No individual who is in the regular full-time employ of the United States and engaged in the administration of this chapter may be a member of any panel. The Secretary shall designate one of the members of each panel to serve as chairman thereof.

(3) Panel members (other than officers or employees of the United States), while attending meetings or conferences of a panel or otherwise engaged in its business, shall be entitled to receive compensation at rates to be fixed by the Secretary, but not at rates exceeding the daily equivalent of the rate in effect for grade GS–18 of the General Schedule, for each day so engaged, including traveltime; and while so serving away from their homes or regular places of business each member may be allowed travel expenses (including per diem in lieu of subsist-

ence) as authorized by section 5703 of title 5, for persons in the Government service employed intermittently.

(4) The Secretary shall furnish each panel with adequate clerical and other necessary assistance.

(5)(A) Classification panels covering each type of device shall be scheduled to meet at such times as may be appropriate for the Secretary to meet applicable statutory deadlines.

(B) When a device is specifically the subject of review by a classification panel, the Secretary shall—

(i) ensure that adequate expertise is represented on the classification panel to assess—

(I) the disease or condition which the device is intended to cure, treat, mitigate, prevent, or diagnose; and

(II) the technology of the device; and

(ii) provide an opportunity for the person whose device is specifically the subject of panel review to provide recommendations on the expertise needed among the voting members of the panel.

(C) For purposes of subparagraph (B)(i), the term ''adequate expertise'' means that the membership of the classification panel includes—

(i) two or more voting members, with a specialty or other expertise clinically relevant to the device under review; and

(ii) at least one voting member who is knowledgeable about the technology of the device.

(D) The Secretary shall provide an annual opportunity for patients, representatives of patients, and sponsors of medical devices that may be specifically the subject of a review by a classification panel to provide recommendations for individuals with appropriate expertise to fill voting member positions on classification panels.

(6)(A) Any person whose device is specifically the subject of review by a classification panel shall have—

(i) the same access to data and information submitted to a classification panel (except for data and information that are not available for public disclosure under section 552 of title 5) as the Secretary;

(ii) the opportunity to submit, for review by a classification panel, information that is based on the data or information provided in the application submitted under section 360e of this title by the person, which information shall be submitted to the Secretary for prompt transmittal to the classification panel; and

(iii) the same opportunity as the Secretary to participate in meetings of the panel, including, subject to the discretion of the panel chairperson, by designating a representative who will be provided a time during the panel meeting to address the panel for the purpose of correcting misstatements of fact or providing clarifying information, and permitting the person or representative to call on experts within the person's organization to address such specific issues in the time provided.

(B)(i) Any meeting of a classification panel with respect to the review of a device shall—

(I) provide adequate time for initial presentations by the person whose device is specifically the subject of such review and by the Secretary; and

(II) encourage free and open participation by all interested persons.

(ii) Following the initial presentations described in clause (i), the panel may—

(I) pose questions to a designated representative described in subparagraph (A)(iii); and

(II) consider the responses to such questions in the panel's review of the device.

(7) After receiving from a classification panel the conclusions and recommendations of the panel on a matter that the panel has reviewed, the Secretary shall review the conclusions and recommendations, shall make a final decision on the matter in accordance with section 360e(d)(2) of this title, and shall notify the affected persons of the decision in writing and, if the decision differs from the conclusions and recommendations of the panel, shall include the reasons for the difference.

(8) A classification panel under this subsection shall not be subject to the annual chartering and annual report requirements of the[1] chapter 10 of title 5.

(c) Classification panel organization and operation

(1) The Secretary shall organize the panels according to the various fields of clinical medicine and fundamental sciences in which devices intended for human use are used. The Secretary shall refer a device to be classified under this section to an appropriate panel established or authorized to be used under subsection (b) for its review and for its recommendation respecting the classification of the device. The Secretary shall by regulation prescribe the procedure to be followed by the panels in making their reviews and recommendations. In making their reviews of devices, the panels, to the maximum extent practicable, shall provide an opportunity for interested persons to submit data and views on the classification of the devices.

(2)(A) Upon completion of a panel's review of a device referred to it under paragraph (1), the panel shall, subject to subparagraphs (B) and (C), submit to the Secretary its recommendation for the classification of the device. Any such recommendation shall (i) contain (I) a summary of the reasons for the recommendation, (II) a summary of the data upon which the recommendation is based, and (III) an identification of the risks to health (if any) presented by the device with respect to which the recommendation is made, and (ii) to the extent practicable, include a recommendation for the assignment of a priority for the application of the requirements of section 360d or 360e of this title to a device recommended to be classified in class II or class III.

(B) A recommendation of a panel for the classification of a device in class I shall include a recommendation as to whether the device should be exempted from the requirements of section 360, 360i, or 360j(f) of this title.

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[1] So in original. The word ''the'' probably should not appear.

(C) In the case of a device which has been referred under paragraph (1) to a panel, and which—

(i) is intended to be implanted in the human body or is purported or represented to be for a use in supporting or sustaining human life, and

(ii)(I) has been introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, or

(II) is within a type of device which was so introduced or delivered before such date and is substantially equivalent to another device within that type,

such panel shall recommend to the Secretary that the device be classified in class III unless the panel determines that classification of the device in such class is not necessary to provide reasonable assurance of its safety and effectiveness. If a panel does not recommend that such a device be classified in class III, it shall in its recommendation to the Secretary for the classification of the device set forth the reasons for not recommending classification of the device in such class.

(3) The panels shall submit to the Secretary within one year of the date funds are first appropriated for the implementation of this section their recommendations respecting all devices of a type introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976.

(d) Panel recommendation; publication; priorities

(1) Upon receipt of a recommendation from a panel respecting a device, the Secretary shall publish in the Federal Register the panel's recommendation and a proposed regulation classifying such device and shall provide interested persons an opportunity to submit comments on such recommendation and the proposed regulation. After reviewing such comments, the Secretary shall, subject to paragraph (2), by regulation classify such device.

(2)(A) A regulation under paragraph (1) classifying a device in class I shall prescribe which, if any, of the requirements of section 360, 360i, or 360j(f) of this title shall not apply to the device. A regulation which makes a requirement of section 360, 360i, or 360j(f) of this title inapplicable to a device shall be accompanied by a statement of the reasons of the Secretary for making such requirement inapplicable.

(B) A device described in subsection (c)(2)(C) shall be classified in class III unless the Secretary determines that classification of the device in such class is not necessary to provide reasonable assurance of its safety and effectiveness. A proposed regulation under paragraph (1) classifying such a device in a class other than class III shall be accompanied by a full statement of the reasons of the Secretary (and supporting documentation and data) for not classifying such device in such class and an identification of the risks to health (if any) presented by such device.

(3) In the case of devices classified in class II and devices classified under this subsection in class III and described in section 360e(b)(1) of this title the Secretary may establish priorities which, in his discretion, shall be used in applying sections 360d and 360e of this title, as appropriate, to such devices.

(e) Classification changes

(1)(A)(i) Based on new information respecting a device, the Secretary may, upon the initiative of the Secretary or upon petition of an interested person, change the classification of such device, and revoke, on account of the change in classification, any regulation or requirement in effect under section 360d or 360e of this title with respect to such device, by administrative order published in the Federal Register following publication of a proposed reclassification order in the Federal Register, a meeting of a device classification panel described in subsection (b), and consideration of comments to a public docket, notwithstanding subchapter II of chapter 5 of title 5. The proposed reclassification order published in the Federal Register shall set forth the proposed reclassification, and a substantive summary of the valid scientific evidence concerning the proposed reclassification, including—

(I) the public health benefit of the use of the device, and the nature and, if known, incidence of the risk of the device;

(II) in the case of a reclassification from class II to class III, why general controls pursuant to subsection (a)(1)(A) and special controls pursuant to subsection (a)(1)(B) together are not sufficient to provide a reasonable assurance of safety and effectiveness for such device; and

(III) in the case of reclassification from class III to class II, why general controls pursuant to subsection (a)(1)(A) and special controls pursuant to subsection (a)(1)(B) together are sufficient to provide a reasonable assurance of safety and effectiveness for such device.

(ii) An order under this subsection changing the classification of a device from class III to class II may provide that such classification shall not take effect until the effective date of a performance standard established under section 360d of this title for such device.

(B) Authority to issue such administrative order shall not be delegated below the Director of the Center for Devices and Radiological Health, acting in consultation with the Commissioner.

(2) By an order issued under paragraph (1), the Secretary may change the classification of a device from class III—

(A) to class II if the Secretary determines that special controls would provide reasonable assurance of the safety and effectiveness of the device and that general controls would not provide reasonable assurance of the safety and effectiveness of the device, or

(B) to class I if the Secretary determines that general controls would provide reasonable assurance of the safety and effectiveness of the device.

(f) Initial classification and reclassification of certain devices

(1) Any device intended for human use which was not introduced or delivered for introduction

into interstate commerce for commercial distribution before May 28, 1976, is classified in class III unless—

(A) the device—

(i) is within a type of device (I) which was introduced or delivered for introduction into interstate commerce for commercial distribution before such date and which is to be classified pursuant to subsection (b), or (II) which was not so introduced or delivered before such date and has been classified in class I or II, and

(ii) is substantially equivalent to another device within such type;

(B) the Secretary in response to a petition submitted under paragraph (3) has classified such device in class I or II; or

(C) the device is classified pursuant to a request submitted under paragraph (2).

A device classified in class III under this paragraph shall be classified in that class until the effective date of an order of the Secretary under paragraph (2) or (3) classifying the device in class I or II.

(2)(A)(i) Any person who submits a report under section 360(k) of this title for a type of device that has not been previously classified under this chapter, and that is classified into class III under paragraph (1), may request, after receiving written notice of such a classification, the Secretary to classify the device.

(ii) In lieu of submitting a report under section 360(k) of this title and submitting a request for classification under clause (i) for a device, if a person determines there is no legally marketed device upon which to base a determination of substantial equivalence (as defined in subsection (i)), a person may submit a request under this clause for the Secretary to classify the device.

(iii) Upon receipt of a request under clause (i) or (ii), the Secretary shall classify the device subject to the request under the criteria set forth in subparagraphs (A) through (C) of subsection (a)(1) within 120 days.

(iv) Notwithstanding clause (iii), the Secretary may decline to undertake a classification request submitted under clause (ii) if the Secretary identifies a legally marketed device that could provide a reasonable basis for review of substantial equivalence under paragraph (1), or when the Secretary determines that the device submitted is not of low to moderate risk or that general controls would be inadequate to control the risks and special controls to mitigate the risks cannot be developed.

(v) The person submitting the request for classification under this subparagraph may recommend to the Secretary a classification for the device and shall, if recommending classification in class II, include in the request an initial draft proposal for applicable special controls, as described in subsection (a)(1)(B), that are necessary, in conjunction with general controls, to provide reasonable assurance of safety and effectiveness and a description of how the special controls provide such assurance. Any such request shall describe the device and provide detailed information and reasons for the recommended classification.

(B)(i) The Secretary shall by written order classify the device involved. Such classification shall be the initial classification of the device for purposes of paragraph (1) and any device classified under this paragraph shall be a predicate device for determining substantial equivalence under paragraph (1).

(ii) A device that remains in class III under this subparagraph shall be deemed to be adulterated within the meaning of section 351(f)(1)(B) of this title until approved under section 360e of this title or exempted from such approval under section 360j(g) of this title.

(C) Within 30 days after the issuance of an order classifying a device under this paragraph, the Secretary shall publish a notice in the Federal Register announcing such classification.

(3)(A) The Secretary may initiate the reclassification of a device classified into class III under paragraph (1) of this subsection or the manufacturer or importer of a device classified under paragraph (1) may petition the Secretary (in such form and manner as he shall prescribe) for the issuance of an order classifying the device in class I or class II. Within thirty days of the filing of such a petition, the Secretary shall notify the petitioner of any deficiencies in the petition which prevent the Secretary from making a decision on the petition.

(B)(i) Upon determining that a petition does not contain any deficiency which prevents the Secretary from making a decision on the petition, the Secretary may for good cause shown refer the petition to an appropriate panel established or authorized to be used under subsection (b). A panel to which such a petition has been referred shall not later than ninety days after the referral of the petition make a recommendation to the Secretary respecting approval or denial of the petition. Any such recommendation shall contain (I) a summary of the reasons for the recommendation, (II) a summary of the data upon which the recommendation is based, and (III) an identification of the risks to health (if any) presented by the device with respect to which the petition was filed. In the case of a petition for a device which is intended to be implanted in the human body or which is purported or represented to be for a use in supporting or sustaining human life, the panel shall recommend that the petition be denied unless the panel determines that the classification in class III of the device is not necessary to provide reasonable assurance of its safety and effectiveness. If the panel recommends that such petition be approved, it shall in its recommendation to the Secretary set forth its reasons for such recommendation.

(ii) The requirements of paragraphs (1) and (2) of subsection (c) (relating to opportunities for submission of data and views and recommendations respecting priorities and exemptions from sections 360, 360i, and 360j(f) of this title) shall apply with respect to consideration by panels of petitions submitted under subparagraph (A).

(C)(i) Within ninety days from the date the Secretary receives the recommendation of a panel respecting a petition (but not later than 210 days after the filing of such petition) the Secretary shall by order deny or approve the petition. If the Secretary approves the petition,

the Secretary shall order the classification of the device into class I or class II in accordance with the criteria prescribed by subsection (a)(1)(A) or (a)(1)(B). In the case of a petition for a device which is intended to be implanted in the human body or which is purported or represented to be for a use in supporting or sustaining human life, the Secretary shall deny the petition unless the Secretary determines that the classification in class III of the device is not necessary to provide reasonable assurance of its safety and effectiveness. An order approving such petition shall be accompanied by a full statement of the reasons of the Secretary (and supporting documentation and data) for approving the petition and an identification of the risks to health (if any) presented by the device to which such order applies.

(ii) The requirements of paragraphs (1) and (2)(A) of subsection (d) (relating to publication of recommendations, opportunity for submission of comments, and exemption from sections 360, 360i, and 360j(f) of this title) shall apply with respect to action by the Secretary on petitions submitted under subparagraph (A).

(4) If a manufacturer reports to the Secretary under section 360(k) of this title that a device is substantially equivalent to another device—

(A) which the Secretary has classified as a class III device under subsection (b),

(B) which was introduced or delivered for introduction into interstate commerce for commercial distribution before December 1, 1990, and

(C) for which no final regulation requiring premarket approval has been promulgated under section 360e(b) of this title,

the manufacturer shall certify to the Secretary that the manufacturer has conducted a reasonable search of all information known or otherwise available to the manufacturer respecting such other device and has included in the report under section 360(k) of this title a summary of and a citation to all adverse safety and effectiveness data respecting such other device and respecting the device for which the section 360(k) report is being made and which has not been submitted to the Secretary under section 360i of this title. The Secretary may require the manufacturer to submit the adverse safety and effectiveness data described in the report.

(5) The Secretary may not withhold a determination of the initial classification of a device under paragraph (1) because of a failure to comply with any provision of this chapter unrelated to a substantial equivalence decision, including a finding that the facility in which the device is manufactured is not in compliance with good manufacturing requirements as set forth in regulations of the Secretary under section 360j(f) of this title (other than a finding that there is a substantial likelihood that the failure to comply with such regulations will potentially present a serious risk to human health).

(6)(A) Subject to the succeeding subparagraphs of this paragraph, the Secretary shall, by written order, classify an accessory under this section based on the risks of the accessory when used as intended and the level of regulatory controls necessary to provide a reasonable assurance of safety and effectiveness of the accessory, notwithstanding the classification of any other device with which such accessory is intended to be used.

(B) The classification of any accessory distinct from another device by regulation or written order issued prior to December 13, 2016, shall continue to apply unless and until the accessory is reclassified by the Secretary, notwithstanding the classification of any other device with which such accessory is intended to be used. Nothing in this paragraph shall preclude the Secretary's authority to initiate the classification of an accessory through regulation or written order, as appropriate.

(C)(i) In the case of a device intended to be used with an accessory, where the accessory has been included in an application for premarket approval of such device under section 360e of this title or a report under section 360(k) of this title for clearance of such device and the Secretary has not classified such accessory distinctly from another device in accordance with subparagraph (A), the person filing the application or report (as applicable) at the time such application or report is filed—

(I) may include a written request for the proper classification of the accessory pursuant to subparagraph (A);

(II) shall include in any such request such information as may be necessary for the Secretary to evaluate, based on the least burdensome approach, the appropriate class for the accessory under subsection (a); and

(III) shall, if the request under subclause (I) is requesting classification of the accessory in class II, include in the application an initial draft proposal for special controls, if special controls would be required pursuant to subsection (a)(1)(B).

(ii) The Secretary's response under section 360e(d) or section 360(n) of this title (as applicable) to an application or report described in clause (i) shall also contain the Secretary's granting or denial of the request for classification of the accessory involved.

(iii) The Secretary's evaluation of an accessory under clause (i) shall constitute an order establishing a new classification for such accessory for the specified intended use or uses of such accessory and for any accessory with the same intended use or uses as such accessory.

(D) For accessories that have been granted marketing authorization as part of a submission for another device with which the accessory involved is intended to be used, through an application for such other device under section 360e(c) of this title, a report under section 360(k) of this title, or a request for classification under paragraph (2) of this subsection, the following shall apply:

(i) Not later than the date that is one year after August 18, 2017, and at least once every 5 years thereafter, and as the Secretary otherwise determines appropriate, pursuant to this paragraph, the Secretary shall publish in the Federal Register a notice proposing a list of such accessories that the Secretary determines may be suitable for a distinct classification in class I and the proposed regulations for such classifications. In developing such list, the Secretary shall consider recommendations

from sponsors of device submissions and other stakeholders for accessories to be included on such list. The notices shall provide for a period of not less than 60 calendar days for public comment. Within 180 days after the end of the comment period, the Secretary shall publish in the Federal Register a final action classifying such suitable accessories into class I.

(ii) A manufacturer or importer of an accessory that has been granted such marketing authorization may submit to the Secretary a written request for the appropriate classification of the accessory based on the risks and appropriate level of regulatory controls as described in subparagraph (A), and shall, if the request is requesting classification of the accessory in class II, include in the submission an initial draft proposal for special controls, if special controls would be required pursuant to subsection (a)(1)(B). Such request shall include such information as may be necessary for the Secretary to evaluate, based on the least burdensome approach, the appropriate class for the accessory under subsection (a). The Secretary shall provide an opportunity for a manufacturer or importer to meet with appropriate personnel of the Food and Drug Administration to discuss the appropriate classification of such accessory prior to submitting a written request under this clause for classification of the accessory.

(iii) The Secretary shall respond to a request made under clause (ii) not later than 85 calendar days after receiving such request by issuing a written order classifying the accessory or denying the request. If the Secretary does not agree with the recommendation for classification submitted by the manufacturer or importer, the response shall include a detailed description and justification for such determination. Within 30 calendar days after granting such a request, the Secretary shall publish a notice in the Federal Register announcing such response.

(E) Nothing in this paragraph may be construed as precluding a manufacturer of an accessory of a new type from using the classification process described in subsection (f)(2) to obtain classification of such accessory in accordance with the criteria and requirements set forth in that subsection.

(g) Information

Within sixty days of the receipt of a written request of any person for information respecting the class in which a device has been classified or the requirements applicable to a device under this chapter, the Secretary shall provide such person a written statement of the classification (if any) of such device and the requirements of this chapter applicable to the device.

(h) Definitions

For purposes of this section and sections 351, 360, 360d, 360e, 360f, 360i, and 360j of this title

(1) a reference to ''general controls'' is a reference to the controls authorized by or under sections 351, 352, 360, 360f, 360h, 360i, and 360j of this title,

(2) a reference to ''class I'', ''class II'', or ''class III'' is a reference to a class of medical devices described in subparagraph (A), (B), or (C) of subsection (a)(1), and

(3) a reference to a ''panel under section 360c of this title'' is a reference to a panel established or authorized to be used under this section.

(i) Substantial equivalence

(1)(A) For purposes of determinations of substantial equivalence under subsection (f) and section 360j(*l*) of this title, the term ''substantially equivalent'' or ''substantial equivalence'' means, with respect to a device being compared to a predicate device, that the device has the same intended use as the predicate device and that the Secretary by order has found that the device—

(i) has the same technological characteristics as the predicate device, or

(ii)(I) has different technological characteristics and the information submitted that the device is substantially equivalent to the predicate device contains information, including appropriate clinical or scientific data if deemed necessary by the Secretary or a person accredited under section 360m of this title, that demonstrates that the device is as safe and effective as a legally marketed device, and (II) does not raise different questions of safety and effectiveness than the predicate device.

(B) For purposes of subparagraph (A), the term ''different technological characteristics'' means, with respect to a device being compared to a predicate device, that there is a significant change in the materials, design, energy source, or other features of the device from those of the predicate device.

(C) To facilitate reviews of reports submitted to the Secretary under section 360(k) of this title, the Secretary shall consider the extent to which reliance on postmarket controls may expedite the classification of devices under subsection (f)(1) of this section.

(D)(i) Whenever the Secretary requests information to demonstrate that devices with differing technological characteristics are substantially equivalent, the Secretary shall only request information that is necessary to making substantial equivalence determinations. In making such request, the Secretary shall consider the least burdensome means of demonstrating substantial equivalence and request information accordingly.

(ii) For purposes of clause (i), the term ''necessary'' means the minimum required information that would support a determination of substantial equivalence between a new device and a predicate device.

(iii) Nothing in this subparagraph shall alter the standard for determining substantial equivalence between a new device and a predicate device.

(E)(i) Any determination by the Secretary of the intended use of a device shall be based upon the proposed labeling submitted in a report for the device under section 360(k) of this title. However, when determining that a device can be found substantially equivalent to a legally marketed device, the director of the organizational unit responsible for regulating devices (in this subparagraph referred to as the ''Director'') may

require a statement in labeling that provides appropriate information regarding a use of the device not identified in the proposed labeling if, after providing an opportunity for consultation with the person who submitted such report, the Director determines and states in writing—

(I) that there is a reasonable likelihood that the device will be used for an intended use not identified in the proposed labeling for the device; and

(II) that such use could cause harm.

(ii) Such determination shall—

(I) be provided to the person who submitted the report within 10 days from the date of the notification of the Director's concerns regarding the proposed labeling;

(II) specify the limitations on the use of the device not included in the proposed labeling; and

(III) find the device substantially equivalent if the requirements of subparagraph (A) are met and if the labeling for such device conforms to the limitations specified in subclause (II).

(iii) The responsibilities of the Director under this subparagraph may not be delegated.

(F) Not later than 270 days after November 21, 1997, the Secretary shall issue guidance specifying the general principles that the Secretary will consider in determining when a specific intended use of a device is not reasonably included within a general use of such device for purposes of a determination of substantial equivalence under subsection (f) or section 360j(*l*) of this title.

(2) A device may not be found to be substantially equivalent to a predicate device that has been removed from the market at the initiative of the Secretary or that has been determined to be misbranded or adulterated by a judicial order.

(3)(A) As part of a submission under section 360(k) of this title respecting a device, the person required to file a premarket notification under such section shall provide an adequate summary of any information respecting safety and effectiveness or state that such information will be made available upon request by any person.

(B) Any summary under subparagraph (A) respecting a device shall contain detailed information regarding data concerning adverse health effects and shall be made available to the public by the Secretary within 30 days of the issuance of a determination that such device is substantially equivalent to another device.

(j) Training and oversight of least burdensome requirements

(1) The Secretary shall—

(A) ensure that each employee of the Food and Drug Administration who is involved in the review of premarket submissions, including supervisors, receives training regarding the meaning and implementation of the least burdensome requirements under subsections (a)(3)(D) and (i)(1)(D) of this section and section 360e(c)(5) of this title; and

(B) periodically assess the implementation of the least burdensome requirements, including the employee training under subparagraph (A), to ensure that the least burdensome requirements are fully and consistently applied.

(2) Not later than 18 months after December 13, 2016, the ombudsman for any organizational unit of the Food and Drug Administration responsible for the premarket review of devices shall—

(A) conduct an audit of the training described in paragraph (1)(A), including the effectiveness of such training in implementing the least burdensome requirements;

(B) include in such audit interviews of persons who are representatives of the device industry regarding their experiences in the device premarket review process, including with respect to the application of least burdensome concepts to premarket review and decision-making;

(C) include in such audit a list of the measurement tools the Secretary uses to assess the implementation of the least burdensome requirements, including under paragraph (1)(B) and section 360g–1(a)(3) of this title, and may also provide feedback on the effectiveness of such tools in the implementation of the least burdensome requirements;

(D) summarize the findings of such audit in a final audit report; and

(E) within 30 calendar days of completion of such final audit report, make such final audit report available—

(i) to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives; and

(ii) on the Internet website of the Food and Drug Administration.

(k) Dual submission for certain devices

For a device authorized for emergency use under section 360bbb–3 of this title for which, in accordance with section 360bbb–3(m) of this title, the Secretary has deemed a laboratory examination or procedure associated with such device to be in the category of examinations and procedures described in section 263a(d)(3) of title 42, the sponsor of such device may, when submitting a request for classification under subsection (f)(2), submit a single submission containing—

(1) the information needed for such a request; and

(2) sufficient information to enable the Secretary to determine whether such laboratory examination or procedure satisfies the criteria to be categorized under section 263a(d)(3) of title 42.

(June 25, 1938, ch. 675, § 513, as added Pub. L. 94–295, § 2, May 28, 1976, 90 Stat. 540; amended Pub. L. 101–629, §§ 4(a), 5(a)–(c)(1), (3), 12(a), 18(a), Nov. 28, 1990, 104 Stat. 4515, 4517, 4518, 4523, 4528; Pub. L. 102–300, § 6(e), June 16, 1992, 106 Stat. 240; Pub. L. 103–80, § 3(s), Aug. 13, 1993, 107 Stat. 778; Pub. L. 105–115, title II, §§ 205(a), (b), 206(b), (c), 207, 208, 217, Nov. 21, 1997, 111 Stat. 2336, 2337, 2339, 2340, 2350; Pub. L. 107–250, title II, § 208, Oct. 26, 2002, 116 Stat. 1613; Pub. L. 112–144, title VI, §§ 602, 607–608(a)(2)(A), July 9, 2012, 126 Stat. 1051, 1054–1056; Pub. L. 114–255, div. A, title III, §§ 3055,

3058(a), 3060(c), 3101(a)(2)(I), Dec. 13, 2016, 130 Stat. 1127, 1128, 1133, 1154; Pub. L. 115–52, title VII, §707(a), (b), title IX, §901(h), Aug. 18, 2017, 131 Stat. 1060, 1062, 1077; Pub. L. 117–286, §4(a)(155), Dec. 27, 2022, 136 Stat. 4323; Pub. L. 117–328, div. FF, title III, §3301, Dec. 29, 2022, 136 Stat. 5831.)

Editorial Notes

AMENDMENTS

2022—Subsec. (b)(1). Pub. L. 117–286, §4(a)(155)(A), substituted ''Section 1013 of title 5'' for ''Section 14 of the Federal Advisory Committee Act'' in concluding provisions.

Subsec. (b)(8). Pub. L. 117–286, §4(a)(155)(B), substituted ''chapter 10 of title 5.'' for ''Federal Advisory Committee Act.''

Subsec. (k). Pub. L. 117–328 added subsec. (k).

2017—Subsec. (b)(5)(D). Pub. L. 115–52, §901(h), substituted ''medical devices that may be specifically the subject of a review by a classification panel'' for ''medical device submissions''.

Subsec. (b)(9). Pub. L. 115–52, §707(b), struck out par. (9) which read as follows: ''The Secretary shall classify an accessory under this section based on the intended use of the accessory, notwithstanding the classification of any other device with which such accessory is intended to be used.''

Subsec. (f)(6). Pub. L. 115–52, §707(a), added par. (6).

2016—Subsec. (b)(5). Pub. L. 114–255, §3055(a), designated existing provisions as subpar. (A) and added subpars. (B) to (D).

Subsec. (b)(6)(A)(iii). Pub. L. 114–255, §3055(b)(1), inserted before period at end '', including, subject to the discretion of the panel chairperson, by designating a representative who will be provided a time during the panel meeting to address the panel for the purpose of correcting misstatements of fact or providing clarifying information, and permitting the person or representative to call on experts within the person's organization to address such specific issues in the time provided''.

Subsec. (b)(6)(B). Pub. L. 114–255, §3055(b)(2), added subpar. (B) and struck out former subpar. (B) which read as follows: ''Any meetings of a classification panel shall provide adequate time for initial presentations and for response to any differing views by persons whose devices are specifically the subject of a classification panel review, and shall encourage free and open participation by all interested persons.''

Subsec. (b)(9). Pub. L. 114–255, §3060(c), added par. (9).

Subsec. (f)(2)(A)(i). Pub. L. 114–255, §3101(a)(2)(I)(i), struck out ''within 30 days'' after ''may request,''.

Subsec. (f)(2)(A)(iv). Pub. L. 114–255, §3101(a)(2)(I)(ii), substituted ''low to moderate'' for ''low-moderate''.

Subsec. (j). Pub. L. 114–255, §3058(a), added subsec. (j).

2012—Subsec. (a)(3)(D)(iii) to (v). Pub. L. 112–144, §602(a), added cls. (iii) and (iv) and redesignated former cl. (iii) as (v).

Subsec. (e)(1). Pub. L. 112–144, §608(a)(1), amended par. (1) generally. Prior to amendment, par. (1) read as follows: ''Based on new information respecting a device, the Secretary may, upon his own initiative or upon petition of an interested person, by regulation (A) change such device's classification, and (B) revoke, because of the change in classification, any regulation or requirement in effect under section 360d or 360e of this title with respect to such device. In the promulgation of such a regulation respecting a device's classification, the Secretary may secure from the panel to which the device was last referred pursuant to subsection (c) of this section a recommendation respecting the proposed change in the device's classification and shall publish in the Federal Register any recommendation submitted to the Secretary by the panel respecting such change. A regulation under this subsection changing the classification of a device from class III to class II may provide that such classification shall not take effect until the effective date of a performance standard established under section 360d of this title for such device.''

Subsec. (e)(2). Pub. L. 112–144, §608(a)(2)(A), substituted ''an order issued'' for ''regulation promulgated'' in introductory provisions.

Subsec. (f)(1)(C). Pub. L. 112–144, §607(b), added subpar. (C).

Subsec. (f)(2)(A). Pub. L. 112–144, §607(a)(1)–(3), designated existing provisions as cl. (i), struck out ''under the criteria set forth in subparagraphs (A) through (C) of subsection (a)(1) of this section. The person may, in the request, recommend to the Secretary a classification for the device. Any such request shall describe the device and provide detailed information and reasons for the recommended classification'' before period at end, and added cls. (ii) to (v).

Subsec. (f)(2)(B)(i). Pub. L. 112–144, §607(a)(4), substituted ''The Secretary'' for ''Not later than 60 days after the date of the submission of the request under subparagraph (A), the Secretary''.

Subsec. (i)(1)(D). Pub. L. 112–144, §602(b), designated existing provisions as cl. (i) and added cls. (ii) and (iii).

2002—Subsec. (i)(1)(E)(iv). Pub. L. 107–250 struck out cl. (iv) which read as follows: ''This subparagraph has no legal effect after the expiration of the five-year period beginning on November 21, 1997.''

1997—Subsec. (a)(3)(A). Pub. L. 105–115, §217, substituted ''1 or more clinical investigations'' for ''clinical investigations''.

Subsec. (a)(3)(C), (D). Pub. L. 105–115, §205(a), added subpars. (C) and (D).

Subsec. (b)(5) to (8). Pub. L. 105–115, §208, added pars. (5) to (8).

Subsec. (f)(1). Pub. L. 105–115, §207(1)(B), substituted ''paragraph (2) or (3)'' for ''paragraph (2)'' in closing provisions.

Subsec. (f)(1)(B). Pub. L. 105–115, §207(1)(A), substituted ''paragraph (3)'' for ''paragraph (2)''.

Subsec. (f)(2) to (4). Pub. L. 105–115, §207(2), (3), added par. (2) and redesignated former pars. (2) and (3) as (3) and (4), respectively.

Subsec. (f)(5). Pub. L. 105–115, §206(b), added par. (5).

Subsec. (i)(1)(A)(ii). Pub. L. 105–115, §206(c)(1), substituted ''appropriate clinical or scientific data'' for ''clinical data'', inserted ''or a person accredited under section 360m of this title'' after ''Secretary'', and substituted ''effectiveness'' for ''efficacy''.

Subsec. (i)(1)(C) to (E). Pub. L. 105–115, §205(b), added subpars. (C) to (E).

Subsec. (i)(1)(F). Pub. L. 105–115, §206(c)(2), added subpar. (F).

1993—Subsec. (b)(3). Pub. L. 103–80 substituted ''5703'' for ''5703(b)''.

1992—Subsec. (f)(3). Pub. L. 102–300 redesignated clauses (i) to (iii) as subpars. (A) to (C), respectively, and substituted ''the section 360(k) report'' for ''the 360(k) report'' in closing provisions.

1990—Subsec. (a)(1)(A)(ii). Pub. L. 101–629, §5(a)(1), substituted ''or to establish special controls'' for ''or to establish a performance standard''.

Subsec. (a)(1)(B). Pub. L. 101–629, §5(a)(2), amended subpar. (B) generally. Prior to amendment, subpar. (B) read as follows: ''CLASS II, PERFORMANCE STANDARDS.—A device which cannot be classified as a class I device because the controls authorized by or under sections 351, 352, 360, 360f, 360h, 360i, and 360j of this title by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device, for which there is sufficient information to establish a performance standard to provide such assurance, and for which it is therefore necessary to establish for the device a performance standard under section 360d of this title to provide reasonable assurance of its safety and effectiveness.''

Subsec. (a)(1)(C)(i). Pub. L. 101–629, §5(a)(3), amended cl. (i) generally. Prior to amendment, cl. (i) read as follows: ''it (I) cannot be classified as a class I device because insufficient information exists to determine that the controls authorized by or under sections 351, 352,

360, 360f, 360h, 360i, and 360j of this title are sufficient to provide reasonable assurance of the safety and effectiveness of the device and (II) cannot be classified as a class II device because insufficient information exists for the establishment of a performance standard to provide reasonable assurance of its safety and effectiveness, and''.

Subsec. (e). Pub. L. 101–629, § 5(b), designated existing provisions as par. (1), redesignated cls. (1) and (2) as (A) and (B), respectively, and added par. (2).

Subsec. (f). Pub. L. 101–629, § 5(c)(3), inserted ''and reclassification'' before ''of'' in heading.

Subsec. (f)(2)(A). Pub. L. 101–629, § 5(c)(1), substituted ''The Secretary may initiate the reclassification of a device classified into class III under paragraph (1) of this subsection or the manufacturer'' for ''The manufacturer''.

Subsec. (f)(2)(B)(i). Pub. L. 101–629, § 18(a), substituted ''the Secretary may for good cause shown'' for ''the Secretary shall''.

Subsec. (f)(3). Pub. L. 101–629, § 4(a), added par. (3).

Subsec. (i). Pub. L. 101–629, § 12(a), added subsec. (i).

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 2017 AMENDMENT

Pub. L. 115–52, title VII, § 707(c), Aug. 18, 2017, 131 Stat. 1062, provided that: ''The amendments made by subsections (a) and (b) [amending this section] shall take effect on the date that is 60 days after the date of enactment of this Act [Aug. 18, 2017].''

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by Pub. L. 105–115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as a note under section 321 of this title.

SHORT TITLE OF 1976 AMENDMENT

Pub. L. 94–295, § 1(a), May 28, 1976, 90 Stat. 539, provided that: ''This Act [enacting sections 360c to 360k, 379, and 379a of this title and section 3512 of Title 42, The Public Health and Welfare, and amending sections 321, 331, 334, 351, 352, 358, 360, 374, 379e, and 381 of this title and section 55 of Title 15, Commerce and Trade] may be cited as the 'Medical Device Amendments of 1976'.''

REGULATIONS

Pub. L. 101–629, § 12(b), Nov. 28, 1990, 104 Stat. 4524, provided that: ''Within 12 months of the date of the enactment of this Act [Nov. 28, 1990], the Secretary of Health and Human Services shall issue regulations establishing the requirements of the summaries under section 513(i)(3) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360c(i)(3)], as added by the amendment made by subsection (a).''

DEVICES RECLASSIFIED PRIOR TO JULY 9, 2012

Pub. L. 112–144, title VI, § 608(a)(3), July 9, 2012, 126 Stat. 1056, provided that:

''(A) IN GENERAL.—The amendments made by this subsection [amending this section and sections 360d and 360g of this title] shall have no effect on a regulation promulgated with respect to the classification of a device under section 513(e) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360c(e)] prior to the date of enactment of this Act [July 9, 2012].

''(B) APPLICABILITY OF OTHER PROVISIONS.—In the case of a device reclassified under section 513(e) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360c(e)] by regulation prior to the date of enactment of this Act [July 9, 2012], section 517(a)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360g(a)(1)) shall apply to such regulation promulgated under section 513(e) of such Act with respect to such device in the same manner such section 517(a)(1) applies to an administrative order issued with respect to a device reclassified after the date of enactment of this Act.''

DAILY WEAR SOFT OR DAILY WEAR NONHYDROPHILIC PLASTIC CONTACT LENSES

Pub. L. 101–629, § 4(b)(3), Nov. 28, 1990, 104 Stat. 4517, provided that:

''(A) Notwithstanding section 520(*l*)(5) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360j(*l*)(5)], the Secretary of Health and Human Services shall not retain any daily wear soft or daily wear nonhydrophilic plastic contact lens in class III under such Act [this chapter] unless the Secretary finds that it meets the criteria set forth in section 513(a)(1)(C) of such Act [21 U.S.C. 360c(a)(1)(C)]. The finding and the grounds for the finding shall be published in the Federal Register. For any such lens, the Secretary shall make the determination respecting reclassification required in section 520(*l*)(5)(B) of such Act within 24 months of the date of the enactment of this paragraph [Nov. 28, 1990].

''(B) The Secretary of Health and Human Services may by notice published in the Federal Register extend the two-year period prescribed by subparagraph (A) for a lens for an additional period not to exceed one year.

''(C)(i) Before classifying a lens in class II pursuant to subparagraph (A), the Secretary of Health and Human Services shall pursuant to section 513(a)(1)(B) of such Act assure that appropriate regulatory safeguards are in effect which provide reasonable assurance of the safety and effectiveness of such lens, including clinical and preclinical data if deemed necessary by the Secretary.

''(ii) Prior to classifying a lens in class I pursuant to subparagraph (A), the Secretary shall assure that appropriate regulatory safeguards are in effect which provide reasonable assurance of the safety and effectiveness of such lens, including clinical and preclinical data if deemed necessary by the Secretary.

''(D) Notwithstanding section 520(*l*)(5) of such Act, if the Secretary of Health and Human Services has not made the finding and published the finding required by subparagraph (A) within 36 months of the date of the enactment of this subparagraph [Nov. 28, 1990], the Secretary shall issue an order placing the lens in class II.

''(E) Any person adversely affected by a final regulation under this paragraph revising the classification of a lens may challenge the revision of the classification of such lens only by filing a petition under section 513(e) for a classification change.''

REFERENCES IN OTHER LAWS TO GS–16, 17, OR 18 PAY RATES

References in laws to the rates of pay for GS–16, 17, or 18, or to maximum rates of pay under the General Schedule, to be considered references to rates payable under specified sections of Title 5, Government Organization and Employees, see section 529 [title I, § 101(c)(1)] of Pub. L. 101–509, set out in a note under section 5376 of Title 5.

§ 360c–1. Reporting

The Secretary of Health and Human Services shall annually post on the Internet Web site of the Food and Drug Administration—

(1) the number and type of class I and class II devices reclassified as class II or class III in the previous calendar year under section 360c(e)(1) of this title;

(2) the number and type of class II and class III devices reclassified as class I or class II in the previous calendar year under such section 360c(e)(1) of this title; and

(3) the number and type of devices reclassified in the previous calendar year under section 360e of this title.

(Pub. L. 112–144, title VI, § 608(c), July 9, 2012, 126 Stat. 1059.)

Editorial Notes

CODIFICATION

Section was enacted as part of the Food and Drug Administration Safety and Innovation Act, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

§ 360d. Performance standards

(a) Reasonable assurance of safe and effective performance; periodic evaluation

(1) The special controls required by section 360c(a)(1)(B) of this title shall include performance standards for a class II device if the Secretary determines that a performance standard is necessary to provide reasonable assurance of the safety and effectiveness of the device. A class III device may also be considered a class II device for purposes of establishing a standard for the device under subsection (b) if the device has been reclassified as a class II device under an administrative order under section 360c(e) of this title (or a regulation promulgated under such section prior to July 9, 2012) but such order (or regulation) provides that the reclassification is not to take effect until the effective date of such a standard for the device.

(2) A performance standard established under subsection (b) for a device—

(A) shall include provisions to provide reasonable assurance of its safe and effective performance;

(B) shall, where necessary to provide reasonable assurance of its safe and effective performance, include—

(i) provisions respecting the construction, components, ingredients, and properties of the device and its compatibility with power systems and connections to such systems,

(ii) provisions for the testing (on a sample basis or, if necessary, on an individual basis) of the device or, if it is determined that no other more practicable means are available to the Secretary to assure the conformity of the device to the standard, provisions for the testing (on a sample basis or, if necessary, on an individual basis) by the Secretary or by another person at the direction of the Secretary,

(iii) provisions for the measurement of the performance characteristics of the device,

(iv) provisions requiring that the results of each or of certain of the tests of the device required to be made under clause (ii) show that the device is in conformity with the portions of the standard for which the test or tests were required, and

(v) a provision requiring that the sale and distribution of the device be restricted but only to the extent that the sale and distribution of a device may be restricted under a regulation under section 360j(e) of this title; and

(C) shall, where appropriate, require the use and prescribe the form and content of labeling for the proper installation, maintenance, operation, and use of the device.

(3) The Secretary shall provide for periodic evaluation of performance standards established under subsection (b) to determine if such standards should be changed to reflect new medical, scientific, or other technological data.

(4) In carrying out his duties under this subsection and subsection (b), the Secretary shall, to the maximum extent practicable—

(A) use personnel, facilities, and other technical support available in other Federal agencies,

(B) consult with other Federal agencies concerned with standard-setting and other nationally or internationally recognized standard-setting entities, and

(C) invite appropriate participation, through joint or other conferences, workshops, or other means, by informed persons representative of scientific, professional, industry, or consumer organizations who in his judgment can make a significant contribution.

(b) Establishment of a standard

(1)(A) The Secretary shall publish in the Federal Register a notice of proposed rulemaking for the establishment, amendment, or revocation of any performance standard for a device.

(B) A notice of proposed rulemaking for the establishment or amendment of a performance standard for a device shall—

(i) set forth a finding with supporting justification that the performance standard is appropriate and necessary to provide reasonable assurance of the safety and effectiveness of the device,

(ii) set forth proposed findings with respect to the risk of illness or injury that the performance standard is intended to reduce or eliminate,

(iii) invite interested persons to submit to the Secretary, within 30 days of the publication of the notice, requests for changes in the classification of the device pursuant to section 360c(e) of this title based on new information relevant to the classification, and

(iv) invite interested persons to submit an existing performance standard for the device, including a draft or proposed performance standard, for consideration by the Secretary.

(C) A notice of proposed rulemaking for the revocation of a performance standard shall set forth a finding with supporting justification that the performance standard is no longer necessary to provide reasonable assurance of the safety and effectiveness of a device.

(D) The Secretary shall provide for a comment period of not less than 60 days.

(2) If, after publication of a notice in accordance with paragraph (1), the Secretary receives a request for a change in the classification of the device, the Secretary shall, within 60 days of the publication of the notice, after consultation with the appropriate panel under section 360c of this title, either deny the request or give notice of an intent to initiate such change under section 360c(e) of this title.

(3)(A) After the expiration of the period for comment on a notice of proposed rulemaking published under paragraph (1) respecting a performance standard and after consideration of such comments and any report from an advisory committee under paragraph (5), the Secretary shall (i) promulgate a regulation establishing a performance standard and publish in the Federal

Register findings on the matters referred to in paragraph (1), or (ii) publish a notice terminating the proceeding for the development of the standard together with the reasons for such termination. If a notice of termination is published, the Secretary shall (unless such notice is issued because the device is a banned device under section 360f of this title) initiate a proceeding under section 360c(e) of this title to reclassify the device subject to the proceeding terminated by such notice.

(B) A regulation establishing a performance standard shall set forth the date or dates upon which the standard shall take effect, but no such regulation may take effect before one year after the date of its publication unless (i) the Secretary determines that an earlier effective date is necessary for the protection of the public health and safety, or (ii) such standard has been established for a device which, effective upon the effective date of the standard, has been reclassified from class III to class II. Such date or dates shall be established so as to minimize, consistent with the public health and safety, economic loss to, and disruption or dislocation of, domestic and international trade.

(4)(A) The Secretary, upon his own initiative or upon petition of an interested person may by regulation, promulgated in accordance with the requirements of paragraphs (1), (2), and (3)(B) of this subsection, amend or revoke a performance standard.

(B) The Secretary may declare a proposed amendment of a performance standard to be effective on and after its publication in the Federal Register and until the effective date of any final action taken on such amendment if he determines that making it so effective is in the public interest. A proposed amendment of a performance standard made so effective under the preceding sentence may not prohibit, during the period in which it is so effective, the introduction or delivery for introduction into interstate commerce of a device which conforms to such standard without the change or changes provided by such proposed amendment.

(5)(A) The Secretary—

(i) may on his own initiative refer a proposed regulation for the establishment, amendment, or revocation of a performance standard, or

(ii) shall, upon the request of an interested person which demonstrates good cause for referral and which is made before the expiration of the period for submission of comments on such proposed regulation refer such proposed regulation,

to an advisory committee of experts, established pursuant to subparagraph (B), for a report and recommendation with respect to any matter involved in the proposed regulation which requires the exercise of scientific judgment. If a proposed regulation is referred under this subparagraph to an advisory committee, the Secretary shall provide the advisory committee with the data and information on which such proposed regulation is based. The advisory committee shall, within sixty days of the referral of a proposed regulation and after independent study of the data and information furnished to it by the Secretary and other data and information before it, submit to the Secretary a report and recommendation respecting such regulation, together with all underlying data and information and a statement of the reason or basis for the recommendation. A copy of such report and recommendation shall be made public by the Secretary.

(B) The Secretary shall establish advisory committees (which may not be panels under section 360c of this title) to receive referrals under subparagraph (A). The Secretary shall appoint as members of any such advisory committee persons qualified in the subject matter to be referred to the committee and of appropriately diversified professional background, except that the Secretary may not appoint to such a committee any individual who is in the regular full-time employ of the United States and engaged in the administration of this chapter. Each such committee shall include as nonvoting members a representative of consumer interests and a representative of interests of the device manufacturing industry. Members of an advisory committee who are not officers or employees of the United States, while attending conferences or meetings of their committee or otherwise serving at the request of the Secretary, shall be entitled to receive compensation at rates to be fixed by the Secretary, which rates may not exceed the daily equivalent of the rate in effect for grade GS–18 of the General Schedule, for each day (including traveltime) they are so engaged; and while so serving away from their homes or regular places of business each member may be allowed travel expenses, including per diem in lieu of subsistence, as authorized by section 5703 of title 5 for persons in the Government service employed intermittently. The Secretary shall designate one of the members of each advisory committee to serve as chairman thereof. The Secretary shall furnish each advisory committee with clerical and other assistance, and shall by regulation prescribe the procedures to be followed by each such committee in acting on referrals made under subparagraph (A).

(c) Recognition of standard

(1)(A) In addition to establishing a performance standard under this section, the Secretary shall, by publication in the Federal Register (or, with respect to a susceptibility test interpretive criteria standard under section 360a–2 of this title, by posting on the Interpretive Criteria Website in accordance with such section), recognize all or part of an appropriate standard established by a nationally or internationally recognized standard development organization for which a person may submit a declaration of conformity in order to meet a premarket submission requirement or other requirement under this chapter to which such standard is applicable.

(B) If a person elects to use a standard recognized by the Secretary under subparagraph (A) to meet the requirements described in such subparagraph, the person shall provide a declaration of conformity to the Secretary that certifies that the device is in conformity with such standard. A person may elect to use data, or information, other than data required by a standard recognized under subparagraph (A) to meet

any requirement regarding devices under this chapter.

(C)(i) Any person may submit a request for recognition under subparagraph (A) of all or part of an appropriate standard established by a nationally or internationally recognized standard organization.[1]

(ii) Not later than 60 calendar days after the Secretary receives such a request, the Secretary shall—

(I) make a determination to recognize all, part, or none of the standard that is the subject of the request; and

(II) issue to the person who submitted such request a response in writing that states the Secretary's rationale for that determination, including the scientific, technical, regulatory, or other basis for such determination.

(iii) The Secretary shall make a response issued under clause (ii)(II) publicly available, in such a manner as the Secretary determines appropriate.

(iv) The Secretary shall take such actions as may be necessary to implement all or part of a standard recognized under clause (ii)(I), in accordance with subparagraph (A).

(D) The Secretary shall make publicly available, in such manner as the Secretary determines appropriate, the rationale for recognition under subparagraph (A) of all, part, or none of a standard, including the scientific, technical, regulatory, or other basis for the decision regarding such recognition.

(2) The Secretary may withdraw such recognition of a standard through publication of a notice in the Federal Register if the Secretary determines that the standard is no longer appropriate for meeting a requirement regarding devices under this chapter.

(3)(A) Subject to subparagraph (B), the Secretary shall accept a declaration of conformity that a device is in conformity with a standard recognized under paragraph (1) unless the Secretary finds—

(i) that the data or information submitted to support such declaration does not demonstrate that the device is in conformity with the standard identified in the declaration of conformity; or

(ii) that the standard identified in the declaration of conformity is not applicable to the particular device under review.

(B) The Secretary may request, at any time, the data or information relied on by the person to make a declaration of conformity with respect to a standard recognized under paragraph (1).

(C) A person making a declaration of conformity with respect to a standard recognized under paragraph (1) shall maintain the data and information demonstrating conformity of the device to the standard for a period of two years after the date of the classification or approval of the device by the Secretary or a period equal to the expected design life of the device, whichever is longer.

(4) The Secretary shall provide to all employees of the Food and Drug Administration who review premarket submissions for devices periodic training on the concept and use of recognized standards for purposes of meeting a premarket submission requirement or other applicable requirement under this chapter, including standards relevant to an employee's area of device review.

(d) Accreditation scheme for conformity assessment

(1) In general

The Secretary shall establish a program under which—

(A) testing laboratories meeting criteria specified in guidance by the Secretary may be accredited, by accreditation bodies meeting criteria specified in guidance by the Secretary, to conduct testing to support the assessment of the conformity of a device to certain standards recognized under this section; and

(B) subject to paragraph (2), results from tests conducted to support the assessment of conformity of devices as described in subparagraph (A) conducted by testing laboratories accredited pursuant to this subsection shall be accepted by the Secretary for purposes of demonstrating such conformity unless the Secretary finds that certain results of such tests should not be so accepted.

(2) Secretarial review of accredited laboratory results

The Secretary may—

(A) review the results of tests conducted by testing laboratories accredited pursuant to this subsection, including by conducting periodic audits of such results or of the processes of accredited bodies or testing laboratories;

(B) following such review, take additional measures under this chapter, as the Secretary determines appropriate, such as—

(i) suspension or withdrawal of accreditation of a testing laboratory or recognition of an accreditation body under paragraph (1)(A); or

(ii) requesting additional information with respect to a device; and

(C) if the Secretary becomes aware of information materially bearing on the safety or effectiveness of a device for which an assessment of conformity was supported by testing conducted by a testing laboratory accredited under this subsection, take such additional measures under this chapter, as the Secretary determines appropriate, such as—

(i) suspension or withdrawal of accreditation of a testing laboratory or recognition of an accreditation body under paragraph (1)(A); or

(ii) requesting additional information with regard to such device.

(3) Report

The Secretary shall make available on the internet website of the Food and Drug Administration an annual report on the progress of the program under this subsection.

(June 25, 1938, ch. 675, §514, as added Pub. L. 94–295, §2, May 28, 1976, 90 Stat. 546; amended

[1] So in original. Probably should be ''standard development organization.''

Pub. L. 94–460, title III, § 304, Oct. 8, 1976, 90 Stat. 1960; Pub. L. 101–629, §§ 6(a), (b)(1), 18(b), Nov. 28, 1990, 104 Stat. 4519, 4528; Pub. L. 102–300, § 6(g), June 16, 1992, 106 Stat. 241; Pub. L. 103–80, § 4(a)(1), Aug. 13, 1993, 107 Stat. 779; Pub. L. 105–115, title II, § 204(a), (d), Nov. 21, 1997, 111 Stat. 2335, 2336; Pub. L. 112–144, title VI, § 608(a)(2)(B), July 9, 2012, 126 Stat. 1056; Pub. L. 114–255, div. A, title III, §§ 3044(b)(3), 3053(a), Dec. 13, 2016, 130 Stat. 1121, 1125; Pub. L. 115–52, title II, § 205(a), Aug. 18, 2017, 131 Stat. 1016; Pub. L. 117–180, div. F, title II, § 2005, Sept. 30, 2022, 136 Stat. 2153.)

Editorial Notes

Amendments

2022—Subsec. (d). Pub. L. 117–180 amended subsec. (d) generally. Prior to amendment, subsec. (d) related to a pilot program for accrediting laboratories to assess device conformance.

2017—Subsec. (d). Pub. L. 115–52 added subsec. (d).

2016—Subsec. (c)(1)(A). Pub. L. 114–255, § 3044(b)(3), inserted ''(or, with respect to a susceptibility test interpretive criteria standard under section 360a–2 of this title, by posting on the Interpretive Criteria Website in accordance with such section)'' after ''the Secretary shall, by publication in the Federal Register''.

Subsec. (c)(1)(C), (D). Pub. L. 114–255, § 3053(a)(1), added subpars. (C) and (D).

Subsec. (c)(4). Pub. L. 114–255, § 3053(a)(2), added par. (4).

2012—Subsec. (a)(1). Pub. L. 112–144 substituted ''under an administrative order under section 360c(e) of this title (or a regulation promulgated under such section prior to July 9, 2012) but such order (or regulation)'' for ''under a regulation under section 360c(e) of this title but such regulation''.

1997—Subsec. (a)(1). Pub. L. 105–115, § 204(d)(1), substituted ''under subsection (b)'' for ''under this section''.

Subsec. (a)(2). Pub. L. 105–115, § 204(d)(2), substituted ''under subsection (b)'' for ''under this section'' in introductory provisions.

Subsec. (a)(3). Pub. L. 105–115, § 204(d)(3), substituted ''under subsection (b)'' for ''under this section''.

Subsec. (a)(4). Pub. L. 105–115, § 204(d)(4), substituted ''this subsection and subsection (b)'' for ''this section'' in introductory provisions.

Subsec. (c). Pub. L. 105–115, § 204(a), added subsec. (c).

1993—Subsec. (b)(4)(B), (5)(A)(ii). Pub. L. 103–80 amended directory language of Pub. L. 101–619, § 18(b), identical to amendment by Pub. L. 102–300, § 6(g)(1). See 1992 and 1990 Amendment notes below.

1992—Subsec. (b)(4)(B), (5)(A)(ii). Pub. L. 102–300 made technical corrections to directory language of Pub. L. 101–629, § 18(b)(1), (2). See 1990 Amendment note below.

1990—Subsec. (a)(1). Pub. L. 101–629, § 6(a)(1), substituted ''The special controls required by section 360c(a)(1)(B) of this title shall include performance standards for a class II device if the Secretary determines that a performance standard is necessary to provide reasonable assurance of the safety and effectiveness of the device.'' for ''The Secretary may by regulation, promulgated in accordance with this section, establish a performance standard for a class II device.''

Subsec. (b). Pub. L. 101–629, § 6(a)(2), (3), redesignated subsec. (g) as (b) and struck out former subsec. (b) which read as follows:

''(1) A proceeding for the development of a performance standard for a device shall be initiated by the Secretary by the publication in the Federal Register of notice of the opportunity to submit to the Secretary a request (within fifteen days of the date of the publication of the notice) for a change in the classification of the device based on new information relevant to its classification.

''(2) If, after publication of a notice pursuant to paragraph (1) the Secretary receives a request for a change in the device's classification, he shall, within sixty days of the publication of such notice and after consultation with the appropriate panel under section 360c of this title, by order published in the Federal Register, either deny the request for change in classification or give notice of his intent to initiate such a change under section 360c(e) of this title.''

Subsec. (b)(1), (2). Pub. L. 101–629, § 6(a)(4), amended pars. (1) and (2) generally. Prior to amendment, pars. (1) and (2) read as follows:

''(1)(A) After publication pursuant to subsection (c) of this section of a notice respecting a performance standard for a device, the Secretary shall either—

''(i) publish, in the Federal Register in a notice of proposed rulemaking, a proposed performance standard for the device (I) developed by an offeror under such notice and accepted by the Secretary, (II) developed under subsection (c)(4) of this section, (III) accepted by the Secretary under subsection (d) of this section, or (IV) developed by him under subsection (f) of this section, or

''(ii) issue a notice in the Federal Register that the proceeding is terminated together with the reasons for such termination.

''(B) If the Secretary issues under subparagraph (A)(ii) a notice of termination of a proceeding to establish a performance standard for a device, he shall (unless such notice is issued because the device is a banned device under section 360f of this title) initiate a proceeding under section 360c(e) of this title to reclassify the device subject to the proceeding terminated by such notice.

''(2) A notice of proposed rulemaking for the establishment of a performance standard for a device published under paragraph (1)(A)(i) shall set forth proposed findings with respect to the degree of the risk of illness or injury designed to be eliminated or reduced by the proposed standard and the benefit to the public from the device.''

Subsec. (b)(3)(A)(i). Pub. L. 101–629, § 6(b)(1)(A), substituted ''paragraph (1)'' for ''paragraph (2)''.

Subsec. (b)(4)(A). Pub. L. 101–629, § 6(b)(1)(B), substituted ''paragraphs (1), (2), and (3)(B)'' for ''paragraphs (2) and (3)(B)''.

Subsec. (b)(4)(B). Pub. L. 101–629, § 18(b)(1), as amended by Pub. L. 102–300, § 6(g)(1), (2), and Pub. L. 103–80, § 4(a)(1), struck out '', after affording all interested persons an opportunity for an informal hearing,'' after ''if he determines''.

Subsec. (b)(5)(A)(ii). Pub. L. 101–629, § 18(b)(2), as amended by Pub. L. 102–300, § 6(g)(1), (3), and Pub. L. 103–80, § 4(a)(1), substituted ''which demonstrates good cause for referral and which is made before the expiration of the period for submission of comments on such proposed regulation refer such proposed regulation,'' for ''unless the Secretary finds the request to be without good cause or the request is made after the expiration of the period for submission of comments on such proposed regulation refer such proposed regulation,''.

Subsecs. (c) to (f). Pub. L. 101–629, § 6(a)(2), struck out subsec. (c) relating to invitations for standards, subsec. (d) relating to acceptance of certain existing standards, subsec. (e) relating to acceptance of offers to develop standards, and subsec. (f) relating to development of standards by the Secretary after publication of notice inviting submissions or offers of standards.

Subsec. (g). Pub. L. 101–629, § 6(a)(3), redesignated subsec. (g) as (b).

1976—Subsec. (a). Pub. L. 94–460 redesignated pars. (4) and (5) as (3) and (4), respectively. Section as originally enacted contained no par. (3).

Statutory Notes and Related Subsidiaries

Effective Date of 2022 Amendment

Pub. L. 117–180, div. F, title II, § 2008, Sept. 30, 2022, 136 Stat. 2154, provided that: ''The amendments made by this title [amending this section and sections 360m and 379i to 379j–1 of this title and repealing provisions set

out as notes under sections 379i and 379j–1 of this title] shall take effect on October 1, 2022, or the date of the enactment of this Act [Sept. 30, 2022], whichever is later, except that fees under part 3 of subchapter C of chapter VII of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 379i et seq.) shall be assessed for all submissions listed in section 738(a)(2)(A) of such Act [21 U.S.C. 379j(a)(2)(A)] received on or after October 1, 2022, regardless of the date of the enactment of this Act.''

EFFECTIVE DATE OF 2017 AMENDMENT

Amendment by Pub. L. 115–52 effective Oct. 1, 2017, with fees under subpart 3 of part C of subchapter VII of this chapter to be assessed for all submissions listed in section 379j(a)(2)(A) of this title received on or after Oct. 1, 2017, see section 209 of Pub. L. 115–52, set out as a note under section 379i of this title.

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by Pub. L. 105–115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as a note under section 321 of this title.

CONSTRUCTION OF 2016 AMENDMENT

Nothing in amendment by section 3044(b)(3) of Pub. L. 114–255 to be construed to restrict the prescribing of antimicrobial drugs or other products, including drugs approved under section 356(h) of this title, by health care professionals, or to limit the practice of health care, see section 3043 of Pub. L. 114–255, set out as a note under section 356 of this title.

TERMINATION OF ADVISORY COMMITTEES

Advisory committees in existence on Jan. 5, 1973, to terminate not later than the expiration of the 2-year period following Jan. 5, 1973, and advisory committees established after Jan. 5, 1973, to terminate not later than the expiration of the 2-year period beginning on the date of their establishment, unless in the case of a committee established by the President or an officer of the Federal Government, such committee is renewed by appropriate action prior to the expiration of such 2-year period, or in the case of a committee established by Congress, its duration is otherwise provided by law. See section 1013 of Title 5, Government Organization and Employees.

GUIDANCE

Pub. L. 114–255, div. A, title III, § 3053(b), Dec. 13, 2016, 130 Stat. 1125, provided that: ''The Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs, shall review and update, if necessary, previously published guidance and standard operating procedures identifying the principles for recognizing standards, and for withdrawing the recognition of standards, under section 514(c) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360d(c)), taking into account the experience with and reliance on a standard by foreign regulatory authorities and the device industry, and whether recognition of a standard will promote harmonization among regulatory authorities in the regulation of devices.''

REFERENCES IN OTHER LAWS TO GS–16, 17, OR 18 PAY RATES

References in laws to the rates of pay for GS–16, 17, or 18, or to maximum rates of pay under the General Schedule, to be considered references to rates payable under specified sections of Title 5, Government Organization and Employees, see section 529 [title I, § 101(c)(1)] of Pub. L. 101–509, set out in a note under section 5376 of Title 5.

§ 360e. Premarket approval

(a) General requirement

A class III device—

(1) which is subject to an order issued under subsection (b) (or a regulation promulgated under such subsection prior to July 9, 2012); or

(2) which is a class III device because of section 360c(f) of this title,

is required to have, unless exempt under section 360j(g) of this title, an approval under this section of an application for premarket approval or, as applicable, an approval under subsection (c)(2) of a report seeking premarket approval.

(b) Order to require premarket approval

(1) In the case of a class III device which—

(A) was introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976; or

(B) is (i) of a type so introduced or delivered, and (ii) is substantially equivalent to another device within that type,

the Secretary shall by administrative order following publication of a proposed order in the Federal Register, a meeting of a device classification panel described in section 360c(b) of this title, and consideration of comments from all affected stakeholders, including patients, payors, and providers, notwithstanding subchapter II of chapter 5 of title 5, require that such device have an approval under this section of an application for premarket approval. Authority to issue such administrative order shall not be delegated below the Director of the Center for Devices and Radiological Health, acting in consultation with the Commissioner.

(2) A proposed order required under paragraph (1) shall contain—

(A) the proposed order;

(B) proposed findings with respect to the degree of risk of illness or injury designed to be eliminated or reduced by requiring the device to have an approved application for premarket approval and the benefit to the public from use of the device;

(C) opportunity for the submission of comments on the proposed order and the proposed findings; and

(D) opportunity to request a change in the classification of the device based on new information relevant to the classification of the device.

(3) After the expiration of the period for comment on a proposed order and proposed findings published under paragraph (2), consideration of comments submitted on such proposed order and findings, and a meeting of a device classification panel described in section 360c(b) of this title, the Secretary shall (A) issue an administrative order under paragraph (1) and publish in the Federal Register findings on the matters referred to in paragraph (2)(B), or (B) publish a notice terminating the proceeding for the issuance of the administrative order together with the reasons for such termination. If a notice of termination is published, the Secretary shall (unless such notice is issued because the device is a banned device under section 360f of this title) initiate a proceeding under section 360c(e) of this title to reclassify the device subject to the proceeding terminated by such notice.

(c) Application for premarket approval

(1) Any person may file with the Secretary an application for premarket approval for a class

III device. Such an application for a device shall contain—

(A) full reports of all information, published or known to or which should reasonably be known to the applicant, concerning investigations which have been made to show whether or not such device is safe and effective;

(B) a full statement of the components, ingredients, and properties and of the principle or principles of operation, of such device;

(C) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and, when relevant, packing and installation of, such device;

(D) an identifying reference to any performance standard under section 360d of this title which would be applicable to any aspect of such device if it were a class II device, and either adequate information to show that such aspect of such device fully meets such performance standard or adequate information to justify any deviation from such standard;

(E) such samples of such device and of components thereof as the Secretary may reasonably require, except that where the submission of such samples is impracticable or unduly burdensome, the requirement of this subparagraph may be met by the submission of complete information concerning the location of one or more such devices readily available for examination and testing;

(F) specimens of the labeling proposed to be used for such device;

(G) the certification required under section 282(j)(5)(B) of title 42 (which shall not be considered an element of such application); and

(H) such other information relevant to the subject matter of the application as the Secretary, with the concurrence of the appropriate panel under section 360c of this title, may require.

(2)(A) Any person may file with the Secretary a report seeking premarket approval for a class III device referred to in subsection (a) that is a reprocessed single-use device. Such a report shall contain the following:

(i) The device name, including both the trade or proprietary name and the common or usual name.

(ii) The establishment registration number of the owner or operator submitting the report.

(iii) Actions taken to comply with performance standards under section 360d of this title.

(iv) Proposed labels, labeling, and advertising sufficient to describe the device, its intended use, and directions for use.

(v) Full reports of all information, published or known to or which should be reasonably known to the applicant, concerning investigations which have been made to show whether or not the device is safe or effective.

(vi) A description of the device's components, ingredients, and properties.

(vii) A full description of the methods used in, and the facilities and controls used for, the reprocessing and packing of the device.

(viii) Such samples of the device that the Secretary may reasonably require.

(ix) A financial certification or disclosure statement or both, as required by part 54 of title 21, Code of Federal Regulations.

(x) A statement that the applicant believes to the best of the applicant's knowledge that all data and information submitted to the Secretary are truthful and accurate and that no material fact has been omitted in the report.

(xi) Any additional data and information, including information of the type required in paragraph (1) for an application under such paragraph, that the Secretary determines is necessary to determine whether there is reasonable assurance of safety and effectiveness for the reprocessed device.

(xii) Validation data described in section 360(*o*)(1)(A) of this title that demonstrates that the reasonable assurance of the safety or effectiveness of the device will remain after the maximum number of times the device is reprocessed as intended by the person submitting such report.

(B) In the case of a class III device referred to in subsection (a) that is a reprocessed single-use device:

(i) Subparagraph (A) of this paragraph applies in lieu of paragraph (1).

(ii) Subject to clause (i), the provisions of this section apply to a report under subparagraph (A) to the same extent and in the same manner as such provisions apply to an application under paragraph (1).

(iii) Each reference in other sections of this chapter to an application under this section, other than such a reference in section 379i or 379j of this title, shall be considered to be a reference to a report under subparagraph (A).

(iv) Each reference in other sections of this chapter to a device for which an application under this section has been approved, or has been denied, suspended, or withdrawn, other than such a reference in section 379i or 379j of this title, shall be considered to be a reference to a device for which a report under subparagraph (A) has been approved, or has been denied, suspended, or withdrawn, respectively.

(3) Upon receipt of an application meeting the requirements set forth in paragraph (1), the Secretary—

(A) may on the Secretary's own initiative, or

(B) shall, upon the request of an applicant unless the Secretary finds that the information in the application which would be reviewed by a panel substantially duplicates information which has previously been reviewed by a panel appointed under section 360c of this title,

refer such application to the appropriate panel under section 360c of this title for study and for submission (within such period as he may establish) of a report and recommendation respecting approval of the application, together with all underlying data and the reasons or basis for the recommendation. Where appropriate, the Secretary shall ensure that such panel includes, or consults with, one or more pediatric experts.

(4)(A) Prior to the submission of an application under this subsection, the Secretary shall accept and review any portion of the application that the applicant and the Secretary agree is complete, ready, and appropriate for review, except that such requirement does not apply, and the Secretary has discretion whether to accept

and review such portion, during any period in which, under section 379j(g) of this title, the Secretary does not have the authority to collect fees under section 379j(a) of this title.

(B) Each portion of a submission reviewed under subparagraph (A) and found acceptable by the Secretary shall not be further reviewed after receipt of an application that satisfies the requirements of paragraph (1), unless a significant issue of safety or effectiveness provides the Secretary reason to review such accepted portion.

(C) Whenever the Secretary determines that a portion of a submission under subparagraph (A) is unacceptable, the Secretary shall, in writing, provide to the applicant a description of any deficiencies in such portion and identify the information that is required to correct these deficiencies, unless the applicant is no longer pursuing the application.

(5)(A) In requesting additional information with respect to an application under this section, the Secretary shall consider the least burdensome appropriate means necessary to demonstrate a reasonable assurance of device safety and effectiveness.

(B) For purposes of subparagraph (A), the term ''necessary'' means the minimum required information that would support a determination by the Secretary that an application provides a reasonable assurance of the safety and effectiveness of the device.

(C) For purposes of this paragraph, the Secretary shall consider the role of postmarket information in determining the least burdensome means of demonstrating a reasonable assurance of device safety and effectiveness.

(D) Nothing in this paragraph alters the standards for premarket approval of a device.

(d) Action on application for premarket approval

(1)(A) As promptly as possible, but in no event later than one hundred and eighty days after the receipt of an application under subsection (c) (except as provided in section 360j(*l*)(3)(D)(ii) of this title or unless, in accordance with subparagraph (B)(i), an additional period as agreed upon by the Secretary and the applicant), the Secretary, after considering the report and recommendation submitted under paragraph (2) of such subsection, shall—

(i) issue an order approving the application if he finds that none of the grounds for denying approval specified in paragraph (2) of this subsection applies; or

(ii) deny approval of the application if he finds (and sets forth the basis for such finding as part of or accompanying such denial) that one or more grounds for denial specified in paragraph (2) of this subsection apply.

In making the determination whether to approve or deny the application, the Secretary shall rely on the conditions of use included in the proposed labeling as the basis for determining whether or not there is a reasonable assurance of safety and effectiveness, if the proposed labeling is neither false nor misleading. In determining whether or not such labeling is false or misleading, the Secretary shall fairly evaluate all material facts pertinent to the proposed labeling.

(B)(i) The Secretary may not enter into an agreement to extend the period in which to take action with respect to an application submitted for a device subject to a regulation promulgated under subsection (b) unless he finds that the continued availability of the device is necessary for the public health.

(ii) An order approving an application for a device may require as a condition to such approval that the sale and distribution of the device be restricted but only to the extent that the sale and distribution of a device may be restricted under a regulation under section 360j(e) of this title.

(iii) The Secretary shall accept and review statistically valid and reliable data and any other information from investigations conducted under the authority of regulations required by section 360j(g) of this title to make a determination of whether there is a reasonable assurance of safety and effectiveness of a device subject to a pending application under this section if—

(I) the data or information is derived from investigations of an earlier version of the device, the device has been modified during or after the investigations (but prior to submission of an application under subsection (c)) and such a modification of the device does not constitute a significant change in the design or in the basic principles of operation of the device that would invalidate the data or information; or

(II) the data or information relates to a device approved under this section, is available for use under this chapter, and is relevant to the design and intended use of the device for which the application is pending.

(2) The Secretary shall deny approval of an application for a device if, upon the basis of the information submitted to the Secretary as part of the application and any other information before him with respect to such device, the Secretary finds that—

(A) there is a lack of a showing of reasonable assurance that such device is safe under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof;

(B) there is a lack of a showing of reasonable assurance that the device is effective under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof;

(C) the methods used in, or the facilities or controls used for, the manufacture, processing, packing, or installation of such device do not conform to the requirements of section 360j(f) of this title;

(D) based on a fair evaluation of all material facts, the proposed labeling is false or misleading in any particular; or

(E) such device is not shown to conform in all respects to a performance standard in effect under section 360d of this title compliance with which is a condition to approval of the application and there is a lack of adequate information to justify the deviation from such standard.

Any denial of an application shall, insofar as the Secretary determines to be practicable, be accompanied by a statement informing the applicant of the measures required to place such application in approvable form (which measures

may include further research by the applicant in accordance with one or more protocols prescribed by the Secretary).

(3)(A)(i) The Secretary shall, upon the written request of an applicant, meet with the applicant, not later than 100 days after the receipt of an application that has been filed as complete under subsection (c), to discuss the review status of the application.

(ii) The Secretary shall, in writing and prior to the meeting, provide to the applicant a description of any deficiencies in the application that, at that point, have been identified by the Secretary based on an interim review of the entire application and identify the information that is required to correct those deficiencies.

(iii) The Secretary shall notify the applicant promptly of—

(I) any additional deficiency identified in the application, or

(II) any additional information required to achieve completion of the review and final action on the application,

that was not described as a deficiency in the written description provided by the Secretary under clause (ii).

(B) The Secretary and the applicant may, by mutual consent, establish a different schedule for a meeting required under this paragraph.

(4) An applicant whose application has been denied approval may, by petition filed on or before the thirtieth day after the date upon which he receives notice of such denial, obtain review thereof in accordance with either paragraph (1) or (2) of subsection (g), and any interested person may obtain review, in accordance with paragraph (1) or (2) of subsection (g), of an order of the Secretary approving an application.

(5)(A)(i) Unless the change is consistent with a predetermined change control plan approved under section 360e–4 of this title, a supplemental application shall be required for any change to a device subject to an approved application under this subsection that affects safety or effectiveness, unless such change is a modification in a manufacturing procedure or method of manufacturing and the holder of the approved application submits a written notice to the Secretary that describes in detail the change, summarizes the data or information supporting the change, and informs the Secretary that the change has been made under the requirements of section 360j(f) of this title.

(ii) The holder of an approved application who submits a notice under clause (i) with respect to a manufacturing change of a device may distribute the device 30 days after the date on which the Secretary receives the notice, unless the Secretary within such 30-day period notifies the holder that the notice is not adequate and describes such further information or action that is required for acceptance of such change. If the Secretary notifies the holder that a supplemental application is required, the Secretary shall review the supplement within 135 days after the receipt of the supplement. The time used by the Secretary to review the notice of the manufacturing change shall be deducted from the 135-day review period if the notice meets appropriate content requirements for premarket approval supplements.

(B)(i) Subject to clause (ii), in reviewing a supplement to an approved application, for an incremental change to the design of a device that affects safety or effectiveness, the Secretary shall approve such supplement if—

(I) nonclinical data demonstrate that the design modification creates the intended additional capacity, function, or performance of the device; and

(II) clinical data from the approved application and any supplement to the approved application provide a reasonable assurance of safety and effectiveness for the changed device.

(ii) The Secretary may require, when necessary, additional clinical data to evaluate the design modification of the device to provide a reasonable assurance of safety and effectiveness.

(e) Withdrawal and temporary suspension of approval of application

(1) The Secretary shall, upon obtaining, where appropriate, advice on scientific matters from a panel or panels under section 360c of this title, and after due notice and opportunity for informal hearing to the holder of an approved application for a device, issue an order withdrawing approval of the application if the Secretary finds—

(A) that such device is unsafe or ineffective under the conditions of use prescribed, recommended, or suggested in the labeling thereof;

(B) on the basis of new information before him with respect to such device, evaluated together with the evidence available to him when the application was approved, that there is a lack of a showing of reasonable assurance that the device is safe or effective under the conditions of use prescribed, recommended, or suggested in the labeling thereof;

(C) that the application contained or was accompanied by an untrue statement of a material fact;

(D) that the applicant (i) has failed to establish a system for maintaining records, or has repeatedly or deliberately failed to maintain records or to make reports, required by an applicable regulation under section 360i(a) of this title, (ii) has refused to permit access to, or copying or verification of, such records as required by section 374 of this title, or (iii) has not complied with the requirements of section 360 of this title;

(E) on the basis of new information before him with respect to such device, evaluated together with the evidence before him when the application was approved, that the methods used in, or the facilities and controls used for, the manufacture, processing, packing, or installation of such device do not conform with the requirements of section 360j(f) of this title and were not brought into conformity with such requirements within a reasonable time after receipt of written notice from the Secretary of nonconformity;

(F) on the basis of new information before him, evaluated together with the evidence before him when the application was approved, that the labeling of such device, based on a fair evaluation of all material facts, is false or

misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary of such fact; or

(G) on the basis of new information before him, evaluated together with the evidence before him when the application was approved, that such device is not shown to conform in all respects to a performance standard which is in effect under section 360d of this title compliance with which was a condition to approval of the application and that there is a lack of adequate information to justify the deviation from such standard.

(2) The holder of an application subject to an order issued under paragraph (1) withdrawing approval of the application may, by petition filed on or before the thirtieth day after the date upon which he receives notice of such withdrawal, obtain review thereof in accordance with either paragraph (1) or (2) of subsection (g).

(3) If, after providing an opportunity for an informal hearing, the Secretary determines there is reasonable probability that the continuation of distribution of a device under an approved application would cause serious, adverse health consequences or death, the Secretary shall by order temporarily suspend the approval of the application approved under this section. If the Secretary issues such an order, the Secretary shall proceed expeditiously under paragraph (1) to withdraw such application.

(f) Product development protocol

(1) In the case of a class III device which is required to have an approval of an application submitted under subsection (c), such device shall be considered as having such an approval if a notice of completion of testing conducted in accordance with a product development protocol approved under paragraph (4) has been declared completed under paragraph (6).

(2) Any person may submit to the Secretary a proposed product development protocol with respect to a device. Such a protocol shall be accompanied by data supporting it. If, within thirty days of the receipt of such a protocol, the Secretary determines that it appears to be appropriate to apply the requirements of this subsection to the device with respect to which the protocol is submitted, the Secretary—

(A) may, at the initiative of the Secretary, refer the proposed protocol to the appropriate panel under section 360c of this title for its recommendation respecting approval of the protocol; or

(B) shall so refer such protocol upon the request of the submitter, unless the Secretary finds that the proposed protocol and accompanying data which would be reviewed by such panel substantially duplicate a product development protocol and accompanying data which have previously been reviewed by such a panel.

(3) A proposed product development protocol for a device may be approved only if—

(A) the Secretary determines that it is appropriate to apply the requirements of this subsection to the device in lieu of the requirement of approval of an application submitted under subsection (c); and

(B) the Secretary determines that the proposed protocol provides—

(i) a description of the device and the changes which may be made in the device,

(ii) a description of the preclinical trials (if any) of the device and a specification of (I) the results from such trials to be required before the commencement of clinical trials of the device, and (II) any permissible variations in preclinical trials and the results therefrom,

(iii) a description of the clinical trials (if any) of the device and a specification of (I) the results from such trials to be required before the filing of a notice of completion of the requirements of the protocol, and (II) any permissible variations in such trials and the results therefrom,

(iv) a description of the methods to be used in, and the facilities and controls to be used for, the manufacture, processing, and, when relevant, packing and installation of the device,

(v) an identifying reference to any performance standard under section 360d of this title to be applicable to any aspect of such device,

(vi) if appropriate, specimens of the labeling proposed to be used for such device,

(vii) such other information relevant to the subject matter of the protocol as the Secretary, with the concurrence of the appropriate panel or panels under section 360c of this title, may require, and

(viii) a requirement for submission of progress reports and, when completed, records of the trials conducted under the protocol which records are adequate to show compliance with the protocol.

(4) The Secretary shall approve or disapprove a proposed product development protocol submitted under paragraph (2) within one hundred and twenty days of its receipt unless an additional period is agreed upon by the Secretary and the person who submitted the protocol. Approval of a protocol or denial of approval of a protocol is final agency action subject to judicial review under chapter 7 of title 5.

(5) At any time after a product development protocol for a device has been approved pursuant to paragraph (4), the person for whom the protocol was approved may submit a notice of completion—

(A) stating (i) his determination that the requirements of the protocol have been fulfilled and that, to the best of his knowledge, there is no reason bearing on safety or effectiveness why the notice of completion should not become effective, and (ii) the data and other information upon which such determination was made, and

(B) setting forth the results of the trials required by the protocol and all the information required by subsection (c)(1).

(6)(A) The Secretary may, after providing the person who has an approved protocol an opportunity for an informal hearing and at any time prior to receipt of notice of completion of such protocol, issue a final order to revoke such protocol if he finds that—

(i) such person has failed substantially to comply with the requirements of the protocol,

(ii) the results of the trials obtained under the protocol differ so substantially from the results required by the protocol that further trials cannot be justified, or

(iii) the results of the trials conducted under the protocol or available new information do not demonstrate that the device tested under the protocol does not present an unreasonable risk to health and safety.

(B) After the receipt of a notice of completion of an approved protocol the Secretary shall, within the ninety-day period beginning on the date such notice is received, by order either declare the protocol completed or declare it not completed. An order declaring a protocol not completed may take effect only after the Secretary has provided the person who has the protocol opportunity for an informal hearing on the order. Such an order may be issued only if the Secretary finds—

(i) such person has failed substantially to comply with the requirements of the protocol,

(ii) the results of the trials obtained under the protocol differ substantially from the results required by the protocol, or

(iii) there is a lack of a showing of reasonable assurance of the safety and effectiveness of the device under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof.

(C) A final order issued under subparagraph (A) or (B) shall be in writing and shall contain the reasons to support the conclusions thereof.

(7) At any time after a notice of completion has become effective, the Secretary may issue an order (after due notice and opportunity for an informal hearing to the person for whom the notice is effective) revoking the approval of a device provided by a notice of completion which has become effective as provided in subparagraph (B) if he finds that any of the grounds listed in subparagraphs (A) through (G) of subsection (e)(1) of this section apply. Each reference in such subparagraphs to an application shall be considered for purposes of this paragraph as a reference to a protocol and the notice of completion of such protocol, and each reference to the time when an application was approved shall be considered for purposes of this paragraph as a reference to the time when a notice of completion took effect.

(8) A person who has an approved protocol subject to an order issued under paragraph (6)(A) revoking such protocol, a person who has an approved protocol with respect to which an order under paragraph (6)(B) was issued declaring that the protocol had not been completed, or a person subject to an order issued under paragraph (7) revoking the approval of a device may, by petition filed on or before the thirtieth day after the date upon which he receives notice of such order, obtain review thereof in accordance with either paragraph (1) or (2) of subsection (g).

(g) Review

(1) Upon petition for review of—

(A) an order under subsection (d) approving or denying approval of an application or an order under subsection (e) withdrawing approval of an application, or

(B) an order under subsection (f)(6)(A) revoking an approved protocol, under subsection (f)(6)(B) declaring that an approved protocol has not been completed, or under subsection (f)(7) revoking the approval of a device,

the Secretary shall, unless he finds the petition to be without good cause or unless a petition for review of such order has been submitted under paragraph (2), hold a hearing, in accordance with section 554 of title 5, on the order. The panel or panels which considered the application, protocol, or device subject to such order shall designate a member to appear and testify at any such hearing upon request of the Secretary, the petitioner, or the officer conducting the hearing, but this requirement does not preclude any other member of the panel or panels from appearing and testifying at any such hearing. Upon completion of such hearing and after considering the record established in such hearing, the Secretary shall issue an order either affirming the order subject to the hearing or reversing such order and, as appropriate, approving or denying approval of the application, reinstating the application's approval, approving the protocol, or placing in effect a notice of completion.

(2)(A) Upon petition for review of—

(i) an order under subsection (d) approving or denying approval of an application or an order under subsection (e) withdrawing approval of an application, or

(ii) an order under subsection (f)(6)(A) revoking an approved protocol, under subsection (f)(6)(B) declaring that an approved protocol has not been completed, or under subsection (f)(7) revoking the approval of a device,

the Secretary shall refer the application or protocol subject to the order and the basis for the order to an advisory committee of experts established pursuant to subparagraph (B) for a report and recommendation with respect to the order. The advisory committee shall, after independent study of the data and information furnished to it by the Secretary and other data and information before it, submit to the Secretary a report and recommendation, together with all underlying data and information and a statement of the reasons or basis for the recommendation. A copy of such report shall be promptly supplied by the Secretary to any person who petitioned for such referral to the advisory committee.

(B) The Secretary shall establish advisory committees (which may not be panels under section 360c of this title) to receive referrals under subparagraph (A). The Secretary shall appoint as members of any such advisory committee persons qualified in the subject matter to be referred to the committee and of appropriately diversified professional backgrounds, except that the Secretary may not appoint to such a committee any individual who is in the regular full-time employ of the United States and engaged in the administration of this chapter. Members of an advisory committee (other than officers or employees of the United States), while attending conferences or meetings of their committee or otherwise serving at the request of the Sec-

retary, shall be entitled to receive compensation at rates to be fixed by the Secretary, which rates may not exceed the daily equivalent for grade GS–18 of the General Schedule for each day (including traveltime) they are so engaged; and while so serving away from their homes or regular places of business each member may be allowed travel expenses, including per diem in lieu of subsistence, as authorized by section 5703 of title 5 for persons in the Government service employed intermittently. The Secretary shall designate the chairman of an advisory committee from its members. The Secretary shall furnish each advisory committee with clerical and other assistance, and shall by regulation prescribe the procedures to be followed by each such committee in acting on referrals made under subparagraph (A).

(C) The Secretary shall make public the report and recommendation made by an advisory committee with respect to an application and shall by order, stating the reasons therefor, either affirm the order referred to the advisory committee or reverse such order and, if appropriate, approve or deny approval of the application, reinstate the application's approval, approve the protocol, or place in effect a notice of completion.

(h) Service of orders

Orders of the Secretary under this section shall be served (1) in person by any officer or employee of the department designated by the Secretary, or (2) by mailing the order by registered mail or certified mail addressed to the applicant at his last known address in the records of the Secretary.

(i) Revision

(1) Before December 1, 1995, the Secretary shall by order require manufacturers of devices, which were introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, and which are subject to revision of classification under paragraph (2), to submit to the Secretary a summary of and citation to any information known or otherwise available to the manufacturer respecting such devices, including adverse safety or effectiveness information which has not been submitted under section 360i of this title. The Secretary may require the manufacturer to submit the adverse safety or effectiveness data for which a summary and citation were submitted, if such data are available to the manufacturer.

(2) After the issuance of an order under paragraph (1) but before the date that is 2 years after July 9, 2012, the Secretary shall issue an administrative order following publication of a proposed order in the Federal Register, a meeting of a device classification panel described in section 360c(b) of this title, and consideration of comments from all affected stakeholders, including patients, payors, and providers, notwithstanding subchapter II of chapter 5 of title 5, for each device—

(A) which the Secretary has classified as a class III device, and

(B) for which no administrative order has been issued under subsection (b) (or no regulation has been promulgated under such subsection prior to July 9, 2012),

revising the classification of the device so that the device is classified into class I or class II, unless the administrative order issued under this paragraph requires the device to remain in class III. In determining whether to revise the classification of a device or to require a device to remain in class III, the Secretary shall apply the criteria set forth in section 360c(a) of this title.

(3) The Secretary shall, as promptly as is reasonably achievable, but not later than 12 months after the effective date of the order requiring a device to remain in class III, establish a schedule for the issuance of an administrative order under subsection (b) for each device which is subject to the order requiring the device to remain in class III.

(June 25, 1938, ch. 675, §515, as added Pub. L. 94–295, §2, May 28, 1976, 90 Stat. 552; amended Pub. L. 101–629, §§4(b)(1), 9(a), 18(c), Nov. 28, 1990, 104 Stat. 4515, 4521, 4528; Pub. L. 103–80, §3(t), Aug. 13, 1993, 107 Stat. 778; Pub. L. 105–115, title II, §§201(b), 202, 205(c), 209(b), 216(b), Nov. 21, 1997, 111 Stat. 2334, 2338, 2341, 2349; Pub. L. 107–250, title II, §§209, 210, title III, §302(c), Oct. 26, 2002, 116 Stat. 1613, 1614, 1618; Pub. L. 108–214, §2(d)(1), Apr. 1, 2004, 118 Stat. 576; Pub. L. 110–85, title VIII, §801(b)(3)(D), Sept. 27, 2007, 121 Stat. 921; Pub. L. 112–144, title II, §203(g), title VI, §608(b)(1), July 9, 2012, 126 Stat. 1006, 1056; Pub. L. 114–255, div. A, title III, §§3051(c)(1), 3058(b), 3101(a)(2)(J), Dec. 13, 2016, 130 Stat. 1124, 1129, 1154; Pub. L. 115–52, title II, §203(f)(2)(A), Aug. 18, 2017, 131 Stat. 1015; Pub. L. 117–328, div. FF, title III, §3308(b)(2), Dec. 29, 2022, 136 Stat. 5836.)

Editorial Notes

AMENDMENTS

2022—Subsec. (d)(5)(A)(i). Pub. L. 117–328 substituted ''Unless the change is consistent with a predetermined change control plan approved under section 360e–4 of this title, a supplemental'' for ''A supplemental''.

2017—Subsec. (c)(4)(A). Pub. L. 115–52 substituted ''section 379j(g)'' for ''section 379j(h)''.

2016—Subsec. (a)(1). Pub. L. 114–255, §3101(a)(2)(J), substituted ''subject to an order'' for ''subject to a an order''.

Subsec. (c)(5). Pub. L. 114–255, §3058(b), added par. (5).

Subsec. (d)(5), (6). Pub. L. 114–255, §3051(c)(1), redesignated par. (6) as (5) and struck out former par. (5) which read as follows: ''In order to provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human diseases or conditions, the Secretary shall provide review priority for devices—

''(A) representing breakthrough technologies,

''(B) for which no approved alternatives exist,

''(C) which offer significant advantages over existing approved alternatives, or

''(D) the availability of which is in the best interest of the patients.''

2012—Subsec. (a)(1). Pub. L. 112–144, §608(b)(1)(A), substituted ''an order issued under subsection (b) (or a regulation promulgated under such subsection prior to July 9, 2012)'' for ''regulation promulgated under subsection (b)''.

Subsec. (b). Pub. L. 112–144, §608(b)(1)(B)(i)(I), which directed substitution of ''Order'' for ''Regulation'' in the heading of par. (1) of subsec. (b), was executed by making the substitution in the heading of subsec. (b), to reflect the probable intent of Congress.

Subsec. (b)(1). Pub. L. 112–144, §608(b)(1)(B)(i)(II), in concluding provisions, substituted ''by administrative order following publication of a proposed order in the

Federal Register, a meeting of a device classification panel described in section 360c(b) of this title, and consideration of comments from all affected stakeholders, including patients, payors, and providers, notwithstanding subchapter II of chapter 5 of title 5'' for ''by regulation, promulgated in accordance with this subsection'' and inserted at end ''Authority to issue such administrative order shall not be delegated below the Director of the Center for Devices and Radiological Health, acting in consultation with the Commissioner.''

Subsec. (b)(2). Pub. L. 112–144, § 608(b)(1)(B)(ii), struck out subpar. (A) designation after ''(2)'' and substituted ''A proposed order required under paragraph (1) shall contain—'' for ''A proceeding for the promulgation of a regulation under paragraph (1) respecting a device shall be initiated by the publication in the Federal Register of a notice of proposed rulemaking. Such notice shall contain—'' in introductory provisions, redesignated cls. (i) to (iv) as subpars. (A) to (D), respectively, substituted ''order'' for ''regulation'' in subpars. (A) and (C), and struck out former subpar. (B) which read as follows: ''If, within fifteen days after publication of a notice under subparagraph (A), the Secretary receives a request for a change in the classification of a device, he shall, within sixty days of the publication of such notice and after consultation with the appropriate panel under section 360c of this title, by order published in the Federal Register, either deny the request for change in classification or give notice of his intent to initiate such a change under section 360c(e) of this title.''

Subsec. (b)(3). Pub. L. 112–144, § 608(b)(1)(B)(iii)(I), (II), (IV), (V), substituted ''proposed order'' for ''proposed regulation'' in two places, ''paragraph (2),'' for ''paragraph (2) and after'', ''(A) issue an administrative order under paragraph (1)'' for ''(A) promulgate such regulation'', ''paragraph (2)(B)'' for ''paragraph (2)(A)(ii)'', and ''issuance of the administrative order'' for ''promulgation of the regulation''.

Pub. L. 112–144, § 608(b)(1)(B)(iii)(III), which directed insertion of ''and a meeting of a device classification panel described in section 360c(b) of this title,'' after ''such proposed regulation and findings,'' was inserted after ''such proposed order and findings,'' to reflect the probable intent of Congress and amendment by Pub. L. 112–144, § 608(b)(1)(B)(iii)(I). See above.

Subsec. (b)(4). Pub. L. 112–144, § 608(b)(1)(B)(iv), struck out par. (4) which read as follows: ''The Secretary, upon his own initiative or upon petition of an interested person, may by regulation amend or revoke any regulation promulgated under this subsection. A regulation to amend or revoke a regulation under this subsection shall be promulgated in accordance with the requirements prescribed by this subsection for the promulgation of the regulation to be amended or revoked.''

Subsec. (c)(4)(A). Pub. L. 112–144, § 203(g), substituted ''379j(h)'' for ''379j(g)''.

Subsec. (i)(2). Pub. L. 112–144, § 608(b)(1)(C)(i)(III), (IV), in concluding provisions, substituted ''administrative order issued under this paragraph requires'' for ''regulation requires'' and struck out at end ''Before the publication of a regulation requiring a device to remain in class III or revising its classification, the Secretary shall publish a proposed regulation respecting the classification of a device under this paragraph and provide reasonable opportunity for the submission of comments on any such regulation. No regulation requiring a device to remain in class III or revising its classification may take effect before the expiration of 90 days from the date of its publication in the Federal Register as a proposed regulation.''

Pub. L. 112–144, § 608(b)(1)(C)(i)(I), in introductory provisions, substituted ''the date that is 2 years after July 9, 2012'' for ''December 1, 1995'' and ''issue an administrative order following publication of a proposed order in the Federal Register, a meeting of a device classification panel described in section 360c(b) of this title, and consideration of comments from all affected stakeholders, including patients, payors, and providers, notwithstanding subchapter II of chapter 5 of title 5,'' for ''publish a regulation in the Federal Register''.

Subsec. (i)(2)(B). Pub. L. 112–144, § 608(b)(1)(C)(i)(II), substituted ''administrative order has been issued under subsection (b) (or no regulation has been promulgated under such subsection prior to July 9, 2012)'' for ''final regulation has been promulgated under subsection (b) of this section''.

Subsec. (i)(3). Pub. L. 112–144, § 608(b)(1)(C)(ii), substituted ''order requiring'' for ''regulation requiring'' in two places and ''issuance of an administrative order under subsection (b)'' for ''promulgation of a subsection (b) of this section regulation''.

2007—Subsec. (c)(1)(G), (H). Pub. L. 110–85 added subpar. (G) and redesignated former subpar. (G) as (H).

2004—Subsec. (c)(3). Pub. L. 108–214, § 2(d)(1)(B), amended directory language of Pub. L. 107–250, § 210. See 2002 Amendment note below.

Pub. L. 108–214, § 2(d)(1)(A)(i), redesignated par. (3) relating to acceptance and review of any portion of the application prior to submission as (4).

Subsec. (c)(4). Pub. L. 108–214, § 2(d)(1)(A), redesignated par. (3) relating to acceptance and review of any portion of the application prior to submission as (4) and substituted ''unless a significant issue of safety'' for ''unless an issue of safety'' in subpar. (B).

2002—Subsec. (a). Pub. L. 107–250, § 302(c)(1), inserted ''or, as applicable, an approval under subsection (c)(2) of a report seeking premarket approval'' before period in concluding provisions.

Subsec. (c)(2). Pub. L. 107–250, § 302(c)(2)(B), added par. (2). Former par. (2) redesignated (3).

Subsec. (c)(3). Pub. L. 107–250, § 302(c)(2)(A), redesignated par. (2) relating to Secretary's referral of application to appropriate panel as (3).

Pub. L. 107–250, § 210, as amended by Pub. L. 108–214, § 2(d)(1)(B), inserted ''Where appropriate, the Secretary shall ensure that such panel includes, or consults with, one or more pediatric experts.'' at the end of the concluding provisions of par. (3) as redesignated by Pub. L. 107–250, § 302(c)(2)(A).

Pub. L. 107–250, § 209, added par. (3) relating to acceptance and review of any portion of the application prior to submission.

1997—Subsec. (d)(1)(A). Pub. L. 105–115, § 205(c)(1), inserted at end ''In making the determination whether to approve or deny the application, the Secretary shall rely on the conditions of use included in the proposed labeling as the basis for determining whether or not there is a reasonable assurance of safety and effectiveness, if the proposed labeling is neither false nor misleading. In determining whether or not such labeling is false or misleading, the Secretary shall fairly evaluate all material facts pertinent to the proposed labeling.''

Subsec. (d)(1)(B)(iii). Pub. L. 105–115, § 201(b), added cl. (iii).

Subsec. (d)(3), (4). Pub. L. 105–115, § 202(1), 209(b), added par. (3) and redesignated former par. (3) as (4).

Subsec. (d)(5). Pub. L. 105–115, § 202(2), added par. (5).

Subsec. (d)(6). Pub. L. 105–115, § 205(c)(2), added par. (6).

Subsec. (f)(2). Pub. L. 105–115, § 216(b), substituted ''the Secretary—'' and subpars. (A) and (B) for ''he shall refer the proposed protocol to the appropriate panel under section 360c of this title for its recommendation respecting approval of the protocol.''

1993—Subsec. (c)(2)(A). Pub. L. 103–80 struck out ''refer such application'' after ''own initiative''.

1990—Subsec. (c)(2). Pub. L. 101–629, § 18(c), substituted ''the Secretary—'' for ''the Secretary shall'' and added subpars. (A) and (B).

Subsec. (e). Pub. L. 101–629, § 9(a)(2), inserted ''and temporary suspension'' after ''Withdrawal'' in heading.

Subsec. (e)(3). Pub. L. 101–629, § 9(a)(1), added par. (3).

Subsec. (i). Pub. L. 101–629, § 4(b)(1), added subsec. (i).

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 2017 AMENDMENT

Amendment by Pub. L. 115–52 effective Oct. 1, 2017, with fees under subpart 3 of part C of subchapter VII of

this chapter to be assessed for all submissions listed in section 379j(a)(2)(A) of this title received on or after Oct. 1, 2017, see section 209 of Pub. L. 115–52, set out as a note under section 379i of this title.

EFFECTIVE DATE OF 2012 AMENDMENT

Amendment by section 203(g) of Pub. L. 112–144 effective Oct. 1, 2012, with additional provision for assessment of certain fees, see section 206 of Pub. L. 112–144, set out as a note under section 379i of this title.

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by Pub. L. 105–115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as a note under section 321 of this title.

TERMINATION OF ADVISORY COMMITTEES

Advisory committees in existence on Jan. 5, 1973, to terminate not later than the expiration of the 2-year period following Jan. 5, 1973, and advisory committees established after Jan. 5, 1973, to terminate not later than the expiration of the 2-year period beginning on the date of their establishment, unless in the case of a committee established by the President or an officer of the Federal Government, such committee is renewed by appropriate action prior to the expiration of such 2-year period, or in the case of a committee established by Congress, its duration is otherwise provided by law. See section 1013 of Title 5, Government Organization and Employees.

REPORT ON CERTAIN DEVICES

Pub. L. 107–250, title II, § 205, Oct. 26, 2002, 116 Stat. 1612, directed the Secretary of Health and Human Services, not later than one year after Oct. 26, 2002, to report to the appropriate committees of Congress on the timeliness and effectiveness of device premarket reviews by centers other than the Center for Devices and Radiological Health, including information on the times required to log in and review original submissions and supplements, times required to review manufacturers' replies to submissions, times to approve or clear such devices, and recommendations on improvement of performance and reassignment of responsibility for regulating such devices.

REFERENCES IN OTHER LAWS TO GS–16, 17, OR 18 PAY RATES

References in laws to the rates of pay for GS–16, 17, or 18, or to maximum rates of pay under the General Schedule, to be considered references to rates payable under specified sections of Title 5, Government Organization and Employees, see section 529 [title I, § 101(c)(1)] of Pub. L. 101–509, set out in a note under section 5376 of Title 5.

§ 360e–1. Pediatric uses of devices

(a) New devices

(1) In general

A person that submits to the Secretary an application under section 360j(m) of this title, or an application (or supplement to an application) or a product development protocol under section 360e of this title, shall include in the application or protocol the information described in paragraph (2).

(2) Required information

The application or protocol described in paragraph (1) shall include, with respect to the device for which approval is sought and if readily available—

(A) a description of any pediatric subpopulations that suffer from the disease or condition that the device is intended to treat, diagnose, or cure; and

(B) the number of affected pediatric patients.

(3) Annual report

Not later than 18 months after September 27, 2007, and annually thereafter, the Secretary shall submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives a report that includes—

(A) the number of devices approved in the year preceding the year in which the report is submitted, for which there is a pediatric subpopulation that suffers from the disease or condition that the device is intended to treat, diagnose, or cure;

(B) any information, based on a review of data available to the Secretary, regarding devices used in pediatric patients but not labeled for such use for which the Secretary determines that approved pediatric labeling could confer a benefit to pediatric patients;

(C) the number of pediatric devices that receive a humanitarian use exemption under section 360j(m) of this title;

(D) the number of devices approved in the year preceding the year in which the report is submitted, labeled for use in pediatric patients;

(E) the number of pediatric devices approved in the year preceding the year in which the report is submitted, exempted from a fee pursuant to section 379j(a)(2)(B)(v) of this title;

(F) the review time for each device described in subparagraphs (A), (C), (D), and (E);

(G) the number of devices for which the Secretary relied on data with respect to adults to support a determination of a reasonable assurance of safety and effectiveness in pediatric patients; and

(H) the number of devices for which the Secretary relied on data from one pediatric subpopulation to support a determination of a reasonable assurance of safety and effectiveness in another pediatric subpopulation.

For the items described in this paragraph, such report shall disaggregate the number of devices by pediatric subpopulation.

(b) Determination of pediatric effectiveness based on similar course of disease or condition or similar effect of device on adults

(1) In general

If the course of the disease or condition and the effects of the device are sufficiently similar in adults and pediatric patients, the Secretary may conclude that adult data may be used to support a determination of a reasonable assurance of effectiveness in pediatric populations, as appropriate.

(2) Extrapolation between subpopulations

A study may not be needed in each pediatric subpopulation if data from one subpopulation can be extrapolated to another subpopulation.

(c) Pediatric subpopulation

For purposes of this section, the term ''pediatric subpopulation'' has the meaning given the term in section 360j(m)(6)(E)(ii) of this title.

(June 25, 1938, ch. 675, § 515A, as added Pub. L. 110–85, title III, § 302, Sept. 27, 2007, 121 Stat. 859; amended Pub. L. 115–52, title V, § 502(a), Aug. 18, 2017, 131 Stat. 1037.)

Editorial Notes

AMENDMENTS

2017—Subsec. (a)(3). Pub. L. 115–52 added subpars. (B), (C), (G), and (H), redesignated former subpars. (B) to (D) as (D) to (F), respectively, substituted ''(C), (D), and (E);'' for ''(B), and (C).'' in subpar. (F), and inserted concluding provisions.

Statutory Notes and Related Subsidiaries

FINAL RULE RELATING TO TRACKING OF PEDIATRIC USES OF DEVICES

Pub. L. 112–144, title VI, § 620(b), July 9, 2012, 126 Stat. 1064, provided that: ''The Secretary of Health and Human Services shall issue—

''(1) a proposed rule implementing section 515A(a)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360e–1(a)(2)) not later than December 31, 2012; and

''(2) a final rule implementing such section not later than December 31, 2013.''

§ 360e–3. Breakthrough devices

(a) Purpose

The purpose of this section is to encourage the Secretary, and provide the Secretary with sufficient authority, to apply efficient and flexible approaches to expedite the development of, and prioritize the Food and Drug Administration's review of, devices that represent breakthrough technologies.

(b) Establishment of program

The Secretary shall establish a program to expedite the development of, and provide for the priority review for, devices, as determined by the Secretary—

(1) that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions; and

(2)(A) that represent breakthrough technologies;

(B) for which no approved or cleared alternatives exist;

(C) that offer significant advantages over existing approved or cleared alternatives, including the potential, compared to existing approved alternatives, to reduce or eliminate the need for hospitalization, improve patient quality of life, facilitate patients' ability to manage their own care (such as through self-directed personal assistance), or establish long-term clinical efficiencies; or

(D) the availability of which is in the best interest of patients.

(c) Request for designation

A sponsor of a device may request that the Secretary designate such device for expedited development and priority review under this section. Any such request for designation may be made at any time prior to the submission of an application under section 360e(c) of this title, a notification under section 360(k) of this title, or a petition for classification under section 360c(f)(2) of this title.

(d) Designation process

(1) In general

Not later than 60 calendar days after the receipt of a request under subsection (c), the Secretary shall determine whether the device that is the subject of the request meets the criteria described in subsection (b). If the Secretary determines that the device meets the criteria, the Secretary shall designate the device for expedited development and priority review.

(2) Review

Review of a request under subsection (c) shall be undertaken by a team that is composed of experienced staff and senior managers of the Food and Drug Administration.

(3) Withdrawal

The Secretary may not withdraw a designation granted under this section on the basis of the criteria under subsection (b) no longer applying because of the subsequent clearance or approval of another device that—

(A) was designated under this section; or

(B) was given priority review under section 360e(d)(5) of this title, as in effect prior to December 13, 2016.

(e) Expedited development and priority review

(1) Actions

For purposes of expediting the development and review of devices designated under subsection (d) the Secretary shall—

(A) assign a team of staff, including a team leader with appropriate subject matter expertise and experience, for each device for which a request is submitted under subsection (c);

(B) provide for oversight of the team by senior agency personnel to facilitate the efficient development of the device and the efficient review of any submission described in subsection (c) for the device;

(C) adopt an efficient process for timely dispute resolution;

(D) provide for interactive and timely communication with the sponsor of the device during the development program and review process;

(E) expedite the Secretary's review of manufacturing and quality systems compliance, as applicable;

(F) disclose to the sponsor, not less than 5 business days in advance, the topics of any consultation the Secretary intends to undertake with external experts or an advisory committee concerning the sponsor's device and provide the sponsor the opportunity to recommend such external experts;

(G) provide for advisory committee input, as the Secretary determines appropriate (including in response to the request of the sponsor) for applications submitted under section 360e(c) of this title; and

(H) assign staff to be available within a reasonable time to address questions by in-

stitutional review committees concerning the conditions and clinical testing requirements applicable to the investigational use of the device pursuant to an exemption under section 360j(g) of this title.

(2) Additional actions

In addition to the actions described in paragraph (1), for purposes of expediting the development and review of devices designated under subsection (d), the Secretary, in collaboration with the device sponsor, may, as appropriate—

(A) coordinate with the sponsor regarding early agreement on a data development plan;

(B) take steps to ensure that the design of clinical trials is as efficient and flexible as practicable, when scientifically appropriate;

(C) facilitate, when scientifically appropriate, expedited and efficient development and review of the device through utilization of timely postmarket data collection with regard to application for approval under section 360e(c) of this title; and

(D) agree in writing to clinical protocols that the Secretary will consider binding on the Secretary and the sponsor, subject to—

(i) changes to such protocols agreed to in writing by the sponsor and the Secretary; or

(ii) a decision, made by the director of the office responsible for reviewing the device submission, that a substantial scientific issue essential to determining the safety or effectiveness of such device exists, provided that such decision is in writing, and is made only after the Secretary provides to the device sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant are present and at which the director documents the substantial scientific issue.

(f) Priority review guidance

(1) Content

Not later than 1 year after December 13, 2016, the Secretary shall issue guidance on the implementation of this section. Such guidance shall—

(A) set forth the process by which a person may seek a designation under subsection (d);

(B) provide a template for requests under subsection (c);

(C) identify the criteria the Secretary will use in evaluating a request for designation under this section; and

(D) identify the criteria and processes the Secretary will use to assign a team of staff, including team leaders, to review devices designated for expedited development and priority review, including any training required for such personnel to ensure effective and efficient review.

(2) Process

Prior to finalizing the guidance under paragraph (1), the Secretary shall seek public comment on a draft version of that guidance.

(g) Rule of construction

Nothing in this section shall be construed to affect—

(1) the criteria and standards for evaluating an application pursuant to section 360e(c) of this title, a report and request for classification under section 360c(f)(2) of this title, or a report under section 360(k) of this title, including the recognition of valid scientific evidence as described in section 360c(a)(3)(B) of this title and consideration and application of the least burdensome means of evaluating device effectiveness or demonstrating substantial equivalence between devices with differing technological characteristics, as applicable;

(2) the authority of the Secretary with respect to clinical holds under section 360j(g)(8)(A) of this title;

(3) the authority of the Secretary to act on an application pursuant to section 360e(d) of this title before completion of an establishment inspection, as the Secretary determines appropriate; or

(4) the authority of the Secretary with respect to postmarket surveillance under sections 360i(h) and 360*l* of this title.

(June 25, 1938, ch. 675, §515B, formerly §515C, as added Pub. L. 114–255, div. A, title III, §3051(a), Dec. 13, 2016, 130 Stat. 1121; renumbered §515B and amended Pub. L. 115–52, title IX, §901(f), (g), Aug. 18, 2017, 131 Stat. 1076, 1077.)

Editorial Notes

AMENDMENTS

2017—Pub. L. 115–52, §901(f)(1), made technical amendment to directory language of Pub. L. 114–255, §3051(a), which added this section.

Subsec. (f)(2). Pub. L. 115–52, §901(g), substituted ''a draft version of that guidance'' for ''a proposed guidance''.

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 2017 AMENDMENT

Pub. L. 115–52, title IX, §901(f), Aug. 18, 2017, 131 Stat. 1076, provided that the renumbering and amendment made by section 901(f) is effective as of the enactment of Pub. L. 114–255.

§360e–4. Predetermined change control plans for devices

(a) Approved devices

(1) In general

Notwithstanding section 360e(d)(5)(A) of this title, a supplemental application shall not be required for a change to a device approved under section 360e of this title, if such change is consistent with a predetermined change control plan that is approved pursuant to paragraph (2).

(2) Predetermined change control plan

The Secretary may approve a predetermined change control plan submitted in an application, including a supplemental application, under section 360e of this title that describes planned changes that may be made to the device (and that would otherwise require a supplemental application under section 360e of this title), if the device remains safe and effective without any change.

(3) Scope

The Secretary may require that a change control plan include labeling required for safe

and effective use of the device as such device changes pursuant to such plan, notification requirements if the device does not function as intended pursuant to such plan, and performance requirements for changes made under the plan.

(b) Cleared devices

(1) In general

Notwithstanding section 360(k) of this title, a premarket notification shall not be required for a change to a device cleared under section 360(k) of this title, if such change is consistent with an established predetermined change control plan granted pursuant to paragraph (2).

(2) Predetermined change control plan

The Secretary may clear a predetermined change control plan submitted in a notification submitted under section 360(k) of this title that describes planned changes that may be made to the device (and that would otherwise require a new notification), if—

(A) the device remains safe and effective without any such change; and

(B) the device would remain substantially equivalent to the predicate.

(3) Scope

The Secretary may require that a change control plan include labeling required for safe and effective use of the device as such device changes pursuant to such plan, notification requirements if the device does not function as intended pursuant to such plan, and performance requirements for changes made under the plan.

(c) Predicate devices

In making a determination of substantial equivalence pursuant to section 360c(i) of this title, the Secretary shall not compare a device to changed versions of a device implemented in accordance with an established predetermined change control plan as a predicate device. Only the version of the device cleared or approved, prior to changes made under the predetermined change control plan, may be used by a sponsor as a predicate device.

(June 25, 1938, ch. 675, § 515C, as added Pub. L. 117–328, div. FF, title III, § 3308(a), Dec. 29, 2022, 136 Stat. 5835.)

Editorial Notes

PRIOR PROVISIONS

A prior section 515C of act June 25, 1938, was renumbered section 515B and is classified to section 360e–3 of this title.

§ 360f. Banned devices

(a) General rule

Whenever the Secretary finds, on the basis of all available data and information, that—

(1) a device intended for human use presents substantial deception or an unreasonable and substantial risk of illness or injury for one or more intended uses; and

(2) in the case of substantial deception or an unreasonable and substantial risk of illness or injury which the Secretary determined could be corrected or eliminated by labeling or change in labeling and with respect to which the Secretary provided written notice to the manufacturer specifying the deception or risk of illness or injury, the labeling or change in labeling to correct the deception or eliminate or reduce such risk, and the period within which such labeling or change in labeling was to be done, such labeling or change in labeling was not done within such period;

he may initiate a proceeding to promulgate a regulation to make such device a banned device or to make such intended use or uses a banned intended use or uses. A device that is banned for one or more intended uses is not a legally marketed device under section 396 of this title when intended for such use or uses.

(b) Special effective date

The Secretary may declare a proposed regulation under subsection (a) to be effective upon its publication in the Federal Register and until the effective date of any final action taken respecting such regulation if (1) he determines, on the basis of all available data and information, that the deception or risk of illness or injury associated with the use of the device which is subject to the regulation presents an unreasonable, direct, and substantial danger to the health of individuals, and (2) before the date of the publication of such regulation, the Secretary notifies the manufacturer of such device that such regulation is to be made so effective. If the Secretary makes a proposed regulation so effective, he shall, as expeditiously as possible, give interested persons prompt notice of his action under this subsection, provide reasonable opportunity for an informal hearing on the proposed regulation, and either affirm, modify, or revoke such proposed regulation.

(June 25, 1938, ch. 675, § 516, as added Pub. L. 94–295, § 2, May 28, 1976, 90 Stat. 560; amended Pub. L. 101–629, § 18(d), Nov. 28, 1990, 104 Stat. 4529; Pub. L. 117–328, div. FF, title III, § 3306(a), Dec. 29, 2022, 136 Stat. 5834.)

Editorial Notes

AMENDMENTS

2022—Subsec. (a). Pub. L. 117–328, § 3306(a)(2), inserted ''or to make such intended use or uses a banned intended use or uses. A device that is banned for one or more intended uses is not a legally marketed device under section 396 of this title when intended for such use or uses'' after ''banned device'' in concluding provisions.

Subsec. (a)(1). Pub. L. 117–328, § 3306(a)(1), inserted ''for one or more intended uses'' before semicolon at end.

1990—Subsec. (a). Pub. L. 101–629 struck out ''and after consultation with the appropriate panel or panels under section 360c of this title'' after ''data and information'' in introductory provisions and struck out at end ''The Secretary shall afford all interested persons opportunity for an informal hearing on a regulation proposed under this subsection.''

Statutory Notes and Related Subsidiaries

CONSTRUCTION OF 2022 AMENDMENT

Pub. L. 117–328, div. FF, title III, § 3306(b), Dec. 29, 2022, 136 Stat. 5834, provided that: ''Nothing in this section [amending this section] shall be construed to limit

the authority of the Secretary [of Health and Human Services] to amend, in accordance with section 516 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360f), as amended by this section, and chapter 5 of title 5, United States Code, regulations promulgated pursuant to such section 516, as amended by this section.''

§ 360g. Judicial review

(a) Petition; record

Not later than thirty days after—

(1) the promulgation of a regulation under section 360c of this title classifying a device in class I, an administrative order changing the classification of a device to class I, or an order under subsection (f)(2) of such section reclassifying a device or denying a petition for reclassification of a device,

(2) the promulgation of a regulation under section 360d of this title establishing, amending, or revoking a performance standard for a device,

(3) the issuance of an order under section 360d(b)(2) or 360e(b)(2)(B) of this title denying a request for reclassification of a device,

(4) the promulgation of a regulation under paragraph (3) of section 360e(b) of this title requiring a device to have an approval of a premarket application, a regulation under paragraph (4) of that section amending or revoking a regulation under paragraph (3), or an order pursuant to section 360e(g)(1) or 360e(g)(2)(C) of this title,

(5) the promulgation of a regulation under section 360f of this title (other than a proposed regulation made effective under subsection (b) of such section upon the regulation's publication) making a device a banned device,

(6) the issuance of an order under section 360j(f)(2) of this title,

(7) an order under section 360j(g)(4) of this title disapproving an application for an exemption of a device for investigational use or an order under section 360j(g)(5) of this title withdrawing such an exemption for a device,

(8) an order pursuant to section 360c(i) of this title, or

(9) a regulation under section 360e(i)(2) or 360j(*l*)(5)(B) of this title,

any person adversely affected by such regulation or order may file a petition with the United States Court of Appeals for the District of Columbia or for the circuit wherein such person resides or has his principal place of business for judicial review of such regulation or order. A copy of the petition shall be transmitted by the clerk of the court to the Secretary or other officer designated by him for that purpose. The Secretary shall file in the court the record of the proceedings on which the Secretary based his regulation or order as provided in section 2112 of title 28. For purposes of this section, the term ''record'' means all notices and other matter published in the Federal Register with respect to the regulation or order reviewed, all information submitted to the Secretary with respect to such regulation or order, proceedings of any panel or advisory committee with respect to such regulation or order, any hearing held with respect to such regulation or order, and any other information identified by the Secretary, in the administrative proceeding held with respect to such regulation or order, as being relevant to such regulation or order.

(b) Additional data, views, and arguments

If the petitioner applies to the court for leave to adduce additional data, views, or arguments respecting the regulation or order being reviewed and shows to the satisfaction of the court that such additional data, views, or arguments are material and that there were reasonable grounds for the petitioner's failure to adduce such data, views, or arguments in the proceedings before the Secretary, the court may order the Secretary to provide additional opportunity for the oral presentation of data, views, or arguments and for written submissions. The Secretary may modify his findings, or make new findings by reason of the additional data, views, or arguments so taken and shall file with the court such modified or new findings, and his recommendation, if any, for the modification or setting aside of the regulation or order being reviewed, with the return of such additional data, views, or arguments.

(c) Standard for review

Upon the filing of the petition under subsection (a) of this section for judicial review of a regulation or order, the court shall have jurisdiction to review the regulation or order in accordance with chapter 7 of title 5 and to grant appropriate relief, including interim relief, as provided in such chapter. A regulation described in paragraph (2) or (5) of subsection (a) and an order issued after the review provided by section 360e(g) of this title shall not be affirmed if it is found to be unsupported by substantial evidence on the record taken as a whole.

(d) Finality of judgments

The judgment of the court affirming or setting aside, in whole or in part, any regulation or order shall be final, subject to review by the Supreme Court of the United States upon certiorari or certification, as provided in section 1254 of title 28.

(e) Remedies

The remedies provided for in this section shall be in addition to and not in lieu of any other remedies provided by law.

(f) Statement of reasons

To facilitate judicial review under this section or under any other provision of law of a regulation or order issued under section 360c, 360d, 360e, 360f, 360h, 360i, 360j, or 360k of this title each such regulation or order shall contain a statement of the reasons for its issuance and the basis, in the record of the proceedings held in connection with its issuance, for its issuance.

(June 25, 1938, ch. 675, § 517, as added Pub. L. 94–295, § 2, May 28, 1976, 90 Stat. 560; amended Pub. L. 101–629, § 13, Nov. 28, 1990, 104 Stat. 4524; Pub. L. 102–300, § 6(f), June 16, 1992, 106 Stat. 240; Pub. L. 105–115, title II, § 216(a)(2), Nov. 21, 1997, 111 Stat. 2349; Pub. L. 112–144, title VI, § 608(a)(2)(C), July 9, 2012, 126 Stat. 1056.)

Editorial Notes

AMENDMENTS

2012—Subsec. (a)(1). Pub. L. 112–144 substituted '', an administrative order changing the classification of a

device to class I,'' for ''or changing the classification of a device to class I''.

1997—Subsec. (a)(8). Pub. L. 105–115, § 216(a)(2)(A), inserted ''or'' at end.

Subsec. (a)(9). Pub. L. 105–115, § 216(a)(2)(B), substituted comma for '', or'' at end.

Subsec. (a)(10). Pub. L. 105–115, § 216(a)(2)(C), struck out par. (10) which read as follows: ''an order under section 360j(h)(4)(B) of this title,''.

1992—Subsec. (a)(10). Pub. L. 102–300 substituted ''360j(h)(4)(B)'' for ''360j(c)(4)(B)''.

1990—Subsec. (a)(8) to (10). Pub. L. 101–629 added pars. (8) to (10).

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by Pub. L. 105–115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as a note under section 321 of this title.

§ 360g–1. Agency documentation and review of significant decisions regarding devices

(a) Documentation of rationale for significant decisions

(1) In general

The Secretary shall provide a substantive summary of the scientific and regulatory rationale for any significant decision of the Center for Devices and Radiological Health regarding submission or review of a report under section 360(k) of this title, a petition for classification under section 360c(f) of this title, an application under section 360e of this title, or an application for an exemption under section 360j(g) of this title, including documentation of significant controversies or differences of opinion and the resolution of such controversies or differences of opinion.

(2) Provision of documentation

Upon request, the Secretary shall furnish such substantive summary to the person who is seeking to submit, or who has submitted, such report or application.

(3) Application of least burdensome requirements

The substantive summary required under this subsection shall include a brief statement regarding how the least burdensome requirements were considered and applied consistent with section 360c(i)(1)(D) of this title, section 360c(a)(3)(D) of this title, and section 360e(c)(5) of this title, as applicable.

(b) Review of significant decisions

(1) Request for supervisory review of significant decision

Any person may request a supervisory review of the significant decision described in subsection (a)(1). Such review may be conducted at the next supervisory level or higher above the individual who made the significant decision.

(2) Submission of request

A person requesting a supervisory review under paragraph (1) shall submit such request to the Secretary not later than 30 days after such decision and shall indicate in the request whether such person seeks an in-person meeting or a teleconference review.

(3) Timeframe

(A) In general

Except as provided in subparagraph (B), the Secretary shall schedule an in-person or teleconference review, if so requested, not later than 30 days after such request is made. The Secretary shall issue a decision to the person requesting a review under this subsection not later than 45 days after the request is made under paragraph (1), or, in the case of a person who requests an in-person meeting or teleconference, 30 days after such meeting or teleconference.

(B) Exception

Subparagraph (A) shall not apply in cases that are referred to experts outside of the Food and Drug Administration.

(June 25, 1938, ch. 675, § 517A, as added Pub. L. 112–144, title VI, § 603, July 9, 2012, 126 Stat. 1051; amended Pub. L. 114–255, div. A, title III, §§ 3051(b), 3058(c), Dec. 13, 2016, 130 Stat. 1124, 1129; Pub. L. 117–328, div. FF, title III, § 3308(b)(3), Dec. 29, 2022, 136 Stat. 5836.)

Editorial Notes

AMENDMENTS

2022—Subsec. (a)(1). Pub. L. 117–328 amended par. (1) generally. Prior to amendment, text read as follows: ''The Secretary shall provide a substantive summary of the scientific and regulatory rationale for any significant decision of the Center for Devices and Radiological Health regarding submission or review of a report under section 360(k) of this title, an application under section 360e of this title, a request for designation under section 360e–3 of this title, or an application for an exemption under section 360j(g) of this title, including documentation of significant controversies or differences of opinion and the resolution of such controversies or differences of opinion.''

2016—Subsec. (a)(1). Pub. L. 114–255, § 3051(b), inserted ''a request for designation under section 360e–3 of this title,'' after ''application under section 360e of this title,''.

Subsec. (a)(3). Pub. L. 114–255, § 3058(c), added par. (3).

§ 360g–2. Third party data transparency

(a) In general

To the extent the Secretary relies on any data, analysis, or other information or findings provided by entities that has been funded in whole or in part by, or otherwise performed under contract with, the Food and Drug Administration, in regulatory decision-making with respect to devices, the Secretary shall—

(1) request access to the datasets, inputs, clinical or other assumptions, methods, analytical code, results, and other components underlying or comprising the analysis, conclusions, or other findings upon which the Secretary seeks to rely; and

(2) in the event that information described in paragraph (1) is used to support regulatory decision-making, and as otherwise appropriate, to the extent practicable, provide the manufacturer or manufacturers subject to such decision a summary of such information, subject to protection of confidential commercial information or trade secret information or personally identifiable information.

(b) Report

Not later than September 30, 2023, and biennially thereafter, the Secretary shall submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives, and publish on the website of the Food and Drug Administration, a report on the number of postmarket device signals communications issued by the Secretary, the sources of data for such signals, and how such signals were revised or resolved.

(c) Rule of construction

Nothing in this section shall be construed to require the delay of any regulatory decision-making or other action of the Food and Drug Administration.

(Pub. L. 117–328, div. FF, title III, § 3307, Dec. 29, 2022, 136 Stat. 5834.)

Editorial Notes

CODIFICATION

Section was enacted as part of the Food and Drug Omnibus Reform Act of 2022, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

Statutory Notes and Related Subsidiaries

DEFINITION OF ''SECRETARY''

Secretary as used in this section means the Secretary of Health and Human Services, see section 3002 of div. FF of Pub. L. 117–328, set out as a note under section 350a–1 of this title.

§ 360h. Notification and other remedies

(a) Notification

If the Secretary determines that—

(1) a device intended for human use which is introduced or delivered for introduction into interstate commerce for commercial distribution presents an unreasonable risk of substantial harm to the public health, and

(2) notification under this subsection is necessary to eliminate the unreasonable risk of such harm and no more practicable means is available under the provisions of this chapter (other than this section) to eliminate such risk,

the Secretary may issue such order as may be necessary to assure that adequate notification is provided in an appropriate form, by the persons and means best suited under the circumstances involved, to all health professionals who prescribe or use the device and to any other person (including manufacturers, importers, distributors, retailers, and device users) who should properly receive such notification in order to eliminate such risk. An order under this subsection shall require that the individuals subject to the risk with respect to which the order is to be issued be included in the persons to be notified of the risk unless the Secretary determines that notice to such individuals would present a greater danger to the health of such individuals than no such notification. If the Secretary makes such a determination with respect to such individuals, the order shall require that the health professionals who prescribe or use the device provide for the notification of the individuals whom the health professionals treated with the device of the risk presented by the device and of any action which may be taken by or on behalf of such individuals to eliminate or reduce such risk. Before issuing an order under this subsection, the Secretary shall consult with the persons who are to give notice under the order.

(b) Repair, replacement, or refund

(1)(A) If, after affording opportunity for an informal hearing, the Secretary determines that—

(i) a device intended for human use which is introduced or delivered for introduction into interstate commerce for commercial distribution presents an unreasonable risk of substantial harm to the public health,

(ii) there are reasonable grounds to believe that the device was not properly designed or manufactured with reference to the state of the art as it existed at the time of its design or manufacture,

(iii) there are reasonable grounds to believe that the unreasonable risk was not caused by failure of a person other than a manufacturer, importer, distributor, or retailer of the device to exercise due care in the installation, maintenance, repair, or use of the device, and

(iv) the notification authorized by subsection (a) would not by itself be sufficient to eliminate the unreasonable risk and action described in paragraph (2) of this subsection is necessary to eliminate such risk,

the Secretary may order the manufacturer, importer, or any distributor of such device, or any combination of such persons, to submit to him within a reasonable time a plan for taking one or more of the actions described in paragraph (2). An order issued under the preceding sentence which is directed to more than one person shall specify which person may decide which action shall be taken under such plan and the person specified shall be the person who the Secretary determines bears the principal, ultimate financial responsibility for action taken under the plan unless the Secretary cannot determine who bears such responsibility or the Secretary determines that the protection of the public health requires that such decision be made by a person (including a device user or health professional) other than the person he determines bears such responsibility.

(B) The Secretary shall approve a plan submitted pursuant to an order issued under subparagraph (A) unless he determines (after affording opportunity for an informal hearing) that the action or actions to be taken under the plan or the manner in which such action or actions are to be taken under the plan will not assure that the unreasonable risk with respect to which such order was issued will be eliminated. If the Secretary disapproves a plan, he shall order a revised plan to be submitted to him within a reasonable time. If the Secretary determines (after affording opportunity for an informal hearing) that the revised plan is unsatisfactory or if no revised plan or no initial plan has been submitted to the Secretary within the prescribed time, the Secretary shall (i) prescribe a plan to be carried out by the person or persons

to whom the order issued under subparagraph (A) was directed, or (ii) after affording an opportunity for an informal hearing, by order prescribe a plan to be carried out by a person who is a manufacturer, importer, distributor, or retailer of the device with respect to which the order was issued but to whom the order under subparagraph (A) was not directed.

(2) The actions which may be taken under a plan submitted under an order issued under paragraph (1) are as follows:

(A) To repair the device so that it does not present the unreasonable risk of substantial harm with respect to which the order under paragraph (1) was issued.

(B) To replace the device with a like or equivalent device which is in conformity with all applicable requirements of this chapter.

(C) To refund the purchase price of the device (less a reasonable allowance for use if such device has been in the possession of the device user for one year or more—

(i) at the time of notification ordered under subsection (a), or

(ii) at the time the device user receives actual notice of the unreasonable risk with respect to which the order was issued under paragraph (1),

whichever first occurs).

(3) No charge shall be made to any person (other than a manufacturer, importer, distributor or retailer) for availing himself of any remedy, described in paragraph (2) and provided under an order issued under paragraph (1), and the person subject to the order shall reimburse each person (other than a manufacturer, importer, distributor, or retailer) who is entitled to such a remedy for any reasonable and foreseeable expenses actually incurred by such person in availing himself of such remedy.

(c) Reimbursement

An order issued under subsection (b) with respect to a device may require any person who is a manufacturer, importer, distributor, or retailer of the device to reimburse any other person who is a manufacturer, importer, distributor, or retailer of such device for such other person's expenses actually incurred in connection with carrying out the order if the Secretary determines such reimbursement is required for the protection of the public health. Any such requirement shall not affect any rights or obligations under any contract to which the person receiving reimbursement or the person making such reimbursement is a party.

(d) Effect on other liability

Compliance with an order issued under this section shall not relieve any person from liability under Federal or State law. In awarding damages for economic loss in an action brought for the enforcement of any such liability, the value to the plaintiff in such action of any remedy provided him under such order shall be taken into account.

(e) Recall authority

(1) If the Secretary finds that there is a reasonable probability that a device intended for human use would cause serious, adverse health consequences or death, the Secretary shall issue an order requiring the appropriate person (including the manufacturers, importers, distributors, or retailers of the device)—

(A) to immediately cease distribution of such device, and

(B) to immediately notify health professionals and device user facilities of the order and to instruct such professionals and facilities to cease use of such device.

The order shall provide the person subject to the order with an opportunity for an informal hearing, to be held not later than 10 days after the date of the issuance of the order, on the actions required by the order and on whether the order should be amended to require a recall of such device. If, after providing an opportunity for such a hearing, the Secretary determines that inadequate grounds exist to support the actions required by the order, the Secretary shall vacate the order.

(2)(A) If, after providing an opportunity for an informal hearing under paragraph (1), the Secretary determines that the order should be amended to include a recall of the device with respect to which the order was issued, the Secretary shall, except as provided in subparagraphs (B) and (C), amend the order to require a recall. The Secretary shall specify a timetable in which the device recall will occur and shall require periodic reports to the Secretary describing the progress of the recall.

(B) An amended order under subparagraph (A)—

(i) shall—

(I) not include recall of a device from individuals, and

(II) not include recall of a device from device user facilities if the Secretary determines that the risk of recalling such device from the facilities presents a greater health risk than the health risk of not recalling the device from use, and

(ii) shall provide for notice to individuals subject to the risks associated with the use of such device.

In providing the notice required by clause (ii), the Secretary may use the assistance of health professionals who prescribed or used such a device for individuals. If a significant number of such individuals cannot be identified, the Secretary shall notify such individuals pursuant to section 375(b) of this title.

(3) The remedy provided by this subsection shall be in addition to remedies provided by subsections (a), (b), and (c).

(June 25, 1938, ch. 675, § 518, as added Pub. L. 94–295, § 2, May 28, 1976, 90 Stat. 562; amended Pub. L. 101–629, § 8, Nov. 28, 1990, 104 Stat. 4520; Pub. L. 102–300, § 4, June 16, 1992, 106 Stat. 239.)

Editorial Notes

AMENDMENTS

1992—Subsec. (b)(1)(A)(ii). Pub. L. 102–300 substituted ''or'' for ''and'' after ''properly designed'' and ''time of its design''.

1990—Subsec. (e). Pub. L. 101–629 added subsec. (e).

§ 360h–1. Program to improve the device recall system

(a) In general

The Secretary shall—

(1) establish a program to routinely and systematically assess information relating to device recalls and use such information to proactively identify strategies for mitigating health risks presented by defective or unsafe devices;

(2) clarify procedures for conducting device recall audit checks to improve the ability of investigators to perform those checks in a consistent manner;

(3) develop detailed criteria for assessing whether a person performing a device recall has performed an effective correction or action plan for the recall; and

(4) document the basis for each termination by the Food and Drug Administration of a device recall.

(b) Assessment content

The program established under subsection (a)(1) shall, at a minimum, identify—

(1) trends in the number and types of device recalls;

(2) devices that are most frequently the subject of a recall; and

(3) underlying causes of device recalls.

(c) Definition

In this section, the term ''recall'' means—

(1) the removal from the market of a device pursuant to an order of the Secretary under subsection (b) or (e) of section 360h of this title; or

(2) the correction or removal from the market of a device at the initiative of the manufacturer or importer of the device that is required to be reported to the Secretary under section 360i(g) of this title.

(June 25, 1938, ch. 675, § 518A, as added Pub. L. 112–144, title VI, § 605, July 9, 2012, 126 Stat. 1053; amended Pub. L. 114–255, div. A, title III, § 3101(a)(2)(K), Dec. 13, 2016, 130 Stat. 1154.)

Editorial Notes

AMENDMENTS

2016—Subsecs. (c), (d). Pub. L. 114–255 redesignated subsec. (d) as (c) and struck out former subsec. (c). Prior to amendment, text read as follows: ''The Secretary shall document the basis for the termination by the Food and Drug Administration of a device recall.''

§ 360i. Records and reports on devices

(a) General rule

Every person who is a manufacturer or importer of a device intended for human use shall establish and maintain such records, make such reports, and provide such information, as the Secretary may by regulation reasonably require to assure that such device is not adulterated or misbranded and to otherwise assure its safety and effectiveness. Regulations prescribed under the preceding sentence—

(1) shall require a device manufacturer or importer to report to the Secretary whenever the manufacturer or importer receives or otherwise becomes aware of information that reasonably suggests that one of its marketed devices—

(A) may have caused or contributed to a death or serious injury, or

(B) has malfunctioned and that such device or a similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur, which report under this subparagraph—

(i) shall be submitted in accordance with part 803 of title 21, Code of Federal Regulations (or successor regulations), unless the Secretary grants an exemption or variance from, or an alternative to, a requirement under such regulations pursuant to section 803.19 of such part, if the device involved is—

(I) a class III device;

(II) a class II device that is permanently implantable, is life supporting, or is life sustaining; or

(III) a type of device which the Secretary has, by notice published in the Federal Register or letter to the person who is the manufacturer or importer of the device, indicated should be subject to such part 803 in order to protect the public health;

(ii) shall, if the device is not subject to clause (i), be submitted in accordance with criteria established by the Secretary for reports made pursuant to this clause, which criteria shall require the reports to be in summary form and made on a quarterly basis; or

(iii) shall, if the device is imported into the United States and for which part 803 of title 21, Code of Federal Regulations (or successor regulations) requires an importer to submit a report to the manufacturer, be submitted by the importer to the manufacturer in accordance with part 803 of title 21, Code of Federal Regulations (or successor regulations)[1]

(2) shall define the term ''serious injury'' to mean an injury that—

(A) is life threatening,

(B) results in permanent impairment of a body function or permanent damage to a body structure, or

(C) necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure;

(3) shall require reporting of other significant adverse device experiences as determined by the Secretary to be necessary to be reported;

(4) shall not impose requirements unduly burdensome to a device manufacturer or importer taking into account his cost of complying with such requirements and the need for the protection of the public health and the implementation of this chapter;

(5) which prescribe the procedure for making requests for reports or information shall re-

[1] So in original. Probably should be followed by a semicolon.

quire that each request made under such regulations for submission of a report or information to the Secretary state the reason or purpose for such request and identify to the fullest extent practicable such report or information;

(6) which require submission of a report or information to the Secretary shall state the reason or purpose for the submission of such report or information and identify to the fullest extent practicable such report or information;

(7) may not require that the identity of any patient be disclosed in records, reports, or information required under this subsection unless required for the medical welfare of an individual, to determine the safety or effectiveness of a device, or to verify a record, report, or information submitted under this chapter; and

(8) may not require a manufacturer or importer of a class I device to—

(A) maintain for such a device records respecting information not in the possession of the manufacturer or importer, or

(B) to submit for such a device to the Secretary any report or information—

(i) not in the possession of the manufacturer or importer, or

(ii) on a periodic basis,

unless such report or information is necessary to determine if the device should be reclassified or if the device is adulterated or misbranded. and[2]

In prescribing such regulations, the Secretary shall have due regard for the professional ethics of the medical profession and the interests of patients. The prohibitions of paragraph (7) of this subsection continue to apply to records, reports, and information concerning any individual who has been a patient, irrespective of whether or when he ceases to be a patient. The Secretary shall by regulation require distributors to keep records and make such records available to the Secretary upon request. Paragraphs (4) and (8) apply to distributors to the same extent and in the same manner as such paragraphs apply to manufacturers and importers.

(b) User reports

(1)(A) Whenever a device user facility receives or otherwise becomes aware of information that reasonably suggests that a device has or may have caused or contributed to the death of a patient of the facility, the facility shall, as soon as practicable but not later than 10 working days after becoming aware of the information, report the information to the Secretary and, if the identity of the manufacturer is known, to the manufacturer of the device. In the case of deaths, the Secretary may by regulation prescribe a shorter period for the reporting of such information.

(B) Whenever a device user facility receives or otherwise becomes aware of—

(i) information that reasonably suggests that a device has or may have caused or contributed to the serious illness of, or serious injury to, a patient of the facility, or

(ii) other significant adverse device experiences as determined by the Secretary by regulation to be necessary to be reported,

the facility shall, as soon as practicable but not later than 10 working days after becoming aware of the information, report the information to the manufacturer of the device or to the Secretary if the identity of the manufacturer is not known.

(C) Each device user facility shall submit to the Secretary on an annual basis a summary of the reports made under subparagraphs (A) and (B). Such summary shall be submitted on January 1 of each year. The summary shall be in such form and contain such information from such reports as the Secretary may require and shall include—

(i) sufficient information to identify the facility which made the reports for which the summary is submitted,

(ii) in the case of any product which was the subject of a report, the product name, serial number, and model number,

(iii) the name and the address of the manufacturer of such device, and

(iv) a brief description of the event reported to the manufacturer.

(D) For purposes of subparagraphs (A), (B), and (C), a device user facility shall be treated as having received or otherwise become aware of information with respect to a device of that facility when medical personnel who are employed by or otherwise formally affiliated with the facility receive or otherwise become aware of information with respect to that device in the course of their duties.

(2) The Secretary may not disclose the identity of a device user facility which makes a report under paragraph (1) except in connection with—

(A) an action brought to enforce section 331(q) of this title, or

(B) a communication to a manufacturer of a device which is the subject of a report under paragraph (1).

This paragraph does not prohibit the Secretary from disclosing the identity of a device user facility making a report under paragraph (1) or any information in such a report to employees of the Department of Health and Human Services, to the Department of Justice, or to the duly authorized committees and subcommittees of the Congress.

(3) No report made under paragraph (1) by—

(A) a device user facility,

(B) an individual who is employed by or otherwise formally affiliated with such a facility, or

(C) a physician who is not required to make such a report,

shall be admissible into evidence or otherwise used in any civil action involving private parties unless the facility, individual, or physician who made the report had knowledge of the falsity of the information contained in the report.

(4) A report made under paragraph (1) does not affect any obligation of a manufacturer who receives the report to file a report as required under subsection (a).

[2] So in original. The word ''and'' probably should not appear.

(5) With respect to device user facilities:

(A) The Secretary shall by regulation plan and implement a program under which the Secretary limits user reporting under paragraphs (1) through (4) to a subset of user facilities that constitutes a representative profile of user reports for device deaths and serious illnesses or serious injuries.

(B) During the period of planning the program under subparagraph (A), paragraphs (1) through (4) continue to apply.

(C) During the period in which the Secretary is providing for a transition to the full implementation of the program, paragraphs (1) through (4) apply except to the extent that the Secretary determines otherwise.

(D) On and after the date on which the program is fully implemented, paragraphs (1) through (4) do not apply to a user facility unless the facility is included in the subset referred to in subparagraph (A).

(E) Not later than 2 years after November 21, 1997, the Secretary shall submit to the Committee on Commerce of the House of Representatives, and to the Committee on Labor and Human Resources of the Senate, a report describing the plan developed by the Secretary under subparagraph (A) and the progress that has been made toward the implementation of the plan.

(6) For purposes of this subsection:

(A) The term ''device user facility'' means a hospital, ambulatory surgical facility, nursing home, or outpatient treatment facility which is not a physician's office. The Secretary may by regulation include an outpatient diagnostic facility which is not a physician's office in such term.

(B) The terms ''serious illness'' and ''serious injury'' mean illness or injury, respectively, that—

(i) is life threatening,

(ii) results in permanent impairment of a body function or permanent damage to a body structure, or

(iii) necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.

(c) Persons exempt

Subsection (a) shall not apply to—

(1) any practitioner who is licensed by law to prescribe or administer devices intended for use in humans and who manufactures or imports devices solely for use in the course of his professional practice;

(2) any person who manufactures or imports devices intended for use in humans solely for such person's use in research or teaching and not for sale (including any person who uses a device under an exemption granted under section 360j(g) of this title); and

(3) any other class of persons as the Secretary may by regulation exempt from subsection (a) upon a finding that compliance with the requirements of such subsection by such class with respect to a device is not necessary to (A) assure that a device is not adulterated or misbranded or (B) otherwise to assure its safety and effectiveness.

(d) Repealed. Pub. L. 105–115, title II, § 213(a)(2), Nov. 21, 1997, 111 Stat. 2347

(e) Device tracking

(1) The Secretary may by order require a manufacturer to adopt a method of tracking a class II or class III device—

(A) the failure of which would be reasonably likely to have serious adverse health consequences; or

(B) which is—

(i) intended to be implanted in the human body for more than one year, or

(ii) a life sustaining or life supporting device used outside a device user facility.

(2) Any patient receiving a device subject to tracking under paragraph (1) may refuse to release, or refuse permission to release, the patient's name, address, social security number, or other identifying information for the purpose of tracking.

(f) Unique device identification system

Not later than December 31, 2012, the Secretary shall issue proposed regulations establishing a unique device identification system for medical devices requiring the label of devices to bear a unique identifier, unless the Secretary requires an alternative placement or provides an exception for a particular device or type of device. The unique identifier shall adequately identify the device through distribution and use, and may include information on the lot or serial number. The Secretary shall finalize the proposed regulations not later than 6 months after the close of the comment period and shall implement the final regulations with respect to devices that are implantable, life-saving, or life sustaining not later than 2 years after the regulations are finalized, taking into account patient access to medical devices and therapies.

(g) Reports of removals and corrections

(1) Except as provided in paragraph (2), the Secretary shall by regulation require a manufacturer or importer of a device to report promptly to the Secretary any correction or removal of a device undertaken by such manufacturer or importer if the removal or correction was undertaken—

(A) to reduce a risk to health posed by the device, or

(B) to remedy a violation of this chapter caused by the device which may present a risk to health.

A manufacturer or importer of a device who undertakes a correction or removal of a device which is not required to be reported under this paragraph shall keep a record of such correction or removal.

(2) No report of the corrective action or removal of a device may be required under paragraph (1) if a report of the corrective action or removal is required and has been submitted under subsection (a).

(3) For purposes of paragraphs (1) and (2), the terms ''correction'' and ''removal'' do not include routine servicing.

(h) Inclusion of devices in the postmarket risk identification and analysis system

(1) In general

(A) Application to devices

The Secretary shall amend the procedures established and maintained under clauses (i), (ii), (iii), and (v) of section 355(k)(3)(C) of this title in order to expand the postmarket risk identification and analysis system established under such section to include and apply to devices.

(B) Exception

Subclause (II) of clause (i) of section 355(k)(3)(C) of this title shall not apply to devices.

(C) Clarification

With respect to devices, the private sector health-related electronic data provided under section 355(k)(3)(C)(i)(III)(bb) of this title may include medical device utilization data, health insurance claims data, and procedure and device registries.

(2) Data

In expanding the system as described in paragraph (1)(A), the Secretary shall use relevant data with respect to devices cleared under section 360(k) of this title or approved under section 360e of this title, including claims data, patient survey data, and any other data deemed appropriate by the Secretary.

(3) Stakeholder input

To help ensure effective implementation of the system as described in paragraph (1) with respect to devices, the Secretary shall engage outside stakeholders in development of the system, and gather information from outside stakeholders regarding the content of an effective sentinel program, through a public hearing, advisory committee meeting, maintenance of a public docket, or other similar public measures.

(4) Voluntary surveys

Chapter 35 of title 44 shall not apply to the collection of voluntary information from health care providers, such as voluntary surveys or questionnaires, initiated by the Secretary for purposes of postmarket risk identification, mitigation, and analysis for devices.

(i) Postmarket pilot

(1) In general

In order to provide timely and reliable information on the safety and effectiveness of devices approved under section 360e of this title, cleared under section 360(k) of this title, or classified under section 360c(f)(2) of this title, including responses to adverse events and malfunctions, and to advance the objectives of part 803 of title 21, Code of Federal Regulations (or successor regulations), and advance the objectives of, and evaluate innovative new methods of compliance with, this section and section 360*l* of this title, the Secretary shall, within one year of August 18, 2017, initiate one or more pilot projects for voluntary participation by a manufacturer or manufacturers of a device or device type, or continue existing projects, in accordance with paragraph (3), that—

(A) are designed to efficiently generate reliable and timely safety and active surveillance data for use by the Secretary or manufacturers of the devices that are involved in the pilot project;

(B) inform the development of methods, systems, data criteria, and programs that could be used to support safety and active surveillance activities for devices included or not included in such project;

(C) may be designed and conducted in coordination with a comprehensive system for evaluating medical device technology that operates under a governing board with appropriate representation of stakeholders, including patient groups and device manufacturers;

(D) use electronic health data including claims data, patient survey data, or any other data, as the Secretary determines appropriate; and

(E) prioritize devices and device types that meet one or more of the following criteria:

(i) Devices and device types for which the collection and analysis of real world evidence regarding a device's safety and effectiveness is likely to advance public health.

(ii) Devices and device types that are widely used.

(iii) Devices and device types, the failure of which has significant health consequences.

(iv) Devices and device types for which the Secretary—

(I) has received public recommendations in accordance with paragraph (2)(B); and

(II) has determined to meet one or more of the criteria under clause (i), (ii), or (iii) and is appropriate for such a pilot project.

(2) Participation

The Secretary shall establish the conditions and processes—

(A) under which a manufacturer of a device may voluntarily participate in a pilot project described in paragraph (1); and

(B) for facilitating public recommendations for devices to be prioritized under such a pilot project, including requirements for the data necessary to support such a recommendation.

(3) Continuation of ongoing projects

The Secretary may continue or expand projects, with respect to providing timely and reliable information on the safety and effectiveness of devices approved under section 360e of this title, cleared under section 360(k) of this title, or classified under section 360c(f)(2) of this title, that are being carried out as of August 18, 2017. The Secretary shall, beginning on such date, take such steps as may be necessary—

(A) to ensure such projects meet the requirements of subparagraphs (A) through (E) of paragraph (1); and

(B) to increase the voluntary participation in such projects of manufacturers of devices and facilitate public recommendations for any devices prioritized under such a project.

(4) Implementation

(A) Contracting authority

The Secretary may carry out a pilot project meeting the criteria specified in subparagraphs (A) through (E) of paragraph (1) or a project continued or expanded under paragraph (3) by entering into contracts, cooperative agreements, grants, or other appropriate agreements with public or private entities that have a significant presence in the United States and meet the following conditions:

(i) If such an entity is a component of another organization, the entity and the organization have established an agreement under which appropriate security measures are implemented to maintain the confidentiality and privacy of the data described in paragraph (1)(D) and such agreement ensures that the entity will not make an unauthorized disclosure of such data to the other components of the organization in breach of requirements with respect to confidentiality and privacy of such data established under such security measures.

(ii) In the case of the termination or nonrenewal of such a contract, cooperative agreement, grant, or other appropriate agreement, the entity or entities involved shall comply with each of the following:

(I) The entity or entities shall continue to comply with the requirements with respect to confidentiality and privacy referred to in clause (i) with respect to all data disclosed to the entity under such an agreement.

(II) The entity or entities shall return any data disclosed to such entity pursuant to this subsection and to which it would not otherwise have access or, if returning such data is not practicable, destroy the data.

(iii) The entity or entities shall have one or more qualifications with respect to—

(I) research, statistical, epidemiologic, or clinical capability and expertise to conduct and complete the activities under this subsection, including the capability and expertise to provide the Secretary access to de-identified data consistent with the requirements of this subsection;

(II) an information technology infrastructure to support electronic data and operational standards to provide security for such data, as appropriate;

(III) experience with, and expertise on, the development of research on, and surveillance of, device safety and effectiveness using electronic health data; or

(IV) such other expertise which the Secretary determines necessary to carry out such a project.

(B) Review of contract in the event of a merger or acquisition

The Secretary shall review any contract, cooperative agreement, grant, or other appropriate agreement entered into under this paragraph with an entity meeting the conditions specified in subparagraph (A) in the event of a merger or acquisition of the entity in order to ensure that the requirements specified in this subsection will continue to be met.

(5) Compliance with requirements for records or reports on devices

The participation of a manufacturer in pilot projects under this subsection or a project continued or expanded under paragraph (3) shall not affect the eligibility of such manufacturer to participate in any quarterly reporting program with respect to devices carried out under this section 360i[3] or section 360*l* of this title. The Secretary may determine that, for a specified time period to be determined by the Secretary, a manufacturer's participation in a pilot project under this subsection or a project continued or expanded under paragraph (3) may meet the applicable requirements of this section or section 360*l* of this title, if—

(A) the project has demonstrated success in capturing relevant adverse event information; and

(B) the Secretary has established procedures for making adverse event and safety information collected from such project public, to the extent possible.

(6) Privacy requirements

With respect to the disclosure of any health information collected through a project conducted under this subsection—

(A) individually identifiable health information so collected shall not be disclosed when presenting any information from such project; and

(B) any such disclosure shall be made in compliance with regulations issued pursuant to section 264(c) of the Health Insurance Portability and Accountability Act of 1996 (42 U.S.C. 1320d–2 note) and sections 552 and 552a of title 5.

(7) Limitations

No pilot project under this subsection, or in coordination with the comprehensive system described in paragraph (1)(C), may allow for an entity participating in such project, other than the Secretary, to make determinations of safety or effectiveness, or substantial equivalence, for purposes of this chapter.

(8) Other projects required to comply

Paragraphs (1)(B), (4)(A)(i), (4)(A)(ii), (5), (6), and (7) shall apply with respect to any pilot project undertaken in coordination with the comprehensive system described in paragraph (1)(C) that relates to the use of real world evidence for devices in the same manner and to the same extent as such paragraphs apply with

[3] So in original. The section number probably should not appear.

respect to pilot projects conducted under this subsection.

(9) Report to Congress

Not later than 18 months after August 18, 2017, and annually thereafter, the Secretary shall submit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor and Pensions of the Senate a report containing a description of the pilot projects being conducted under this subsection and projects continued or expanded pursuant to paragraph (3), including for each such project—

(A) how the project is being implemented in accordance with paragraph (4), including how such project is being implemented through a contract, cooperative agreement, grant, or other appropriate agreement, if applicable;

(B) the number of manufacturers that have agreed to participate in such project;

(C) the data sources used to conduct such project;

(D) the devices or device categories involved in such project;

(E) the number of patients involved in such project; and

(F) the findings of the project in relation to device safety, including adverse events, malfunctions, and other safety information.

(10) Sunset

The Secretary may not carry out a pilot project initiated by the Secretary under this subsection after October 1, 2022.

(June 25, 1938, ch. 675, § 519, as added Pub. L. 94–295, § 2, May 28, 1976, 90 Stat. 564; amended Pub. L. 101–629, §§ 2(a), 3(a)(1), (b)(1), 7, Nov. 28, 1990, 104 Stat. 4511, 4513, 4514, 4520; Pub. L. 102–300, § 5(a), June 16, 1992, 106 Stat. 239; Pub. L. 103–80, § 3(u), Aug. 13, 1993, 107 Stat. 778; Pub. L. 105–115, title II, §§ 211, 213(a), (c), Nov. 21, 1997, 111 Stat. 2345–2347; Pub. L. 110–85, title II, §§ 226(a), 227, Sept. 27, 2007, 121 Stat. 854; Pub. L. 112–144, title VI, §§ 614, 615, July 9, 2012, 126 Stat. 1061; Pub. L. 114–255, div. A, title III, § 3101(a)(2)(L), Dec. 13, 2016, 130 Stat. 1154; Pub. L. 115–52, title VII, § 708(a), Aug. 18, 2017, 131 Stat. 1062.)

Editorial Notes

REFERENCES IN TEXT

Section 264(c) of the Health Insurance Portability and Accountability Act of 1996, referred to in subsec. (i)(6)(B), is section 264(c) of Pub. L. 104–191, which is set out as a note under section 1320d–2 of Title 42, The Public Health and Welfare.

AMENDMENTS

2017—Subsec. (i). Pub. L. 115–52 added subsec. (i).

2016—Subsec. (f). Pub. L. 114–255 substituted ''or life sustaining'' for ''and life sustaining''.

2012—Subsec. (f). Pub. L. 112–144, § 614, substituted ''Not later than December 31, 2012, the Secretary shall issue proposed'' for ''The Secretary shall promulgate'' and inserted at end ''The Secretary shall finalize the proposed regulations not later than 6 months after the close of the comment period and shall implement the final regulations with respect to devices that are implantable, life-saving, and life sustaining not later than 2 years after the regulations are finalized, taking into account patient access to medical devices and therapies.''

Subsec. (h). Pub. L. 112–144, § 615, added subsec. (h).

2007—Subsec. (a)(1)(B). Pub. L. 110–85, § 227, substituted ''were to recur, which report under this subparagraph—'' for ''were to recur;'' and added cls. (i) to (iii).

Subsecs. (f), (g). Pub. L. 110–85, § 226(a), added subsec. (f) and redesignated former subsec. (f) as (g).

1997—Subsec. (a). Pub. L. 105–115, § 213(a)(1)(A), (F), in introductory provisions, substituted ''manufacturer or importer'' for ''manufacturer, importer, or distributor'' and, in closing provisions, inserted at end ''The Secretary shall by regulation require distributors to keep records and make such records available to the Secretary upon request. Paragraphs (4) and (8) apply to distributors to the same extent and in the same manner as such paragraphs apply to manufacturers and importers.''

Subsec. (a)(4). Pub. L. 105–115, § 213(a)(1)(B), substituted ''manufacturer or importer'' for ''manufacturer, importer, or distributor''.

Subsec. (a)(7). Pub. L. 105–115, § 213(a)(1)(C), inserted ''and'' after semicolon at end.

Subsec. (a)(8). Pub. L. 105–115, § 213(a)(1)(D), substituted ''manufacturer or importer'' for ''manufacturer, importer, or distributor'' wherever appearing and substituted period for semicolon after ''misbranded''.

Subsec. (a)(9). Pub. L. 105–115, § 213(a)(1)(E), struck out par. (9) which read as follows: ''shall require distributors who submit such reports to submit copies of the reports to the manufacturer of the device for which the report was made.''

Subsec. (b)(1)(C). Pub. L. 105–115, § 213(c)(1)(A), in introductory provisions, substituted ''on an annual basis'' for ''on a semi-annual basis'' and struck out ''and July 1'' after ''January 1'' and struck out closing provisions which read as follows: ''The Secretary may by regulation alter the frequency and timing of reports required by this subparagraph.''

Subsec. (b)(2)(A). Pub. L. 105–115, § 213(c)(1)(B)(i), inserted ''or'' after comma at end.

Subsec. (b)(2)(B). Pub. L. 105–115, § 213(c)(1)(B)(ii), substituted period for '', or'' at end.

Subsec. (b)(2)(C). Pub. L. 105–115, § 213(c)(1)(B)(iii), struck out subpar. (C) which read as follows: ''a disclosure required under subsection (a) of this section.''

Subsec. (b)(5), (6). Pub. L. 105–115, § 213(c)(2), added par. (5) and redesignated former par. (5) as (6).

Subsec. (d). Pub. L. 105–115, § 213(a)(2), struck out heading and text of subsec. (d). Text read as follows: ''Each manufacturer, importer, and distributor required to make reports under subsection (a) of this section shall submit to the Secretary annually a statement certifying that—

''(1) the manufacturer, importer, or distributor did file a certain number of such reports, or

''(2) the manufacturer, importer, or distributor did not file any report under subsection (a) of this section.''

Subsec. (e). Pub. L. 105–115, § 211, amended heading and text of subsec. (e) generally. Prior to amendment, text read as follows: ''Every person who registers under section 360 of this title and is engaged in the manufacture of—

''(1) a device the failure of which would be reasonably likely to have serious adverse health consequences and which is (A) a permanently implantable device, or (B) a life sustaining or life supporting device used outside a device user facility, or

''(2) any other device which the Secretary may designate,

shall adopt a method of device tracking.''

Subsec. (f)(1). Pub. L. 105–115, § 213(a)(3), substituted ''or importer'' for '', importer, or distributor'' wherever appearing.

1993—Subsec. (a). Pub. L. 103–80 substituted ''paragraph (7)'' for ''paragraph (4)'' in last sentence.

1992—Subsec. (a). Pub. L. 102–300, § 5(a)(1), added pars. (1) to (3) and redesignated former pars. (1) to (6) as (4) to (9), respectively.

Subsec. (b)(1)(A). Pub. L. 102–300, §5(a)(2)(A), substituted ''a device has or may have'' for ''there is a probability that a device has''.

Subsec. (b)(1)(B). Pub. L. 102–300, §5(a)(2)(A), (B), substituted ''a device has or may have'' for ''there is a probability that a device has'', designated existing provisions as cl. (i), and added cl. (ii).

Subsec. (b)(5)(B)(iii). Pub. L. 102–300, §5(a)(2)(C), struck out ''immediate'' before ''medical''.

1990—Subsec. (a)(6). Pub. L. 101–629, §3(a)(1), added par. (6).

Subsecs. (b), (c). Pub. L. 101–629, §2(a), added subsec. (b) and redesignated former subsec. (b) as (c).

Subsecs. (d), (e). Pub. L. 101–629, §3(b)(1), added subsecs. (d) and (e).

Subsec. (f). Pub. L. 101–629, §7, added subsec. (f).

Statutory Notes and Related Subsidiaries

CHANGE OF NAME

Committee on Labor and Human Resources of Senate changed to Committee on Health, Education, Labor, and Pensions of Senate by Senate Resolution No. 20, One Hundred Sixth Congress, Jan. 19, 1999.

EFFECTIVE DATE OF 1997 AMENDMENT

Pub. L. 105–115, title II, §211, Nov. 21, 1997, 111 Stat. 2345, provided in part that the amendment made by that section is effective 90 days after Nov. 21, 1997.

Amendment by section 213(a), (c) of Pub. L. 105–115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as a note under section 321 of this title.

EFFECTIVE DATE OF 1992 AMENDMENT

Pub. L. 102–300, §2(b), June 16, 1992, 106 Stat. 238, provided that: ''The amendments made by subsection (a) [amending sections 3(b)(3) and 3(c) of Pub. L. 101–629, set out as notes below] shall take effect as of May 27, 1992 and any rule to implement section 519(e) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360i(e)] proposed under section 3(c)(2) of the Safe Medical Devices Act of 1990 [Pub. L. 101–629, set out as a note below] shall revert to its proposed status as of such date.''

Pub. L. 102–300, §5(b), June 16, 1992, 106 Stat. 240, provided that: ''The amendments made by subsection (a) [amending this section] shall take effect—

''(1) 1 year after the date of the enactment of this Act [June 16, 1992]; or

''(2) on the effective date of regulations of the Secretary to implement such amendments,

whichever occurs first.''

EFFECTIVE DATE OF 1990 AMENDMENT

Pub. L. 101–629, §2(c), Nov. 28, 1990, 104 Stat. 4513, provided that: ''Section 519(b) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360i(b)], as added by the amendment made by subsection (a), shall take effect—

''(1) upon the effective date of regulations promulgated under subsection (b) [set out below], or

''(2) upon the expiration of 12 months from the date of the enactment of this Act [Nov. 28, 1990],

whichever occurs first.''

Pub. L. 101–629, §3(a)(2), Nov. 28, 1990, 104 Stat. 4514, provided that: ''Section 519(a)(6) [21 U.S.C. 360i(a)(6)], as added by the amendment made by paragraph (1), shall take effect upon the effective date of final regulations under subsection (c) [set out below].''

Pub. L. 101–629, §3(b)(3), Nov. 28, 1990, 104 Stat. 4514, as amended by Pub. L. 102–300, §2(a)(1), June 16, 1992, 106 Stat. 238, provided that: ''Section 519(e) [21 U.S.C. 360i(e)], as added by the amendment made by paragraph (1), shall take effect upon the expiration of 9 months after the issuance of final regulations under subsection (c) [set out below].''

[For effective date of amendment by Pub. L. 102–300, see section 2(b) of Pub. L. 102–300, set out above as an Effective Date of 1992 Amendment note.]

REGULATIONS

Pub. L. 101–629, §2(b), Nov. 28, 1990, 104 Stat. 4512, provided that: ''The Secretary of Health and Human Services shall promulgate regulations to implement section 519(b) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360i(b)], as added by the amendment made by subsection (a) (including a definition of the summary required by paragraph (1)(C) of such section) not later than 12 months after the date of enactment of this Act [Nov. 28, 1990]. In promulgating the regulations, the Secretary shall minimize the administrative burdens on device user facilities consistent with the need to assure adequate information.''

Pub. L. 101–629, §3(c), Nov. 28, 1990, 104 Stat. 4514, as amended by Pub. L. 102–300, §2(a)(2), (3), June 16, 1992, 106 Stat. 238, provided that:

''(1)(A) Not later than 9 months after the date of the enactment of this Act [Nov. 28, 1990], the Secretary of Health and Human Services shall issue proposed regulations—

''(i) to require distributors of devices to establish and maintain records and to make reports (including reports required by part 803 of title 21 of the Code of Federal Regulations) under section 519(a)(6) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360i(a)(6)], and

''(ii) to implement section 519(e) of such Act.

The Secretary may exempt from regulations described in clause (i) classes of distributors of class I and class II devices from whom reports are not necessary for the protection of the public health.

''(B) Regulations under subparagraph (A) shall—

''(i) require appropriate methods for maintenance of records to ensure that patients who receive devices can be provided the notification required by such Act [this chapter],

''(ii) require that manufacturers adopt effective methods of tracking devices,

''(iii) take into account the position of distributors in the device distribution process, and

''(iv) include such other requirements as the Secretary deems necessary for the adoption of an effective user tracking program under section 519(e) of such Act.

''(2) Not later than 18 months after the date of the enactment of this Act, the Secretary shall issue final regulations to implement sections [sic] 519(a)(6) of the Federal Food, Drug, and Cosmetic Act. If the Secretary does not promulgate such final regulations upon the expiration of such 18 months, the Congress finds that there is good cause for the proposed regulations to be considered as the final regulations without response to comment because the implementation of sections [sic] 519(a)(6) of such Act is essential to protect the health of patients who use such devices. Consequently, in such event, the proposed regulations issued under paragraph (1) shall become final regulations as of the expiration of such 18 months. There shall be promptly published in the Federal Register notice of the new status of the proposed regulations.

''(3) Not later than November 28, 1992, the Secretary shall issue final regulations to implement section 519(e) of the Federal Food, Drug, and Cosmetic Act. If the Secretary does not promulgate such final regulations by November 28, 1992, the Congress finds that there is good cause for the proposed regulations to be considered as the final regulations without response to comment because the implementation of section 519(e) of such Act is essential to protect the health of patients who use devices. In such event, the proposed regulations issued under paragraph (1) shall become the issued final regulations on November 29, 1992. There shall be promptly published in the Federal Register notice of the new status of the proposed regulations.''

[For effective date of amendment by Pub. L. 102–300, see section 2(b) of Pub. L. 102–300, set out above as an Effective Date of 1992 Amendment note.]

INFORMATION CONCERNING REPORTING REQUIREMENTS FOR DEVICE USER FACILITIES

Pub. L. 101–629, § 2(d), Nov. 28, 1990, 104 Stat. 4513, directed Secretary of Health and Human Services, during the 18-month period beginning on Nov. 28, 1990, to inform device user facilities (as defined in 21 U.S.C. 360i(b)(5)(A)) and manufacturers and distributors of devices respecting the requirements of 21 U.S.C. 360i(b), and, to the extent practicable, provide persons subject to such requirements assistance in the form of publications regarding such requirements.

STUDY OF REPORTING REQUIREMENTS; COMPLIANCE BY DEVICE USER FACILITIES; ACTIONS BY MANUFACTURERS; COST EFFECTIVENESS; RECOMMENDATIONS

Pub. L. 101–629, § 2(e), Nov. 28, 1990, 104 Stat. 4513, directed Comptroller General of the United States, not more than 36 months after Nov. 28, 1990, to conduct a study of compliance by device user facilities with the requirements of 21 U.S.C. 360i(b), actions taken by manufacturers of devices in response to reports made to them, cost effectiveness of such requirements and their implementation, and any recommendations for improvements to such requirements, with Comptroller General to complete the study and submit a report on the study not later than 45 months from Nov. 28, 1990, to appropriate committees of Congress.

REPORT TO CONGRESS ON REPORTING REQUIREMENTS FOR DEVICE USER FACILITIES

Pub. L. 101–629, § 2(f), Nov. 28, 1990, 104 Stat. 4513, directed Secretary of Health and Human Services, not later than 36 months after Nov. 28, 1990, to prepare and submit to appropriate committees of Congress a report containing an evaluation of the requirements of 21 U.S.C. 360i(b), consisting of an evaluation of the safety benefits of the requirements, the burdens placed on the Food and Drug Administration and on device user facilities by the requirements, and the cost-effectiveness of the requirements and recommendations for legislative reform.

§ 360j. General provisions respecting control of devices intended for human use

(a) General rule

Any requirement authorized by or under section 351, 352, 360, or 360i of this title applicable to a device intended for human use shall apply to such device until the applicability of the requirement to the device has been changed by action taken under section 360c, 360d, or 360e of this title or under subsection (g) of this section, and any requirement established by or under section 351, 352, 360, or 360i of this title which is inconsistent with a requirement imposed on such device under section 360d or 360e of this title or under subsection (g) of this section shall not apply to such device.

(b) Custom devices

(1) In general

The requirements of sections 360d and 360e of this title shall not apply to a device that—

(A) is created or modified in order to comply with the order of an individual physician or dentist (or any other specially qualified person designated under regulations promulgated by the Secretary after an opportunity for an oral hearing);

(B) in order to comply with an order described in subparagraph (A), necessarily deviates from an otherwise applicable performance standard under section 360d of this title or requirement under section 360e of this title;

(C) is not generally available in the United States in finished form through labeling or advertising by the manufacturer, importer, or distributor for commercial distribution;

(D) is designed to treat a unique pathology or physiological condition that no other device is domestically available to treat;

(E)(i) is intended to meet the special needs of such physician or dentist (or other specially qualified person so designated) in the course of the professional practice of such physician or dentist (or other specially qualified person so designated); or

(ii) is intended for use by an individual patient named in such order of such physician or dentist (or other specially qualified person so designated);

(F) is assembled from components or manufactured and finished on a case-by-case basis to accommodate the unique needs of individuals described in clause (i) or (ii) of subparagraph (E); and

(G) may have common, standardized design characteristics, chemical and material compositions, and manufacturing processes as commercially distributed devices.

(2) Limitations

Paragraph (1) shall apply to a device only if—

(A) such device is for the purpose of treating a sufficiently rare condition, such that conducting clinical investigations on such device would be impractical;

(B) production of such device under paragraph (1) is limited to no more than 5 units per year of a particular device type, provided that such replication otherwise complies with this section; and

(C) the manufacturer of such device notifies the Secretary on an annual basis, in a manner prescribed by the Secretary, of the manufacture of such device.

(3) Guidance

Not later than 2 years after July 9, 2012, the Secretary shall issue final guidance on replication of multiple devices described in paragraph (2)(B).

(c) Trade secrets

Any information reported to or otherwise obtained by the Secretary or his representative under section 360c, 360d, 360e, 360f, 360h, 360i, or 374 of this title or under subsection (f) or (g) of this section which is exempt from disclosure pursuant to subsection (a) of section 552 of title 5 by reason of subsection (b)(4) of such section shall be considered confidential and shall not be disclosed and may not be used by the Secretary as the basis for the reclassification of a device from class III to class II or class I or as the basis for the establishment or amendment of a performance standard under section 360d of this title for a device reclassified from class III to class II, except (1) in accordance with subsection (h), and (2) that such information may be disclosed to other officers or employees concerned with carrying out this chapter or when relevant in any proceeding under this chapter (other than section 360c or 360d of this title).

(d) Notices and findings

Each notice of proposed rulemaking under section 360c, 360d, 360e, 360f, 360h, or 360i of this title, or under this section, any other notice which is published in the Federal Register with respect to any other action taken under any such section and which states the reasons for such action, and each publication of findings required to be made in connection with rulemaking under any such section shall set forth—

(1) the manner in which interested persons may examine data and other information on which the notice or findings is based, and

(2) the period within which interested persons may present their comments on the notice or findings (including the need therefor) orally or in writing, which period shall be at least sixty days but may not exceed ninety days unless the time is extended by the Secretary by a notice published in the Federal Register stating good cause therefor.

(e) Restricted devices

(1) The Secretary may by regulation require that a device be restricted to sale, distribution, or use—

(A) only upon the written or oral authorization of a practitioner licensed by law to administer or use such device, or

(B) upon such other conditions as the Secretary may prescribe in such regulation,

if, because of its potentiality for harmful effect or the collateral measures necessary to its use, the Secretary determines that there cannot otherwise be reasonable assurance of its safety and effectiveness. No condition prescribed under subparagraph (B) may restrict the use of a device to persons with specific training or experience in its use or to persons for use in certain facilities unless the Secretary determines that such a restriction is required for the safe and effective use of the device. No such condition may exclude a person from using a device solely because the person does not have the training or experience to make him eligible for certification by a certifying board recognized by the American Board of Medical Specialties or has not been certified by such a Board. A device subject to a regulation under this subsection is a restricted device.

(2) The label of a restricted device shall bear such appropriate statements of the restrictions required by a regulation under paragraph (1) as the Secretary may in such regulation prescribe.

(f) Good manufacturing practice requirements

(1)(A) The Secretary may, in accordance with subparagraph (B), prescribe regulations requiring that the methods used in, and the facilities and controls used for, the manufacture, pre-production design validation (including a process to assess the performance of a device but not including an evaluation of the safety or effectiveness of a device), packing, storage, and installation of a device conform to current good manufacturing practice, as prescribed in such regulations, to assure that the device will be safe and effective and otherwise in compliance with this chapter.

(B) Before the Secretary may promulgate any regulation under subparagraph (A) he shall—

(i) afford the advisory committee established under paragraph (3) an opportunity to submit recommendations to him with respect to the regulation proposed to be promulgated;

(ii) afford opportunity for an oral hearing; and

(iii) ensure that such regulation conforms, to the extent practicable, with internationally recognized standards defining quality systems, or parts of the standards, for medical devices.

The Secretary shall provide the advisory committee a reasonable time to make its recommendation with respect to proposed regulations under subparagraph (A).

(2)(A) Any person subject to any requirement prescribed by regulations under paragraph (1) may petition the Secretary for an exemption or variance from such requirement. Such a petition shall be submitted to the Secretary in such form and manner as he shall prescribe and shall—

(i) in the case of a petition for an exemption from a requirement, set forth the basis for the petitioner's determination that compliance with the requirement is not required to assure that the device will be safe and effective and otherwise in compliance with this chapter,

(ii) in the case of a petition for a variance from a requirement, set forth the methods proposed to be used in, and the facilities and controls proposed to be used for, the manufacture, packing, storage, and installation of the device in lieu of the methods, facilities, and controls prescribed by the requirement, and

(iii) contain such other information as the Secretary shall prescribe.

(B) The Secretary may refer to the advisory committee established under paragraph (3) any petition submitted under subparagraph (A). The advisory committee shall report its recommendations to the Secretary with respect to a petition referred to it within sixty days of the date of the petition's referral. Within sixty days after—

(i) the date the petition was submitted to the Secretary under subparagraph (A), or

(ii) if the petition was referred to an advisory committee, the expiration of the sixty-day period beginning on the date the petition was referred to the advisory committee,

whichever occurs later, the Secretary shall by order either deny the petition or approve it.

(C) The Secretary may approve—

(i) a petition for an exemption for a device from a requirement if he determines that compliance with such requirement is not required to assure that the device will be safe and effective and otherwise in compliance with this chapter, and

(ii) a petition for a variance for a device from a requirement if he determines that the methods to be used in, and the facilities and controls to be used for, the manufacture, packing, storage, and installation of the device in lieu of the methods, controls, and facilities prescribed by the requirement are sufficient to assure that the device will be safe and effective and otherwise in compliance with this chapter.

An order of the Secretary approving a petition for a variance shall prescribe such conditions re-

specting the methods used in, and the facilities and controls used for, the manufacture, packing, storage, and installation of the device to be granted the variance under the petition as may be necessary to assure that the device will be safe and effective and otherwise in compliance with this chapter.

(D) After the issuance of an order under subparagraph (B) respecting a petition, the petitioner shall have an opportunity for an informal hearing on such order.

(3) The Secretary shall establish an advisory committee for the purpose of advising and making recommendations to him with respect to regulations proposed to be promulgated under paragraph (1)(A) and the approval or disapproval of petitions submitted under paragraph (2). The advisory committee shall be composed of nine members as follows:

(A) Three of the members shall be appointed from persons who are officers or employees of any State or local government or of the Federal Government.

(B) Two of the members shall be appointed from persons who are representative of interests of the device manufacturing industry; two of the members shall be appointed from persons who are representative of the interests of physicians and other health professionals; and two of the members shall be representative of the interests of the general public.

Members of the advisory committee who are not officers or employees of the United States, while attending conferences or meetings of the committee or otherwise engaged in its business, shall be entitled to receive compensation at rates to be fixed by the Secretary, which rates may not exceed the daily equivalent of the rate in effect for grade GS–18 of the General Schedule, for each day (including traveltime) they are so engaged; and while so serving away from their homes or regular places of business each member may be allowed travel expenses, including per diem in lieu of subsistence, as authorized by section 5703 of title 5 for persons in the Government service employed intermittently. The Secretary shall designate one of the members of the advisory committee to serve as its chairman. The Secretary shall furnish the advisory committee with clerical and other assistance. Section 1013 of title 5 shall not apply with respect to the duration of the advisory committee established under this paragraph.

(g) Exemption for devices for investigational use

(1) It is the purpose of this subsection to encourage, to the extent consistent with the protection of the public health and safety and with ethical standards, the discovery and development of useful devices intended for human use and to that end to maintain optimum freedom for scientific investigators in their pursuit of that purpose.

(2)(A) The Secretary shall, within the one hundred and twenty-day period beginning on May 28, 1976, by regulation prescribe procedures and conditions under which devices intended for human use may upon application be granted an exemption from the requirements of section 352, 360, 360d, 360e, 360f, 360i, or 379e of this title or subsection (e) or (f) of this section or from any combination of such requirements to permit the investigational use of such devices by experts qualified by scientific training and experience to investigate the safety and effectiveness of such devices.

(B) The conditions prescribed pursuant to subparagraph (A) shall include the following:

(i) A requirement that an application be submitted to the Secretary before an exemption may be granted and that the application be submitted in such form and manner as the Secretary shall specify.

(ii) A requirement that the person applying for an exemption for a device assure the establishment and maintenance of such records, and the making of such reports to the Secretary of safety or effectiveness data obtained as a result of the investigational use of the device during the exemption, as the Secretary determines will enable him to assure compliance with such conditions, review the progress of the investigation, and evaluate the safety and effectiveness of the device.

(iii) Such other requirements as the Secretary may determine to be necessary for the protection of the public health and safety.

(C) Procedures and conditions prescribed pursuant to subparagraph (A) for an exemption may appropriately vary depending on (i) the scope and duration of clinical testing to be conducted under such exemption, (ii) the number of human subjects that are to be involved in such testing, (iii) the need to permit changes to be made in the device subject to the exemption during testing conducted in accordance with a clinical testing plan required under paragraph (3)(A), and (iv) whether the clinical testing of such device is for the purpose of developing data to obtain approval for the commercial distribution of such device.

(3) Procedures and conditions prescribed pursuant to paragraph (2)(A) shall require, as a condition to the exemption of any device to be the subject of testing involving human subjects, that the person applying for the exemption—

(A) submit a plan for any proposed clinical testing of the device and a report of prior investigations of the device (including, where appropriate, tests on animals) adequate to justify the proposed clinical testing—

(i) to the institutional review committee established in accordance with regulations of the Secretary to supervise clinical testing of devices in the facilities where the proposed clinical testing is to be conducted, or

(ii) to the Secretary, if—

(I) no such committee exists, or

(II) the Secretary finds that the process of review by such committee is inadequate (whether or not the plan for such testing has been approved by such committee),

for review for adequacy to justify the commencement of such testing; and, unless the plan and report are submitted to the Secretary, submit to the Secretary a summary of the plan and a report of prior investigations of the device (including, where appropriate, tests on animals);

(B) promptly notify the Secretary (under such circumstances and in such manner as the

Secretary prescribes) of approval by an institutional review committee of any clinical testing plan submitted to it in accordance with subparagraph (A);

(C) in the case of a device to be distributed to investigators for testing, obtain signed agreements from each of such investigators that any testing of the device involving human subjects will be under such investigator's supervision and in accordance with subparagraph (D) and submit such agreements to the Secretary; and

(D) assure that informed consent will be obtained from each human subject (or his representative) of proposed clinical testing involving such device, except where, subject to such conditions as the Secretary may prescribe—

(i) the proposed clinical testing poses no more than minimal risk to the human subject and includes appropriate safeguards to protect the rights, safety, and welfare of the human subject; or

(ii) the investigator conducting or supervising the proposed clinical testing of the device determines in writing that there exists a life threatening situation involving the human subject of such testing which necessitates the use of such device and it is not feasible to obtain informed consent from the subject and there is not sufficient time to obtain such consent from his representative.

The determination required by subparagraph (D)(ii) shall be concurred in by a licensed physician who is not involved in the testing of the human subject with respect to which such determination is made unless immediate use of the device is required to save the life of the human subject of such testing and there is not sufficient time to obtain such concurrence.

(4)(A) An application, submitted in accordance with the procedures prescribed by regulations under paragraph (2), for an exemption for a device (other than an exemption from section 360f of this title) shall be deemed approved on the thirtieth day after the submission of the application to the Secretary unless on or before such day the Secretary by order disapproves the application and notifies the applicant of the disapproval of the application.

(B) The Secretary may disapprove an application only if he finds that the investigation with respect to which the application is submitted does not conform to procedures and conditions prescribed under regulations under paragraph (2). Such a notification shall contain the order of disapproval and a complete statement of the reasons for the Secretary's disapproval of the application and afford the applicant opportunity for an informal hearing on the disapproval order.

(C) Consistent with paragraph (1), the Secretary shall not disapprove an application under this subsection because the Secretary determines that—

(i) the investigation may not support a substantial equivalence or de novo classification determination or approval of the device;

(ii) the investigation may not meet a requirement, including a data requirement, relating to the approval or clearance of a device; or

(iii) an additional or different investigation may be necessary to support clearance or approval of the device.

(5) The Secretary may by order withdraw an exemption granted under this subsection for a device if the Secretary determines that the conditions applicable to the device under this subsection for such exemption are not met. Such an order may be issued only after opportunity for an informal hearing, except that such an order may be issued before the provision of an opportunity for an informal hearing if the Secretary determines that the continuation of testing under the exemption with respect to which the order is to be issued will result in an unreasonable risk to the public health.

(6)(A) Not later than 1 year after November 21, 1997, the Secretary shall by regulation establish, with respect to a device for which an exemption under this subsection is in effect, procedures and conditions that, without requiring an additional approval of an application for an exemption or the approval of a supplement to such an application, permit—

(i) developmental changes in the device (including manufacturing changes) that do not constitute a significant change in design or in basic principles of operation and that are made in response to information gathered during the course of an investigation; and

(ii) changes or modifications to clinical protocols that do not affect—

(I) the validity of data or information resulting from the completion of an approved protocol, or the relationship of likely patient risk to benefit relied upon to approve a protocol;

(II) the scientific soundness of an investigational plan submitted under paragraph (3)(A); or

(III) the rights, safety, or welfare of the human subjects involved in the investigation.

(B) Regulations under subparagraph (A) shall provide that a change or modification described in such subparagraph may be made if—

(i) the sponsor of the investigation determines, on the basis of credible information (as defined by the Secretary) that the applicable conditions under subparagraph (A) are met; and

(ii) the sponsor submits to the Secretary, not later than 5 days after making the change or modification, a notice of the change or modification.

(7)(A) In the case of a person intending to investigate the safety or effectiveness of a class III device or any implantable device, the Secretary shall ensure that the person has an opportunity, prior to submitting an application to the Secretary or to an institutional review committee, to submit to the Secretary, for review, an investigational plan (including a clinical protocol). If the applicant submits a written request for a meeting with the Secretary regarding such review, the Secretary shall, not later than 30 days after receiving the request, meet with the applicant for the purpose of reaching agreement regarding the investigational plan (including a clinical protocol). The written re-

quest shall include a detailed description of the device, a detailed description of the proposed conditions of use of the device, a proposed plan (including a clinical protocol) for determining whether there is a reasonable assurance of effectiveness, and, if available, information regarding the expected performance from the device.

(B) Any agreement regarding the parameters of an investigational plan (including a clinical protocol) that is reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Any such agreement shall not be changed, except—

(i) with the written agreement of the sponsor or applicant; or

(ii) pursuant to a decision, made in accordance with subparagraph (C) by the director of the office in which the device involved is reviewed, that a substantial scientific issue essential to determining the safety or effectiveness of the device involved has been identified.

(C) A decision under subparagraph (B)(ii) by the director shall be in writing, and may be made only after the Secretary has provided to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant are present and at which the director documents the scientific issue involved.

(8)(A) At any time, the Secretary may prohibit the sponsor of an investigation from conducting the investigation (referred to in this paragraph as a ''clinical hold'') if the Secretary makes a determination described in subparagraph (B). The Secretary shall specify the basis for the clinical hold, including the specific information available to the Secretary which served as the basis for such clinical hold, and confirm such determination in writing.

(B) For purposes of subparagraph (A), a determination described in this subparagraph with respect to a clinical hold is a determination that—

(i) the device involved represents an unreasonable risk to the safety of the persons who are the subjects of the clinical investigation, taking into account the qualifications of the clinical investigators, information about the device, the design of the clinical investigation, the condition for which the device is to be investigated, and the health status of the subjects involved; or

(ii) the clinical hold should be issued for such other reasons as the Secretary may by regulation establish.

(C) Any written request to the Secretary from the sponsor of an investigation that a clinical hold be removed shall receive a decision, in writing and specifying the reasons therefor, within 30 days after receipt of such request. Any such request shall include sufficient information to support the removal of such clinical hold.

(9)(A)(i)[1] The sponsor of a device for which submission of an application for an investigational device exemption is required shall submit to the Secretary in such application a diversity action plan for clinical studies of the device, in the form and manner specified in guidance issued by the Secretary.

(ii) The sponsor of a device for which submission of an application for an investigational device exemption is not required, except for a device being studied as described in section 812.2(c) of title 21, Code of Federal Regulations (or successor regulations), shall develop a diversity action plan for any clinical study with respect to the device. Such diversity action plan shall be submitted to the Secretary in any premarket notification under section 360(k) of this title, request for classification under section 360c(f)(2) of this title, or application for premarket approval under section 360e of this title for such device.

(B) A diversity action plan under clause (i) or (ii) of subparagraph (A) shall include—

(i) the sponsor's goals for enrollment in the clinical study;

(ii) the sponsor's rationale for such goals; and

(iii) an explanation of how the sponsor intends to meet such goals.

(C)(i) On the initiative of the Secretary or at the request of a sponsor, the Secretary may waive any requirement in subparagraph (A) or (B) if the Secretary determines that a waiver is necessary based on what is known or can be determined about the prevalence or incidence of the disease or condition for which the device is under investigation (including in terms of the patient population that may use the device), if conducting a clinical investigation in accordance with a diversity action plan would otherwise be impracticable, or if such waiver is necessary to protect public health during a public health emergency.

(ii) The Secretary shall issue a written response granting or denying a request from a sponsor for a waiver within 60 days of receiving such request.

(D) No diversity action plan shall be required for a submission described in section 360bbb of this title.

(h) Release of information respecting safety and effectiveness

(1) The Secretary shall promulgate regulations under which a detailed summary of information respecting the safety and effectiveness of a device which information was submitted to the Secretary and which was the basis for—

(A) an order under section 360e(d)(1)(A) of this title approving an application for premarket approval for the device or denying approval of such an application or an order under section 360e(e) of this title withdrawing approval of such an application for the device,

(B) an order under section 360e(f)(6)(A) of this title revoking an approved protocol for the device, an order under section 360e(f)(6)(B) of this title declaring a protocol for the device completed or not completed, or an order under section 360e(f)(7) of this title revoking the approval of the device, or

(C) an order approving an application under subsection (g) for an exemption for the device from section 360f of this title or an order disapproving, or withdrawing approval of, an application for an exemption under such subsection for the device,

[1] See Delayed Applicability of Amendment note below.

shall be made available to the public upon issuance of the order. Summaries of information made available pursuant to this paragraph respecting a device shall include information respecting any adverse effects on health of the device.

(2) The Secretary shall promulgate regulations under which each advisory committee established under section 360e(g)(2)(B) of this title shall make available to the public a detailed summary of information respecting the safety and effectiveness of a device which information was submitted to the advisory committee and which was the basis for its recommendation to the Secretary made pursuant to section 360e(g)(2)(A) of this title. A summary of information upon which such a recommendation is based shall be made available pursuant to this paragraph only after the issuance of the order with respect to which the recommendation was made and each summary shall include information respecting any adverse effect on health of the device subject to such order.

(3) Except as provided in paragraph (4), any information respecting a device which is made available pursuant to paragraph (1) or (2) of this subsection (A) may not be used to establish the safety or effectiveness of another device for purposes of this chapter by any person other than the person who submitted the information so made available, and (B) shall be made available subject to subsection (c) of this section.

(4)(A) Subject to subparagraph (C), any information contained in an application for premarket approval filed with the Secretary pursuant to section 360e(c) of this title (including information from clinical and preclinical tests or studies that demonstrate the safety and effectiveness of a device, but excluding descriptions of methods of manufacture and product composition and other trade secrets) shall be available, 6 years after the application has been approved by the Secretary, for use by the Secretary in—

(i) approving another device;

(ii) determining whether a product development protocol has been completed, under section 360e of this title for another device;

(iii) establishing a performance standard or special control under this chapter; or

(iv) classifying or reclassifying another device under section 360c of this title and subsection (*l*)(2).

(B) The publicly available detailed summaries of information respecting the safety and effectiveness of devices required by paragraph (1)(A) shall be available for use by the Secretary as the evidentiary basis for the agency actions described in subparagraph (A).

(C) No information contained in an application for premarket approval filed with the Secretary pursuant to section 360e(c) of this title may be used to approve or clear any application submitted under section 360e or 360(k) of this title or to classify a product under section 360c(f)(2) of this title for a combination product containing as a constituent part an approved drug (as defined in section 353(g)(5)(B) of this title) unless—

(i) the application includes the certification or statement referenced in section 353(g)(5)(A) of this title;

(ii) the applicant provides notice as described in section 353(g)(5)(A) of this title; and

(iii) the Secretary's approval of such application is subject to the provisions in section 353(g)(5)(C) of this title.

(i) Proceedings of advisory panels and committees

Each panel under section 360c of this title and each advisory committee established under section 360d(b)(5)(B) or 360e(g) of this title or under subsection (f) of this section shall make and maintain a transcript of any proceeding of the panel or committee. Each such panel and committee shall delete from any transcript made pursuant to this subsection information which under subsection (c) of this section is to be considered confidential.

(j) Traceability

Except as provided in section 360i(e) of this title, no regulation under this chapter may impose on a type or class of device requirements for the traceability of such type or class of device unless such requirements are necessary to assure the protection of the public health.

(k) Research and development

The Secretary may enter into contracts for research, testing, and demonstrations respecting devices and may obtain devices for research, testing, and demonstration purposes without regard to section 3324(a) and (b) of title 31 and section 6101 of title 41.

***(l)* Transitional provisions for devices considered as new drugs**

(1) Any device intended for human use—

(A) for which on May 28, 1976 (hereinafter in this subsection referred to as the ''enactment date'') an approval of an application submitted under section 355(b) of this title was in effect;

(B) for which such an application was filed on or before the enactment date and with respect to which application no order of approval or refusing to approve had been issued on such date under subsection (c) or (d) of such section;

(C) for which on the enactment date an exemption under subsection (i) of such section was in effect;

(D) which is within a type of device described in subparagraph (A), (B), or (C) and is substantially equivalent to another device within that type;

(E) which the Secretary in a notice published in the Federal Register before the enactment date has declared to be a new drug subject to section 355 of this title; or

(F) with respect to which on the enactment date an action is pending in a United States court under section 332, 333, or 334 of this title for an alleged violation of a provision of section 331 of this title which enforces a requirement of section 355 of this title or for an alleged violation of section 355(a) of this title,

is classified in class III unless the Secretary in response to a petition submitted under paragraph (2) has classified such device in class I or II.

(2) The Secretary may initiate the reclassification of a device classified into class III under

paragraph (1) of this subsection or the manufacturer or importer of a device classified under paragraph (1) may petition the Secretary (in such form and manner as he shall prescribe) for the issuance of an order classifying the device in class I or class II. Within thirty days of the filing of such a petition, the Secretary shall notify the petitioner of any deficiencies in the petition which prevent the Secretary from making a decision on the petition. Except as provided in paragraph (3)(D)(ii), within one hundred and eighty days after the filing of a petition under this paragraph, the Secretary shall, after consultation with the appropriate panel under section 360c of this title, by order either deny the petition or order the classification, in accordance with the criteria prescribed by section 360c(a)(1)(A) of this title or 360c(a)(1)(B) of this title, of the device in class I or class II.

(3)(A) In the case of a device which is described in paragraph (1)(A) and which is in class III—

(i) such device shall on the enactment date be considered a device with an approved application under section 360e of this title, and

(ii) the requirements applicable to such device before the enactment date under section 355 of this title shall continue to apply to such device until changed by the Secretary as authorized by this chapter.

(B) In the case of a device which is described in paragraph (1)(B) and which is in class III, an application for such device shall be considered as having been filed under section 360e of this title on the enactment date. The period in which the Secretary shall act on such application in accordance with section 360e(d)(1) of this title shall be one hundred and eighty days from the enactment date (or such greater period as the Secretary and the applicant may agree upon after the Secretary has made the finding required by section 360e(d)(1)(B)(i) of this title) less the number of days in the period beginning on the date an application for such device was filed under section 355 of this title and ending on the enactment date. After the expiration of such period such device is required, unless exempt under subsection (g), to have in effect an approved application under section 360e of this title.

(C) A device which is described in paragraph (1)(C) and which is in class III shall be considered a new drug until the expiration of the ninety-day period beginning on the date of the promulgation of regulations under subsection (g) of this section. After the expiration of such period such device is required, unless exempt under subsection (g), to have in effect an approved application under section 360e of this title.

(D)(i) Except as provided in clauses (ii) and (iii), a device which is described in subparagraph (D), (E), or (F) of paragraph (1) and which is in class III is required, unless exempt under subsection (g) of this section, to have on and after sixty days after the enactment date in effect an approved application under section 360e of this title.

(ii) If—

(I) a petition is filed under paragraph (2) for a device described in subparagraph (D), (E), or (F) of paragraph (1), or

(II) an application for premarket approval is filed under section 360e of this title for such a device,

within the sixty-day period beginning on the enactment date (or within such greater period as the Secretary, after making the finding required under section 360e(d)(1)(B) of this title, and the petitioner or applicant may agree upon), the Secretary shall act on such petition or application in accordance with paragraph (2) or section 360e of this title except that the period within which the Secretary must act on the petition or application shall be within the one hundred and twenty-day period beginning on the date the petition or application is filed. If such a petition or application is filed within such sixty-day (or greater) period, clause (i) of this subparagraph shall not apply to such device before the expiration of such one hundred and twenty-day period, or if such petition is denied or such application is denied approval, before the date of such denial, whichever occurs first.

(iii) In the case of a device which is described in subparagraph (E) of paragraph (1), which the Secretary in a notice published in the Federal Register after March 31, 1976, declared to be a new drug subject to section 355 of this title, and which is in class III—

(I) the device shall, after eighteen months after the enactment date, have in effect an approved application under section 360e of this title unless exempt under subsection (g) of this section, and

(II) the Secretary may, during the period beginning one hundred and eighty days after the enactment date and ending eighteen months after such date, restrict the use of the device to investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of such device, and to investigational use in accordance with the requirements applicable under regulations under subsection (g) of this section to investigational use of devices granted an exemption under such subsection.

If the requirements under subsection (g) of this section are made applicable to the investigational use of such a device, they shall be made applicable in such a manner that the device shall be made reasonably available to physicians meeting appropriate qualifications prescribed by the Secretary.

(4) Repealed. Pub. L. 105–115, title I, § 125(b)(2)(E), Nov. 21, 1997, 111 Stat. 2325.

(5)(A) Before December 1, 1991, the Secretary shall by order require manufacturers of devices described in paragraph (1), which are subject to revision of classification under subparagraph (B), to submit to the Secretary a summary of and citation to any information known or otherwise available to the manufacturers respecting the devices, including adverse safety or effectiveness information which has not been submitted under section 360i of this title. The Secretary may require a manufacturer to submit the adverse safety or effectiveness data for which a summary and citation were submitted, if such data are available to the manufacturer.

(B) Except as provided in subparagraph (C), after the issuance of an order under subpara-

graph (A) but before December 1, 1992, the Secretary shall publish a regulation in the Federal Register for each device which is classified in class III under paragraph (1) revising the classification of the device so that the device is classified into class I or class II, unless the regulation requires the device to remain in class III. In determining whether to revise the classification of a device or to require a device to remain in class III, the Secretary shall apply the criteria set forth in section 360c(a) of this title. Before the publication of a regulation requiring a device to remain in class III or revising its classification, the Secretary shall publish a proposed regulation respecting the classification of a device under this subparagraph and provide an opportunity for the submission of comments on any such regulation. No regulation under this subparagraph requiring a device to remain in class III or revising its classification may take effect before the expiration of 90 days from the date of the publication in the Federal Register of the proposed regulation.

(C) The Secretary may by notice published in the Federal Register extend the period prescribed by subparagraph (B) for a device for an additional period not to exceed 1 year.

(m) Humanitarian device exemption

(1) To the extent consistent with the protection of the public health and safety and with ethical standards, it is the purpose of this subsection to encourage the discovery and use of devices intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect not more than 8,000 individuals in the United States.

(2) The Secretary may grant a request for an exemption from the effectiveness requirements of sections 360d and 360e of this title for a device for which the Secretary finds that—

(A) the device is designed to treat or diagnose a disease or condition that affects not more than 8,000 individuals in the United States,

(B) the device would not be available to a person with a disease or condition referred to in subparagraph (A) unless the Secretary grants such an exemption and there is no comparable device, other than under this exemption, available to treat or diagnose such disease or condition, and

(C) the device will not expose patients to an unreasonable or significant risk of illness or injury and the probable benefit to health from the use of the device outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment.

The request shall be in the form of an application submitted to the Secretary and such application shall include the certification required under section 282(j)(5)(B) of title 42 (which shall not be considered an element of such application). Not later than 75 days after the date of the receipt of the application, the Secretary shall issue an order approving or denying the application.

(3) Except as provided in paragraph (6), no person granted an exemption under paragraph (2) with respect to a device may sell the device for an amount that exceeds the costs of research and development, fabrication, and distribution of the device.

(4) Devices granted an exemption under paragraph (2) may only be used—

(A) in facilities in which clinical testing of devices is supervised by an institutional review committee established in accordance with the regulations of the Secretary; and

(B) if, before the use of a device, an institutional review committee or an appropriate local committee approves the use in the treatment or diagnosis of a disease or condition referred to in paragraph (2)(A), unless a physician determines in an emergency situation that approval from an institutional review committee or an appropriate local committee can not be obtained in time to prevent serious harm or death to a patient.

In a case described in subparagraph (B) in which a physician uses a device without an approval from an institutional review committee or an appropriate local committee, the physician shall, after the use of the device, notify the chairperson of the institutional review committee or an appropriate local committee of such use. Such notification shall include the identification of the patient involved, the date on which the device was used, and the reason for the use.

(5) The Secretary may require a person granted an exemption under paragraph (2) to demonstrate continued compliance with the requirements of this subsection if the Secretary believes such demonstration to be necessary to protect the public health, if the Secretary has reason to believe that the requirements of paragraph (6) are no longer met, or if the Secretary has reason to believe that the criteria for the exemption are no longer met. If the person granted an exemption under paragraph (2) fails to demonstrate continued compliance with the requirements of this subsection, the Secretary may suspend or withdraw the exemption from the effectiveness requirements of sections 360d and 360e of this title for a humanitarian device only after providing notice and an opportunity for an informal hearing.

(6)(A) Except as provided in subparagraph (D), the prohibition in paragraph (3) shall not apply with respect to a person granted an exemption under paragraph (2) if each of the following conditions apply:

(i) The device with respect to which the exemption is granted—

(I) is intended for the treatment or diagnosis of a disease or condition that occurs in pediatric patients or in a pediatric subpopulation, and such device is labeled for use in pediatric patients or in a pediatric subpopulation in which the disease or condition occurs; or

(II) is intended for the treatment or diagnosis of a disease or condition that does not occur in pediatric patients or that occurs in pediatric patients in such numbers that the development of the device for such patients is impossible, highly impracticable, or unsafe.

(ii) During any calendar year, the number of such devices distributed during that year under each exemption granted under this subsection does not exceed the annual distribution number for such device. In this paragraph, the term ''annual distribution number'' means the number of such devices reasonably needed to treat, diagnose, or cure a population of 8,000 individuals in the United States. The Secretary shall determine the annual distribution number when the Secretary grants such exemption.

(iii) Such person immediately notifies the Secretary if the number of such devices distributed during any calendar year exceeds the annual distribution number referred to in clause (ii).

(iv) The request for such exemption is submitted on or before October 1, 2027.

(B) The Secretary may inspect the records relating to the number of devices distributed during any calendar year of a person granted an exemption under paragraph (2) for which the prohibition in paragraph (3) does not apply.

(C) A person may petition the Secretary to modify the annual distribution number determined by the Secretary under subparagraph (A)(ii) with respect to a device if additional information arises, and the Secretary may modify such annual distribution number.

(D) If a person notifies the Secretary, or the Secretary determines through an inspection under subparagraph (B), that the number of devices distributed during any calendar year exceeds the annual distribution number, as required under subparagraph (A)(iii), and modified under subparagraph (C), if applicable, then the prohibition in paragraph (3) shall apply with respect to such person for such device for any sales of such device after such notification.

(E)(i) In this subsection, the term ''pediatric patients'' means patients who are 21 years of age or younger at the time of the diagnosis or treatment.

(ii) In this subsection, the term ''pediatric subpopulation'' means 1 of the following populations:

(I) Neonates.

(II) Infants.

(III) Children.

(IV) Adolescents.

(7) The Secretary shall refer any report of an adverse event regarding a device described in paragraph (6)(A)(i)(I) for which the prohibition under paragraph (3) does not apply pursuant to paragraph (6)(A) that the Secretary receives to the Office of Pediatric Therapeutics, established under section 393a of this title. In considering the report, the Director of the Office of Pediatric Therapeutics, in consultation with experts in the Center for Devices and Radiological Health, shall provide for periodic review of the report by the Pediatric Advisory Committee, including obtaining any recommendations of such committee regarding whether the Secretary should take action under this chapter in response to the report.

(8) The Secretary, acting through the Office of Pediatric Therapeutics and the Center for Devices and Radiological Health, shall provide for an annual review by the Pediatric Advisory Committee of all devices described in paragraph (6)(A)(i)(I) to ensure that the exemption under paragraph (2) remains appropriate for the pediatric populations for which it is granted.

(n) Regulation of contact lenses as devices

(1) All contact lenses shall be deemed to be devices under section 321(h) of this title.

(2) Paragraph (1) shall not be construed as bearing on or being relevant to the question of whether any product other than a contact lens is a device as defined by section 321(h) of this title or a drug as defined by section 321(g) of this title.

***(o)* Regulation of medical and certain decisions support software**

(1) The term device,[2] as defined in section 321(h) of this title, shall not include a software function that is intended—

(A) for administrative support of a health care facility, including the processing and maintenance of financial records, claims or billing information, appointment schedules, business analytics, information about patient populations, admissions, practice and inventory management, analysis of historical claims data to predict future utilization or cost-effectiveness, determination of health benefit eligibility, population health management, and laboratory workflow;

(B) for maintaining or encouraging a healthy lifestyle and is unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition;

(C) to serve as electronic patient records, including patient-provided information, to the extent that such records are intended to transfer, store, convert formats, or display the equivalent of a paper medical chart, so long as—

(i) such records were created, stored, transferred, or reviewed by health care professionals, or by individuals working under supervision of such professionals;

(ii) such records are part of health information technology that is certified under section 300jj–11(c)(5) of title 42; and

(iii) such function is not intended to interpret or analyze patient records, including medical image data, for the purpose of the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition;

(D) for transferring, storing, converting formats, or displaying clinical laboratory test or other device data and results, findings by a health care professional with respect to such data and results, general information about such findings, and general background information about such laboratory test or other device, unless such function is intended to interpret or analyze clinical laboratory test or other device data, results, and findings; or

(E) unless the function is intended to acquire, process, or analyze a medical image or a signal from an in vitro diagnostic device or a pattern or signal from a signal acquisition system, for the purpose of—

[2] So in original. Probably should be ''The term 'device',''.

(i) displaying, analyzing, or printing medical information about a patient or other medical information (such as peer-reviewed clinical studies and clinical practice guidelines);

(ii) supporting or providing recommendations to a health care professional about prevention, diagnosis, or treatment of a disease or condition; and

(iii) enabling such health care professional to independently review the basis for such recommendations that such software presents so that it is not the intent that such health care professional rely primarily on any of such recommendations to make a clinical diagnosis or treatment decision regarding an individual patient.

(2) In the case of a product with multiple functions that contains—

(A) at least one software function that meets the criteria under paragraph (1) or that otherwise does not meet the definition of device under section 321(h) of this title; and

(B) at least one function that does not meet the criteria under paragraph (1) and that otherwise meets the definition of a device under section 321(h) of this title,

the Secretary shall not regulate the software function of such product described in subparagraph (A) as a device. Notwithstanding the preceding sentence, when assessing the safety and effectiveness of the device function or functions of such product described in subparagraph (B), the Secretary may assess the impact that the software function or functions described in subparagraph (A) have on such device function or functions.

(3)(A) Notwithstanding paragraph (1), a software function described in subparagraph (C), (D), or (E) of paragraph (1) shall not be excluded from the definition of device under section 321(h) of this title if—

(i) the Secretary makes a finding that use of such software function would be reasonably likely to have serious adverse health consequences; and

(ii) the software function has been identified in a final order issued by the Secretary under subparagraph (B).

(B) Subparagraph (A) shall apply only if the Secretary—

(i) publishes a notification and proposed order in the Federal Register;

(ii) includes in such notification the Secretary's finding, including the rationale and identification of the evidence on which such finding was based, as described in subparagraph (A)(i); and

(iii) provides for a period of not less than 30 calendar days for public comment before issuing a final order or withdrawing such proposed order.

(C) In making a finding under subparagraph (A)(i) with respect to a software function, the Secretary shall consider—

(i) the likelihood and severity of patient harm if the software function were to not perform as intended;

(ii) the extent to which the software function is intended to support the clinical judgment of a health care professional;

(iii) whether there is a reasonable opportunity for a health care professional to review the basis of the information or treatment recommendation provided by the software function; and

(iv) the intended user and user environment, such as whether a health care professional will use a software function of a type described in subparagraph (E) of paragraph (1).

(4) Nothing in this subsection shall be construed as limiting the authority of the Secretary to—

(A) exercise enforcement discretion as to any device subject to regulation under this chapter;

(B) regulate software used in the manufacture and transfusion of blood and blood components to assist in the prevention of disease in humans; or

(C) regulate software as a device under this chapter if such software meets the criteria under section 360c(a)(1)(C) of this title.

(p) Diagnostic imaging devices intended for use with contrast agents

(1) In general

The Secretary may, subject to the succeeding provisions of this subsection, approve an application (or a supplement to such an application) submitted under section 360e of this title with respect to an applicable medical imaging device, or, in the case of an applicable medical imaging device for which a notification is submitted under section 360(k) of this title, may make a substantial equivalence determination with respect to an applicable medical imaging device, or may grant a request submitted under section 360c(f)(2) of this title for an applicable medical imaging device, if such application, notification, or request involves the use of a contrast agent that is not—

(A) in a concentration, rate of administration, or route of administration that is different from those described in the approved labeling of the contrast agent, except that the Secretary may approve such application, make such substantial equivalence determination, or grant such request if the Secretary determines that such differences in concentration, rate of administration, or route of administration exist but do not adversely affect the safety and effectiveness of the contrast agent when used with the device;

(B) in a region, organ, or system of the body that is different from those described in the approved labeling of the contrast agent, except that the Secretary may approve such application, make such substantial equivalence determination, or grant such request if the Secretary determines that such differences in region, organ, or system of the body exist but do not adversely affect the safety and effectiveness of the contrast agent when used with the device;

(C) in a patient population that is different from those described in the approved labeling of the contrast agent, except that the Secretary may approve such application, make such substantial equivalence deter-

mination, or grant such request if the Secretary determines such differences in patient population exist but do not adversely affect the safety and effectiveness of the contrast agent when used with the device; or

(D) in an imaging modality that is different from those described in the approved labeling of the contrast agent.

(2) Premarket review

The agency center charged with premarket review of devices shall have primary jurisdiction with respect to the review of an application, notification, or request described in paragraph (1). In conducting such review, such agency center may—

(A) consult with the agency center charged with the premarket review of drugs or biological products; and

(B) review information and data provided to the Secretary by the sponsor of a contrast agent in an application submitted under section 355 of this title or section 262 of title 42, so long as the sponsor of such contrast agent has provided to the sponsor of the applicable medical imaging device that is the subject of such review a right of reference and the application is submitted in accordance with this subsection.

(3) Applicable requirements

An application submitted under section 360e of this title, a notification submitted under section 360(k) of this title, or a request submitted under section 360c(f)(2) of this title, as described in paragraph (1), with respect to an applicable medical imaging device shall be subject to the requirements of such respective section. Such application, notification, or request shall only be subject to the requirements of this chapter applicable to devices.

(4) Definitions

For purposes of this subsection—

(A) the term ''applicable medical imaging device'' means a device intended to be used in conjunction with a contrast agent (or class of contrast agents) for an imaging use that is not described in the approved labeling of such contrast agent (or the approved labeling of any contrast agent in the same class as such contrast agent); and

(B) the term ''contrast agent'' means a drug that is approved under section 355 of this title or licensed under section 262 of title 42, is intended for use in conjunction with an applicable medical imaging device, and—

(i) is a diagnostic radiopharmaceutical, as defined in section[3] 315.2 and 601.31 of title 21, Code of Federal Regulations (or any successor regulations); or

(ii) is a diagnostic agent that improves the visualization of structure or function within the body by increasing the relative difference in signal intensity within the target tissue, structure, or fluid.

[3] So in original. Probably should be ''sections''.

(q) Regulation of over-the-counter hearing aids

(1) Definition

(A) In general

In this subsection, the term ''over-the-counter hearing aid'' means a device that—

(i) uses the same fundamental scientific technology as air conduction hearing aids (as defined in section 874.3300 of title 21, Code of Federal Regulations) (or any successor regulation) or wireless air conduction hearing aids (as defined in section 874.3305 of title 21, Code of Federal Regulations) (or any successor regulation);

(ii) is intended to be used by adults age 18 and older to compensate for perceived mild to moderate hearing impairment;

(iii) through tools, tests, or software, allows the user to control the over-the-counter hearing aid and customize it to the user's hearing needs;

(iv) may—

(I) use wireless technology; or

(II) include tests for self-assessment of hearing loss; and

(v) is available over-the-counter, without the supervision, prescription, or other order, involvement, or intervention of a licensed person, to consumers through in-person transactions, by mail, or online.

(B) Exception

Such term does not include a personal sound amplification product intended to amplify sound for nonhearing impaired consumers in situations including hunting and bird-watching.

(2) Regulation

An over-the-counter hearing aid shall be subject to the regulations promulgated in accordance with section 709(b) of the FDA Reauthorization Act of 2017 and shall be exempt from sections 801.420 and 801.421 of title 21, Code of Federal Regulations (or any successor regulations).

(June 25, 1938, ch. 675, § 520, as added Pub. L. 94–295, § 2, May 28, 1976, 90 Stat. 565; amended Pub. L. 101–629, §§ 3(b)(2), 4(b)(2), 5(c)(2), 6(b)(2), 11, 14(a), 18(e), (f), Nov. 28, 1990, 104 Stat. 4514, 4516, 4518, 4519, 4522, 4524, 4529; Pub. L. 102–571, title I, § 107(10), Oct. 29, 1992, 106 Stat. 4499; Pub. L. 105–115, title I, § 125(b)(2)(E), title II, §§ 201(a), 203, 216(a)(1), title IV, § 410(a), Nov. 21, 1997, 111 Stat. 2325, 2332, 2334, 2349, 2372; Pub. L. 109–96, § 1, Nov. 9, 2005, 119 Stat. 2119; Pub. L. 110–85, title III, § 303(a), title VIII, § 801(b)(3)(E), Sept. 27, 2007, 121 Stat. 860, 921; Pub. L. 112–144, title V, § 507(c), title VI, §§ 601, 606, 613(a), 617, July 9, 2012, 126 Stat. 1045, 1051, 1054, 1060, 1062; Pub. L. 114–255, div. A, title III, §§ 3024(a), 3038(b), 3052(a), 3056, 3060(a), Dec. 13, 2016, 130 Stat. 1099, 1110, 1124, 1128, 1130; Pub. L. 115–52, title V, § 502(b), title VII, §§ 706(a), 709(a), Aug. 18, 2017, 131 Stat. 1037, 1058, 1065; Pub. L. 117–180, div. F, title V, § 5002, Sept. 30, 2022, 136 Stat. 2167; Pub. L. 117–229, div. C, title III, § 303, Dec. 16, 2022, 136 Stat. 2312; Pub. L. 117–286, § 4(a)(156), Dec. 27, 2022, 136 Stat. 4323; Pub. L. 117–328, div. FF, title III, §§ 3103, 3601(b), Dec. 29, 2022, 136 Stat. 5807, 5861.)

DELAYED APPLICABILITY OF AMENDMENT

For provisions related to delayed applicability of subsection (g)(9) of this section as added by section 3601(b) of Pub. L. 117–328, see Effective Date of 2022 Amendment note set out under section 355 of this title.

Editorial Notes

REFERENCES IN TEXT

July 9, 2012, referred to in subsec. (b)(3), was in the original ''the date of enactment of this section'', which was translated as meaning the date of enactment of Pub. L. 112–144, which amended subsec. (b) generally, to reflect the probable intent of Congress.

Section 709(b) of the FDA Reauthorization Act of 2017, referred to in subsec. (q)(2), is section 709(b) of Pub. L. 115–52, which is set out as a note below.

CODIFICATION

In subsec. (k), ''section 3324(a) and (b) of title 31 and section 6101 of title 41'' substituted for ''sections 3648 and 3709 of the Revised Statutes (31 U.S.C. 529, 41 U.S.C. 5)'' on authority of Pub. L. 97–258, §4(b), Sept. 13, 1982, 96 Stat. 1067, which Act enacted Title 31, Money and Finance, and Pub. L. 111–350, §6(c), Jan. 4, 2011, 124 Stat. 3854, which Act enacted Title 41, Public Contracts.

AMENDMENTS

2022—Subsec. (f)(3). Pub. L. 117–286 substituted ''Section 1013 of title 5'' for ''Section 14 of the Federal Advisory Committee Act'' in concluding provisions.

Subsec. (g)(9). Pub. L. 117–328, §3601(b), added par. (9).

Subsec. (m)(6)(A)(iv). Pub. L. 117–328, §3103, substituted ''October 1, 2027'' for ''December 24, 2022''.

Pub. L. 117–229 substituted ''December 24, 2022'' for ''December 17, 2022''.

Pub. L. 117–180 substituted ''December 17'' for ''October 1''.

2017—Subsec. (m)(4). Pub. L. 115–52, §502(b)(1)(B), inserted ''or an appropriate local committee'' after ''review committee'' in two places in concluding provisions.

Subsec. (m)(4)(B). Pub. L. 115–52, §502(b)(1)(A), inserted ''or an appropriate local committee'' after ''review committee'' in two places.

Subsec. (m)(6)(A)(iv). Pub. L. 115–52, §502(b)(2), substituted ''2022'' for ''2017''.

Subsec. (p). Pub. L. 115–52, §706(a), added subsec. (p).

Subsec. (q). Pub. L. 115–52, §709(a), added subsec. (q). Amendment was executed to this section as amended by section 706(a) of Pub. L. 115–52, notwithstanding directory language referring to section as amended by section 708 of Pub. L. 115–52, which did not amend this section.

2016—Subsec. (g)(3). Pub. L. 114–255, §3024(a)(2), substituted ''subparagraph (D)(ii)'' for ''subparagraph (D)'' in concluding provisions.

Subsec. (g)(3)(A)(i). Pub. L. 114–255, §3056(1)(A), struck out ''local'' before ''institutional review committee'' and ''which has been'' before ''established in accordance with''.

Subsec. (g)(3)(B). Pub. L. 114–255, §3056(1)(B), substituted ''an institutional'' for ''a local institutional''.

Subsec. (g)(3)(D). Pub. L. 114–255, §3024(a)(1), substituted ''except where, subject to such conditions as the Secretary may prescribe—'' for ''except where subject to such conditions as the Secretary may prescribe,'', added cl. (i), and inserted cl. (ii) designation before ''the investigator''.

Subsec. (h)(4)(A). Pub. L. 114–255, §3038(b)(1), substituted ''Subject to subparagraph (C), any information'' for ''Any information'' in introductory provisions.

Subsec. (h)(4)(C). Pub. L. 114–255, §3038(b)(2), added subpar. (C).

Subsec. (m)(1). Pub. L. 114–255, §3052(a)(1), substituted ''not more than 8,000'' for ''fewer than 4,000''.

Subsec. (m)(2)(A). Pub. L. 114–255, §3052(a)(2), substituted ''not more than 8,000'' for ''fewer than 4,000''.

Subsec. (m)(4). Pub. L. 114–255, §3056(2)(C), struck out ''local'' after ''chairperson of the'' in concluding provisions.

Subsec. (m)(4)(A). Pub. L. 114–255, §3056(2)(A), added subpar. (A) and struck out former subpar. (A) which read as follows: ''in facilities that have established, in accordance with regulations of the Secretary, a local institutional review committee to supervise clinical testing of devices in the facilities, and''.

Subsec. (m)(4)(B). Pub. L. 114–255, §3056(2)(B), substituted ''an institutional'' for ''a local institutional''.

Subsec. (m)(6)(A)(ii). Pub. L. 114–255, §3052(a)(3), substituted ''8,000'' for ''4,000''.

Subsec. (*o*). Pub. L. 114–255, §3060(a), added subsec. (*o*).

2012—Subsec. (b). Pub. L. 112–144, §617, amended subsec. (b) generally. Prior to amendment, subsec. (b) related to custom devices.

Subsec. (g)(2)(B)(ii). Pub. L. 112–144, §601(1), inserted ''safety or effectiveness'' before ''data obtained''.

Subsec. (g)(4)(C). Pub. L. 112–144, §601(2), added subpar. (C).

Subsec. (g)(8). Pub. L. 112–144, §606, added par. (8).

Subsec. (m)(6)(A)(i). Pub. L. 112–144, §613(a)(1)(A)(i), added cl. (i) and struck out former cl. (i) which read as follows:

''(i)(I) The device with respect to which the exemption is granted is intended for the treatment or diagnosis of a disease or condition that occurs in pediatric patients or in a pediatric subpopulation, and such device is labeled for use in pediatric patients or in a pediatric subpopulation in which the disease or condition occurs.

''(II) The device was not previously approved under this subsection for the pediatric patients or the pediatric subpopulation described in subclause (I) prior to September 27, 2007.''

Subsec. (m)(6)(A)(ii). Pub. L. 112–144, §613(a)(1)(A)(ii), added cl. (ii) and struck out former cl. (ii) which read as follows: ''During any calendar year, the number of such devices distributed during that year does not exceed the annual distribution number specified by the Secretary when the Secretary grants such exemption. The annual distribution number shall be based on the number of individuals affected by the disease or condition that such device is intended to treat, diagnose, or cure, and of that number, the number of individuals likely to use the device, and the number of devices reasonably necessary to treat such individuals. In no case shall the annual distribution number exceed the number identified in paragraph (2)(A).''

Subsec. (m)(6)(A)(iv). Pub. L. 112–144, §507(c), substituted ''2017'' for ''2012''.

Subsec. (m)(6)(C). Pub. L. 112–144, §613(a)(1)(B), amended subpar. (C) generally. Prior to amendment, subpar. (C) read as follows: ''A person may petition the Secretary to modify the annual distribution number specified by the Secretary under subparagraph (A)(ii) with respect to a device if additional information on the number of individuals affected by the disease or condition arises, and the Secretary may modify such number but in no case shall the annual distribution number exceed the number identified in paragraph (2)(A).''

Subsec. (m)(7). Pub. L. 112–144, §613(a)(2), substituted ''regarding a device described in paragraph (6)(A)(i)(I)'' for ''regarding a device''.

Subsec. (m)(8). Pub. L. 112–144, §613(a)(3), substituted ''of all devices described in paragraph (6)(A)(i)(I)'' for ''of all devices described in paragraph (6)''.

2007—Subsec. (m)(2). Pub. L. 110–85, §801(b)(3)(E), inserted before period at end of first sentence of concluding provisions ''and such application shall include the certification required under section 282(j)(5)(B) of title 42 (which shall not be considered an element of such application)''.

Subsec. (m)(3). Pub. L. 110–85, §303(a)(1), substituted ''Except as provided in paragraph (6), no'' for ''No''.

Subsec. (m)(5). Pub. L. 110–85, §303(a)(2), inserted '', if the Secretary has reason to believe that the require-

ments of paragraph (6) are no longer met,'' after ''public health'' and inserted at end ''If the person granted an exemption under paragraph (2) fails to demonstrate continued compliance with the requirements of this subsection, the Secretary may suspend or withdraw the exemption from the effectiveness requirements of sections 360d and 360e of this title for a humanitarian device only after providing notice and an opportunity for an informal hearing.''

Subsec. (m)(6) to (8). Pub. L. 110–85, § 303(a)(3), added pars. (6) to (8) and struck out former par. (6) which read as follows: ''The Secretary may suspend or withdraw an exemption from the effectiveness requirements of sections 360d and 360e of this title for a humanitarian device only after providing notice and an opportunity for an informal hearing.''

2005—Subsec. (n). Pub. L. 109–96 added subsec. (n).

1997—Subsec. (f)(1)(B)(iii). Pub. L. 105–115, § 410(a), added cl. (iii).

Subsec. (g)(6), (7). Pub. L. 105–115, § 201(a), added pars. (6) and (7).

Subsec. (h)(4). Pub. L. 105–115, § 216(a)(1), amended par. (4) generally. Prior to amendment, par. (4) related to premarket approval of devices.

Subsec. (*l*). Pub. L. 105–115, § 125(b)(2)(E), struck out ''or antibiotic drugs'' after ''new drugs'' in heading.

Subsec. (*l*)(4). Pub. L. 105–115, § 125(b)(2)(E), struck out par. (4) which read as follows: ''Any device intended for human use which on the enactment date was subject to the requirements of section 357 of this title shall be subject to such requirements as follows:

''(A) In the case of such a device which is classified into class I, such requirements shall apply to such device until the effective date of the regulation classifying the device into such class.

''(B) In the case of such a device which is classified into class II, such requirements shall apply to such device until the effective date of a performance standard applicable to the device under section 360d of this title.

''(C) In the case of such a device which is classified into class III, such requirements shall apply to such device until the date on which the device is required to have in effect an approved application under section 360e of this title.''

Subsec. (m)(2). Pub. L. 105–115, § 203(1), inserted at end ''The request shall be in the form of an application submitted to the Secretary. Not later than 75 days after the date of the receipt of the application, the Secretary shall issue an order approving or denying the application.''

Subsec. (m)(4). Pub. L. 105–115, § 203(2)(B), inserted at end ''In a case described in subparagraph (B) in which a physician uses a device without an approval from an institutional review committee, the physician shall, after the use of the device, notify the chairperson of the local institutional review committee of such use. Such notification shall include the identification of the patient involved, the date on which the device was used, and the reason for the use.''

Subsec. (m)(4)(B). Pub. L. 105–115, § 203(2)(A), inserted before period at end '', unless a physician determines in an emergency situation that approval from a local institutional review committee can not be obtained in time to prevent serious harm or death to a patient''.

Subsec. (m)(5). Pub. L. 105–115, § 203(3), amended par. (5) generally. Prior to amendment, par. (5) read as follows: ''An exemption under paragraph (2) shall be for a term of 18 months and may only be initially granted in the 5-year period beginning on the date regulations under paragraph (6) take effect. The Secretary may extend such an exemption for a period of 18 months if the Secretary is able to make the findings set forth in paragraph (2) and if the applicant supplies information demonstrating compliance with paragraph (3). An exemption may be extended more than once and may be extended after the expiration of such 5-year period.''

Subsec. (m)(6). Pub. L. 105–115, § 203(4), amended par. (6) generally. Prior to amendment, par. (6) read as follows: ''Within one year of November 28, 1990, the Secretary shall issue regulations to implement this subsection.''

1992—Subsec. (g)(2)(A). Pub. L. 102–571 substituted ''379e'' for ''376''.

1990—Subsec. (c). Pub. L. 101–629, § 11(1), substituted ''from class III to class II or class I'' for ''under section 360c of this title from class III to class II'' and inserted ''(1) in accordance with subsection (h), and (2)'' after ''except''.

Subsec. (f)(1)(A). Pub. L. 101–629, § 18(e), inserted ''preproduction design validation (including a process to assess the performance of a device but not including an evaluation of the safety or effectiveness of a device),'' after ''manufacture,''.

Subsec. (h)(3). Pub. L. 101–629, § 11(2)(A), substituted ''Except as provided in paragraph (4), any'' for ''Any''.

Subsec. (h)(4). Pub. L. 101–629, § 11(2)(B), added par. (4).

Subsec. (i). Pub. L. 101–629, § 6(b)(2), substituted ''section 360d(b)(5)(B)'' for ''section 360d(g)(5)(B)''.

Subsec. (j). Pub. L. 101–629, § 3(b)(2), substituted ''Except as provided in section 360i(e) of this title, no'' for ''No''.

Subsec. (*l*)(2). Pub. L. 101–629, § 18(f), struck out ''and after affording the petitioner an opportunity for an informal hearing'' after ''under this paragraph''.

Pub. L. 101–629, § 5(c)(2), substituted ''The Secretary may initiate the reclassification of a device classified into class III under paragraph (1) of this subsection or the manufacturer'' for ''The manufacturer''.

Subsec. (*l*)(5). Pub. L. 101–629, § 4(b)(2), added par. (5).

Subsec. (m). Pub. L. 101–629, § 14(a), added subsec. (m).

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 2022 AMENDMENT

Subsec. (g)(9) of this section, as added by section 3601(b) of Pub. L. 117–328, applicable only with respect to clinical investigations for which enrollment commences after the date that is 180 days after the publication of final guidance required under section 3602 of Pub. L. 117–328, see section 3602(c) of Pub. L. 117–328, set out as a note under section 355 of this title.

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by sections 201(a), 203, 216(a)(1), and 410(a) of Pub. L. 105–115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as a note under section 321 of this title.

EFFECTIVE DATE OF 1990 AMENDMENT

Pub. L. 101–629, § 14(b), Nov. 28, 1990, 104 Stat. 4525, provided that: ''Subsection (m) of section 520 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360j(m)], as added by the amendment made by subsection (a), shall take effect on the effective date of the regulations issued by the Secretary under paragraph (6) of such subsection.''

REGULATIONS AND GUIDANCE CONCERNING OVER-THE-COUNTER HEARING AIDS

Pub. L. 115–52, title VII, § 709(b), (c), Aug. 18, 2017, 131 Stat. 1066, 1067, provided that:

''(b) REGULATIONS TO ESTABLISH CATEGORY.—

''(1) IN GENERAL.—The Secretary of Health and Human Services (referred to in this section [amending this section and enacting this note] as the 'Secretary'), not later than 3 years after the date of enactment of this Act [Aug. 18, 2017], shall promulgate proposed regulations to establish a category of over-the-counter hearing aids, as defined in subsection (q) of section 520 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360j) as amended by subsection (a), and, not later than 180 days after the date on which the public comment period on the proposed regulations closes, shall issue such final regulations.

''(2) REQUIREMENTS.—In promulgating the regulations under paragraph (1), the Secretary shall—

''(A) include requirements that provide reasonable assurances of the safety and effectiveness of over-the-counter hearing aids;

''(B) include requirements that establish or adopt output limits appropriate for over-the-counter hearing aids;

''(C) include requirements for appropriate labeling of over-the-counter hearing aids, including requirements that such labeling include a conspicuous statement that the device is only intended for adults age 18 and older, information on how consumers may report adverse events, information on any contraindications, conditions, or symptoms of medically treatable causes of hearing loss, and advisements to consult promptly with a licensed health care practitioner; and

''(D) describe the requirements under which the sale of over-the-counter hearing aids is permitted, without the supervision, prescription, or other order, involvement, or intervention of a licensed person, to consumers through in-person transactions, by mail, or online.

''(3) PREMARKET NOTIFICATION.—The Secretary shall make findings under section 510(m) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360(m)) to determine whether over-the-counter hearing aids (as defined in section 520(q) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360j[(q)]), as amended by subsection (a)) require a report under section 510(k) [21 U.S.C. 360(k)] to provide reasonable assurance of safety and effectiveness.

''(4) EFFECT ON STATE LAW.—No State or local government shall establish or continue in effect any law, regulation, order, or other requirement specifically related to hearing products that would restrict or interfere with the servicing, marketing, sale, dispensing, use, customer support, or distribution of over-the-counter hearing aids (as defined in section 520(q) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360j[(q)]), as amended by subsection (a)) through in-person transactions, by mail, or online, that is different from, in addition to, or otherwise not identical to, the regulations promulgated under this subsection, including any State or local requirement for the supervision, prescription, or other order, involvement, or intervention of a licensed person for consumers to access over-the-counter hearing aids.

''(5) NO EFFECT ON PRIVATE REMEDIES.—Nothing in this section shall be construed to modify or otherwise affect the ability of any person to exercise a private right of action under any State or Federal product liability, tort, warranty, contract, or consumer protection law.

''(c) NEW GUIDANCE ISSUED.—Not later than the date on which final regulations are issued under subsection (b), the Secretary shall update and finalize the draft guidance of the Department of Health and Human Services entitled 'Regulatory Requirements for Hearing Aid Devices and Personal Sound Amplification Products', issued on November 7, 2013. Such updated and finalized guidance shall clarify which products, on the basis of claims or other marketing, advertising, or labeling material, meet the definition of a device in section 201 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321) and which products meet the definition of a personal sound amplification product, as set forth in such guidance.''

GUIDANCE DOCUMENT ON PROBABLE BENEFIT

Pub. L. 114–255, div. A, title III, §3052(b), Dec. 13, 2016, 130 Stat. 1125, provided that: ''Not later than 18 months after the date of enactment of this Act [Dec. 13, 2016], the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs, shall publish a draft guidance that defines the criteria for establishing 'probable benefit' as that term is used in section 520(m)(2)(C) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360j(m)(2)(C)).''

REPORTS

Pub. L. 114–255, div. A, title III, §3060(b), Dec. 13, 2016, 130 Stat. 1132, provided that: ''The Secretary of Health and Human Services (referred to in this subsection as the 'Secretary'), after consultation with agencies and offices of the Department of Health and Human Services involved in health information technology, shall publish a report, not later than 2 years after the date of enactment of this Act [Dec. 13, 2016] and every 2 years thereafter, that—

''(1) includes input from outside experts, such as representatives of patients, consumers, health care providers, startup companies, health plans or other third-party payers, venture capital investors, information technology vendors, health information technology vendors, small businesses, purchasers, employers, and other stakeholders with relevant expertise, as determined by the Secretary;

''(2) examines information available to the Secretary on any risks and benefits to health associated with software functions described in section 520(*o*)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360j[(*o*)(1)]) (as amended by subsection (a)); and

''(3) summarizes findings regarding the impact of such software functions on patient safety, including best practices to promote safety, education, and competency related to such functions.''

APPLICABILITY TO EXISTING DEVICES

Pub. L. 112–144, title VI, §613(b), July 9, 2012, 126 Stat. 1061, provided that: ''A sponsor of a device for which an exemption was approved under paragraph (2) of section 520(m) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360j(m)) before the date of enactment of this Act [July 9, 2012] may seek a determination under subclause (I) or (II) of section 520(m)(6)(A)(i) (as amended by subsection (a)). If the Secretary of Health and Human Services determines that such subclause (I) or (II) applies with respect to a device, clauses (ii), (iii), and (iv) of subparagraph (A) and subparagraphs (B), (C), (D), and (E) of paragraph (6) of such section 520(m) shall apply to such device, and the Secretary shall determine the annual distribution number for purposes of clause (ii) of such subparagraph (A) when making the determination under this subsection.''

GUIDANCE

Pub. L. 110–85, title III, §303(c), Sept. 27, 2007, 121 Stat. 862, provided that: ''Not later than 180 days after the date of the enactment of this Act [Sept. 27, 2007], the Commissioner of Food and Drugs shall issue guidance for institutional review committees on how to evaluate requests for approval for devices for which a humanitarian device exemption under section 520(m)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360j(m)(2)) has been granted.''

Pub. L. 107–250, title II, §213, Oct. 26, 2002, 116 Stat. 1614, provided that: ''Not later than 270 days after the date of the enactment of this Act [Oct. 26, 2002], the Secretary of Health and Human Services shall issue guidance on the following:

''(1) The type of information necessary to provide reasonable assurance of the safety and effectiveness of medical devices intended for use in pediatric populations.

''(2) Protections for pediatric subjects in clinical investigations of the safety or effectiveness of such devices.''

REPORT ON HUMANITARIAN DEVICE EXEMPTIONS

Pub. L. 101–629, §14(c), Nov. 28, 1990, 104 Stat. 4525, directed Secretary of Health and Human Services, within 4 years after issuance of regulations under 21 U.S.C. 360j(m)(6), to report to Congress on types of devices exempted, an evaluation of effects of such section, and a recommendation on extension of the section.

REFERENCES IN OTHER LAWS TO GS–16, 17, OR 18 PAY RATES

References in laws to the rates of pay for GS–16, 17, or 18, or to maximum rates of pay under the General Schedule, to be considered references to rates payable

under specified sections of Title 5, Government Organization and Employees, see section 529 [title I, § 101(c)(1)] of Pub. L. 101–509, set out in a note under section 5376 of Title 5.

§ 360k. State and local requirements respecting devices

(a) General rule

Except as provided in subsection (b), no State or political subdivision of a State may establish or continue in effect with respect to a device intended for human use any requirement—

(1) which is different from, or in addition to, any requirement applicable under this chapter to the device, and

(2) which relates to the safety or effectiveness of the device or to any other matter included in a requirement applicable to the device under this chapter.

(b) Exempt requirements

Upon application of a State or a political subdivision thereof, the Secretary may, by regulation promulgated after notice and opportunity for an oral hearing, exempt from subsection (a), under such conditions as may be prescribed in such regulation, a requirement of such State or political subdivision applicable to a device intended for human use if—

(1) the requirement is more stringent than a requirement under this chapter which would be applicable to the device if an exemption were not in effect under this subsection; or

(2) the requirement—

(A) is required by compelling local conditions, and

(B) compliance with the requirement would not cause the device to be in violation of any applicable requirement under this chapter.

(June 25, 1938, ch. 675, § 521, as added Pub. L. 94–295, § 2, May 28, 1976, 90 Stat. 574.)

§ 360*l*. Postmarket surveillance

(a) Postmarket surveillance

(1) In general

(A) Conduct

The Secretary may by order, at the time of approval or clearance of a device or at any time thereafter, require a manufacturer to conduct postmarket surveillance for any device of the manufacturer that is a class II or class III device—

(i) the failure of which would be reasonably likely to have serious adverse health consequences;

(ii) that is expected to have significant use in pediatric populations; or

(iii) that is intended to be—

(I) implanted in the human body for more than 1 year; or

(II) a life-sustaining or life-supporting device used outside a device user facility.

(B) Condition

The Secretary may order a postmarket surveillance under subparagraph (A) as a condition to approval or clearance of a device described in subparagraph (A)(ii).

(2) Rule of construction

The provisions of paragraph (1) shall have no effect on authorities otherwise provided under the[1] chapter or regulations issued under this chapter.

(b) Surveillance approval

(1) In general

Each manufacturer required to conduct a surveillance of a device shall, within 30 days of receiving an order from the Secretary prescribing that the manufacturer is required under this section to conduct such surveillance, submit, for the approval of the Secretary, a plan for the required surveillance. The Secretary, within 60 days of the receipt of such plan, shall determine if the person designated to conduct the surveillance has appropriate qualifications and experience to undertake such surveillance and if the plan will result in the collection of useful data that can reveal unforeseen adverse events or other information necessary to protect the public health. The manufacturer shall commence surveillance under this section not later than 15 months after the day on which the Secretary issues an order under this section. Except as provided in paragraph (2), the Secretary, in consultation with the manufacturer, may by order require a prospective surveillance period of up to 36 months. Except as provided in paragraph (2), any determination by the Secretary that a longer period is necessary shall be made by mutual agreement between the Secretary and the manufacturer or, if no agreement can be reached, after the completion of a dispute resolution process as described in section 360bbb–1 of this title.

(2) Longer surveillance for pediatric devices

The Secretary may by order require a prospective surveillance period of more than 36 months with respect to a device that is expected to have significant use in pediatric populations if such period of more than 36 months is necessary in order to assess the impact of the device on growth and development, or the effects of growth, development, activity level, or other factors on the safety or efficacy of the device.

(c) Dispute resolution

A manufacturer may request review under section 360bbb–1 of this title of any order or condition requiring postmarket surveillance under this section. During the pendency of such review, the device subject to such a postmarket surveillance order or condition shall not, because of noncompliance with such order or condition, be deemed in violation of section 331(q)(1)(C) of this title, adulterated under section 351(f)(1) of this title, misbranded under section 352(t)(3) of this title, or in violation of, as applicable, section 360(k) of this title or section 360e of this title, unless deemed necessary to protect the public health.

(June 25, 1938, ch. 675, § 522, as added Pub. L. 101–629, § 10, Nov. 28, 1990, 104 Stat. 4521; amended Pub. L. 102–300, § 3(b), June 16, 1992, 106 Stat. 239;

[1] So in original. Probably should be ''this''.

Pub. L. 105–115, title II, § 212, Nov. 21, 1997, 111 Stat. 2346; Pub. L. 110–85, title III, § 307, Sept. 27, 2007, 121 Stat. 865; Pub. L. 112–144, title VI, § 616, July 9, 2012, 126 Stat. 1062.)

Editorial Notes

AMENDMENTS

2012—Subsec. (a)(1)(A). Pub. L. 112–144, § 616(1), inserted '', at the time of approval or clearance of a device or at any time thereafter,'' after ''by order'' in introductory provisions.

Subsec. (b)(1). Pub. L. 112–144, § 616(2), inserted ''The manufacturer shall commence surveillance under this section not later than 15 months after the day on which the Secretary issues an order under this section.'' after ''the public health.''

2007—Pub. L. 110–85, § 307(1), made technical amendment to section catchline.

Subsec. (a). Pub. L. 110–85, § 307(2), added subsec. (a) and struck out former subsec. (a). Prior to amendment, text read as follows: ''The Secretary may by order require a manufacturer to conduct postmarket surveillance for any device of the manufacturer which is a class II or class III device the failure of which would be reasonably likely to have serious adverse health consequences or which is intended to be—

''(1) implanted in the human body for more than one year, or

''(2) a life sustaining or life supporting device used outside a device user facility.''

Subsec. (b). Pub. L. 110–85, § 307(3), designated existing provisions as par. (1), inserted par. heading, substituted ''Except as provided in paragraph (2), the Secretary, in consultation'' for ''The Secretary, in consultation'' and ''Except as provided in paragraph (2), any determination'' for ''Any determination'', and added par. (2).

Subsec. (c). Pub. L. 110–85, § 307(3)(D), added subsec. (c).

1997—Pub. L. 105–115 amended section generally, substituting present provisions for former provisions which related to required surveillance, discretionary surveillance, and surveillance approval.

1992—Subsec. (b). Pub. L. 102–300 substituted ''(a)(1)'' for ''(a)'', inserted comma after ''commerce'', and inserted after first sentence ''Each manufacturer required to conduct a surveillance of a device under subsection (a)(2) of this section shall, within 30 days after receiving notice that the manufacturer is required to conduct such surveillance, submit, for the approval of the Secretary, a protocol for the required surveillance.''

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 1997 AMENDMENT

Pub. L. 105–115, title II, § 212, Nov. 21, 1997, 111 Stat. 2346, provided in part that the amendment made by that section is effective 90 days after Nov. 21, 1997.

STUDY BY INSTITUTE OF MEDICINE OF POSTMARKET SURVEILLANCE REGARDING PEDIATRIC POPULATIONS

Pub. L. 107–250, title II, § 212, Oct. 26, 2002, 116 Stat. 1614, as amended by Pub. L. 108–214, § 2(d)(3)(C), Apr. 1, 2004, 118 Stat. 577, provided that the Secretary of Health and Human Services would request the Institute of Medicine to study whether the system under the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.) for the postmarket surveillance of medical devices provides adequate safeguards regarding the use of devices in pediatric populations, and provided that the Secretary, not later than four years after Oct. 26, 2002, would submit to Congress a report on the study and legislative and administrative recommendations.

§ 360m. Accredited persons

(a) In general

(1) Review and classification of devices

Not later than 1 year after November 21, 1997, the Secretary shall, subject to paragraph (3), accredit persons for the purpose of reviewing reports submitted under section 360(k) of this title and making recommendations to the Secretary regarding the initial classification of devices under section 360c(f)(1) of this title.

(2) Requirements regarding review

(A) In general

In making a recommendation to the Secretary under paragraph (1), an accredited person shall notify the Secretary in writing of the reasons for the recommendation.

(B) Time period for review

Not later than 30 days after the date on which the Secretary is notified under subparagraph (A) by an accredited person with respect to a recommendation of an initial classification of a device, the Secretary shall make a determination with respect to the initial classification.

(C) Special rule

The Secretary may change the initial classification under section 360c(f)(1) of this title that is recommended under paragraph (1) by an accredited person, and in such case shall provide to such person, and the person who submitted the report under section 360(k) of this title for the device, a statement explaining in detail the reasons for the change.

(3) Certain devices

(A) In general

An accredited person may not be used to perform a review of—

(i) a class III device;

(ii) a device classified under section 360c(f)(2) of this title or designated under section 360e–3(d)[1] of this title;

(iii) a device that is intended to be permanently implantable, life sustaining, or life supporting, unless otherwise determined by the Secretary in accordance with subparagraph (B)(i)(II) and listed as eligible for review under subparagraph (B)(iii); or

(iv) a device that is of a type, or subset of a type, listed as not eligible for review under subparagraph (B)(iii).

(B) Designation for review

The Secretary shall—

(i) issue draft guidance on the factors the Secretary will use in determining whether a class I or class II device type, or subset of such device types, is eligible for review by an accredited person, including—

(I) the risk of the device type, or subset of such device type; and

(II) whether the device type, or subset of such device type, is permanently implantable, life sustaining, or life supporting, and whether there is a detailed

[1] See References in Text note below.

public health justification for permitting the review by an accredited person of such device type or subset;

(ii) not later than 24 months after the date on which the Secretary issues such draft guidance, finalize such guidance; and

(iii) beginning on the date such guidance is finalized, designate and post on the internet website of the Food and Drug Administration, an updated list of class I and class II device types, or subsets of such device types, and the Secretary's determination with respect to whether each such device type, or subset of a device type, is eligible or not eligible for review by an accredited person under this section based on the factors described in clause (i).

(C) Interim rule

Until the date on which the updated list is designated and posted in accordance with subparagraph (B)(iii), the list in effect on August 18, 2017, shall be in effect.

(b) Accreditation

(1) Programs

The Secretary shall provide for such accreditation through programs administered by the Food and Drug Administration, other government agencies, or by other qualified nongovernment organizations.

(2) Accreditation

(A) In general

Not later than 180 days after November 21, 1997, the Secretary shall establish and publish in the Federal Register criteria to accredit or deny accreditation to persons who request to perform the duties specified in subsection (a). The Secretary shall respond to a request for accreditation within 60 days of the receipt of the request. The accreditation of such person shall specify the particular activities under subsection (a) for which such person is accredited.

(B) Withdrawal of accreditation

The Secretary may suspend or withdraw accreditation of any person accredited under this paragraph, after providing notice and an opportunity for an informal hearing, when such person is substantially not in compliance with the requirements of this section or poses a threat to public health or fails to act in a manner that is consistent with the purposes of this section.

(C) Performance auditing

To ensure that persons accredited under this section will continue to meet the standards of accreditation, the Secretary shall—

(i) make onsite visits on a periodic basis to each accredited person to audit the performance of such person; and

(ii) take such additional measures as the Secretary determines to be appropriate.

(D) Periodic reaccreditation

(i) Period

Subject to suspension or withdrawal under subparagraph (B), any accreditation under this section shall be valid for a period of 3 years after its issuance.

(ii) Response to reaccreditation request

Upon the submission of a request by an accredited person for reaccreditation under this section, the Secretary shall approve or deny such request not later than 60 days after receipt of the request.

(iii) Criteria

Not later than 120 days after July 9, 2012, the Secretary shall establish and publish in the Federal Register criteria to reaccredit or deny reaccreditation to persons under this section. The reaccreditation of persons under this section shall specify the particular activities under subsection (a), and the devices, for which such persons are reaccredited.

(3) Qualifications

An accredited person shall, at a minimum, meet the following requirements:

(A) Such person may not be an employee of the Federal Government.

(B) Such person shall be an independent organization which is not owned or controlled by a manufacturer, supplier, or vendor of devices and which has no organizational, material, or financial affiliation with such a manufacturer, supplier, or vendor.

(C) Such person shall be a legally constituted entity permitted to conduct the activities for which it seeks accreditation.

(D) Such person shall not engage in the design, manufacture, promotion, or sale of devices.

(E) The operations of such person shall be in accordance with generally accepted professional and ethical business practices.

(F) Such person shall agree, at a minimum, to include in its request for accreditation a commitment to, at the time of accreditation, and at any time it is performing any review pursuant to this section—

(i) certify that reported information accurately reflects data reviewed;

(ii) limit work to that for which competence and capacity are available;

(iii) treat information received, records, reports, and recommendations as proprietary information;

(iv) promptly respond and attempt to resolve complaints regarding its activities for which it is accredited; and

(v) protect against the use, in carrying out subsection (a) with respect to a device, of any officer or employee of the person who has a financial conflict of interest regarding the device, and annually make available to the public disclosures of the extent to which the person, and the officers and employees of the person, have maintained compliance with requirements under this clause relating to financial conflicts of interest.

(4) Selection of accredited persons

The Secretary shall provide each person who chooses to use an accredited person to receive a section 360(k) of this title report a panel of at least two or more accredited persons from which the regulated person may select one for a specific regulatory function.

(5) Compensation of accredited persons

Compensation for an accredited person shall be determined by agreement between the accredited person and the person who engages the services of the accredited person, and shall be paid by the person who engages such services.

(c) Duration

The authority provided by this section terminates on October 1, 2027.

(June 25, 1938, ch. 675, § 523, as added Pub. L. 105–115, title II, § 210(a), Nov. 21, 1997, 111 Stat. 2342; amended Pub. L. 107–250, title II, § 202, Oct. 26, 2002, 116 Stat. 1609; Pub. L. 110–85, title II, § 221, Sept. 27, 2007, 121 Stat. 852; Pub. L. 111–31, div. A, title I, § 103(f), June 22, 2009, 123 Stat. 1837; Pub. L. 112–144, title VI, § 611, July 9, 2012, 126 Stat. 1059; Pub. L. 114–255, div. A, title III, § 3102(4), Dec. 13, 2016, 130 Stat. 1156; Pub. L. 115–52, title II, § 206, Aug. 18, 2017, 131 Stat. 1018; Pub. L. 117–180, div. F, title II, § 2006, Sept. 30, 2022, 136 Stat. 2154; Pub. L. 117–229, div. C, title III, § 309, Dec. 16, 2022, 136 Stat. 2312; Pub. L. 117–328, div. FF, title III, § 3109, Dec. 29, 2022, 136 Stat. 5808.)

Editorial Notes

REFERENCES IN TEXT

Section 360e–3 of this title, referred to in subsec. (a)(3)(A)(ii), was in the original a reference to section 515C of act June 25, 1938, which was renumbered section 515B by Pub. L. 115–52, title IX, § 901(f)(2), Aug. 18, 2017, 131 Stat. 1077.

AMENDMENTS

2022—Subsec. (c). Pub. L. 117–328 substituted ''on October 1, 2027'' for ''December 24, 2022''.

Pub. L. 117–229 substituted ''December 24, 2022'' for ''December 17, 2022''.

Pub. L. 117–180 substituted ''December 17'' for ''October 1''.

2017—Subsec. (a)(3)(A)(ii) to (iv). Pub. L. 115–52, § 206(1)(A), added cls. (ii) to (iv) and struck out former cls. (ii) and (iii) which read as follows:

''(ii) a class II device which is intended to be permanently implantable or life sustaining or life supporting; or

''(iii) a class II device which requires clinical data in the report submitted under section 360(k) of this title for the device, except that the number of class II devices to which the Secretary applies this clause for a year, less the number of such reports to which clauses (i) and (ii) apply, may not exceed 6 percent of the number that is equal to the total number of reports submitted to the Secretary under such section for such year less the number of such reports to which such clauses apply for such year.''

Subsec. (a)(3)(B). Pub. L. 115–52, § 206(1)(B), added subpar. (B) and struck out former subpar. (B). Prior to amendment, text read as follows: ''In determining for a year the ratio described in subparagraph (A)(iii), the Secretary shall not include in the numerator class III devices that the Secretary reclassified into class II, and the Secretary shall include in the denominator class II devices for which reports under section 360(k) of this title were not required to be submitted by reason of the operation of section 360(m) of this title.''

Subsec. (a)(3)(C). Pub. L. 115–52, § 206(1)(C), added subpar. (C).

Subsec. (b)(2)(D), (E). Pub. L. 115–52, § 206(2)(A), redesignated subpar. (E) as (D) and struck out former subpar. (D). Prior to amendment, text of subpar. (D) read as follows: ''The Secretary shall include in the annual report required under section 393(g) of this title the names of all accredited persons and the particular activities under subsection (a) for which each such person is accredited and the name of each accredited person whose accreditation has been withdrawn during the year.''

Subsec. (b)(3)(E). Pub. L. 115–52, § 206(2)(B)(iii), added subpar. (E). Former subpar. (E) redesignated (F).

Subsec. (b)(3)(F). Pub. L. 115–52, § 206(2)(B)(i), (ii), redesignated subpar. (E) as (F) and substituted ''Such person shall agree, at a minimum, to include in its request for accreditation a commitment to, at the time of accreditation, and at any time it is performing any review pursuant to this section'' for ''The operations of such person shall be in accordance with generally accepted professional and ethical business practices and shall agree in writing that as a minimum it will'' in introductory provisions.

Subsec. (c). Pub. L. 115–52, § 206(3), substituted ''2022'' for ''2017''.

2016—Subsec. (d). Pub. L. 114–255 struck out subsec. (d) which related to report to Congress.

2012—Subsec. (b)(2)(E). Pub. L. 112–144, § 611(a), added subpar. (E).

Subsec. (c). Pub. L. 112–144, § 611(b), substituted ''October 1, 2017'' for ''October 1, 2012''.

2009—Subsec. (b)(2)(D). Pub. L. 111–31 made technical amendment to reference in original act which appears in text as reference to section 393(g) of this title.

2007—Subsec. (c). Pub. L. 110–85 substituted ''2012'' for ''2007''.

2002—Subsec. (c). Pub. L. 107–250, § 202(1), substituted ''The authority provided by this section terminates October 1, 2007.'' for ''The authority provided by this section terminates—

''(1) 5 years after the date on which the Secretary notifies Congress that at least 2 persons accredited under subsection (b) of this section are available to review at least 60 percent of the submissions under section 360(k) of this title, or

''(2) 4 years after the date on which the Secretary notifies Congress that the Secretary has made a determination described in paragraph (2)(B) of subsection (a) of this section for at least 35 percent of the devices that are subject to review under paragraph (1) of such subsection,

whichever occurs first.''

Subsec. (d). Pub. L. 107–250, § 202(2), added subsec. (d).

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 2022 AMENDMENT

Amendment by Pub. L. 117–180 effective Oct. 1, 2022, with fees under subpart 3 of part C of subchapter VII of this chapter to be assessed for all submissions listed in section 379j(a)(2)(A) of this title received on or after Oct. 1, 2022, see section 2008 of Pub. L. 117–180, set out as a note under section 360d of this title.

EFFECTIVE DATE OF 2017 AMENDMENT

Amendment by Pub. L. 115–52 effective Oct. 1, 2017, with fees under subpart 3 of part C of subchapter VII of this chapter to be assessed for all submissions listed in section 379j(a)(2)(A) of this title received on or after Oct. 1, 2017, see section 209 of Pub. L. 115–52, set out as a note under section 379i of this title.

EFFECTIVE DATE

Section effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as a note under section 321 of this title.

REPORTS ON PROGRAM OF ACCREDITATION

Pub. L. 105–115, title II, § 210(d), Nov. 21, 1997, 111 Stat. 2345, provided that:

''(1) COMPTROLLER GENERAL.—

''(A) IMPLEMENTATION OF PROGRAM.—Not later than 5 years after the date of the enactment of this Act [Nov. 21, 1997], the Comptroller General of the United

States shall submit to the Committee on Commerce [now Committee on Energy and Commerce] of the House of Representatives and the Committee on Labor and Human Resources [now Committee on Health, Education, Labor, and Pensions] of the Senate a report describing the extent to which the program of accreditation required by the amendment made by subsection (a) [enacting this section] has been implemented.

''(B) EVALUATION OF PROGRAM.—Not later than 6 months prior to the date on which, pursuant to subsection (c) of section 523 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360m(c)] (as added by subsection (a)), the authority provided under subsection (a) of such section will terminate, the Comptroller General shall submit to the Committee on Commerce [now Committee on Energy and Commerce] of the House of Representatives and the Committee on Labor and Human Resources [now Committee on Health, Education, Labor, and Pensions] of the Senate a report describing the use of accredited persons under such section 523, including an evaluation of the extent to which such use assisted the Secretary in carrying out the duties of the Secretary under such Act [21 U.S.C. 301 et seq.] with respect to devices, and the extent to which such use promoted actions which are contrary to the purposes of such Act.

''(2) INCLUSION OF CERTAIN DEVICES WITHIN PROGRAM.—Not later than 3 years after the date of the enactment of this Act [Nov. 21, 1997], the Secretary of Health and Human Services shall submit to the Committee on Commerce of the House of Representatives and the Committee on Labor and Human Resources [now Committee on Health, Education, Labor, and Pensions] of the Senate a report providing a determination by the Secretary of whether, in the program of accreditation established pursuant to the amendment made by subsection (a), the limitation established in clause (iii) of section 523(a)(3)(A) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360m(a)(3)(A)] (relating to class II devices for which clinical data are required in reports under section 510(k) [21 U.S.C. 360(k)]) should be removed.''

§ 360n. Priority review to encourage treatments for tropical diseases

(a) Definitions

In this section:

(1) Priority review

The term ''priority review'', with respect to a human drug application as defined in section 379g(1) of this title, means review and action by the Secretary on such application not later than 6 months after receipt by the Secretary of such application, as described in the Manual of Policies and Procedures of the Food and Drug Administration and goals identified in the letters described in section 101(c) of the Food and Drug Administration Amendments Act of 2007.

(2) Priority review voucher

The term ''priority review voucher'' means a voucher issued by the Secretary to the sponsor of a tropical disease product application that entitles the holder of such voucher to priority review of a single human drug application submitted under section 355(b)(1) of this title or section 262 of title 42 after the date of approval of the tropical disease product application.

(3) Tropical disease

The term ''tropical disease'' means any of the following:

(A) Tuberculosis.
(B) Malaria.
(C) Blinding trachoma.
(D) Buruli Ulcer.
(E) Cholera.
(F) Dengue/dengue haemorrhagic fever.
(G) Dracunculiasis (guinea-worm disease).
(H) Fascioliasis.
(I) Human African trypanosomiasis.
(J) Leishmaniasis.
(K) Leprosy.
(L) Lymphatic filariasis.
(M) Onchocerciasis.
(N) Schistosomiasis.
(O) Soil transmitted helmithiasis.
(P) Yaws.
(Q) Filovirus Diseases.
(R) Zika Virus Disease.
(S) Any other infectious disease for which there is no significant market in developed nations and that disproportionately affects poor and marginalized populations, designated by order of the Secretary.

(4) Tropical disease product application

The term ''tropical disease product application'' means an application that—

(A) is a human drug application as defined in section 379g(1) of this title—

(i) for prevention or treatment of a tropical disease;

(ii) the Secretary deems eligible for priority review;

(iii) that contains reports of one or more new clinical investigations (other than bioavailability studies) that are essential to the approval of the application and conducted or sponsored by the sponsor of such application; and

(iv) that contains an attestation from the sponsor of the application that such reports were not submitted as part of an application for marketing approval or licensure by a regulatory authority in India, Brazil, Thailand, or any country that is a member of the Pharmaceutical Inspection Convention or the Pharmaceutical Inspection Cooperation Scheme prior to September 27, 2007.[1]

(B) is approved after September 27, 2007, by the Secretary for use in the prevention, detection, or treatment of a tropical disease; and

(C) is for—

(i) a human drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under section 355(b)(1) of this title; or

(ii) a biological product, no active ingredient of which has been approved in any other application under section 262 of title 42.

(b) Priority review voucher

(1) In general

The Secretary shall award a priority review voucher to the sponsor of a tropical disease product application upon approval by the Sec-

[1] So in original. The period probably should be a semicolon.

retary of such tropical disease product application.

(2) Transferability

The sponsor of a tropical disease product that receives a priority review voucher under this section may transfer (including by sale) the entitlement to such voucher to a sponsor of a human drug for which an application under section 355(b)(1) of this title or section 262 of title 42 will be submitted after the date of the approval of the tropical disease product application. There is no limit on the number of times a priority review voucher may be transferred before such voucher is used.

(3) Limitation

(A) No award for prior approved application

A sponsor of a tropical disease product may not receive a priority review voucher under this section if the tropical disease product application was submitted to the Secretary prior to September 27, 2007.

(B) One-year waiting period

The Secretary shall issue a priority review voucher to the sponsor of a tropical disease product no earlier than the date that is 1 year after September 27, 2007.

(4) Notification

The sponsor of a human drug application shall notify the Secretary not later than 90 days prior to submission of the human drug application that is the subject of a priority review voucher of an intent to submit the human drug application, including the date on which the sponsor intends to submit the application. Such notification shall be a legally binding commitment to pay for the user fee to be assessed in accordance with this section.

(c) Priority review user fee

(1) In general

The Secretary shall establish a user fee program under which a sponsor of a human drug application that is the subject of a priority review voucher shall pay to the Secretary a fee determined under paragraph (2). Such fee shall be in addition to any fee required to be submitted by the sponsor under subchapter VII.

(2) Fee amount

The amount of the priority review user fee shall be determined each fiscal year by the Secretary and based on the average cost incurred by the agency in the review of a human drug application subject to priority review in the previous fiscal year.

(3) Annual fee setting

The Secretary shall establish, before the beginning of each fiscal year beginning after September 30, 2007, for that fiscal year, the amount of the priority review user fee.

(4) Payment

(A) In general

The priority review user fee required by this subsection shall be due upon the submission of a human drug application under section 355(b)(1) of this title or section 262 of title 42 for which the priority review voucher is used.

(B) Complete application

An application described under subparagraph (A) for which the sponsor requests the use of a priority review voucher shall be considered incomplete if the fee required by this subsection and all other applicable user fees are not paid in accordance with the Secretary's procedures for paying such fees.

(C) No waivers, exemptions, reductions, or refunds

The Secretary may not grant a waiver, exemption, reduction, or refund of any fees due and payable under this section.

(5) Offsetting collections

Fees collected pursuant to this subsection for any fiscal year—

(A) shall be deposited and credited as offsetting collections to the account providing appropriations to the Food and Drug Administration; and

(B) shall not be collected for any fiscal year except to the extent provided in advance in appropriation Acts.

(June 25, 1938, ch. 675, §524, as added Pub. L. 110–85, title XI, §1102, Sept. 27, 2007, 121 Stat. 972; amended Pub. L. 113–233, §2, Dec. 16, 2014, 128 Stat. 2127; Pub. L. 114–146, §2, Apr. 19, 2016, 130 Stat. 357; Pub. L. 114–255, div. A, title III, §3101(a)(2)(M), Dec. 13, 2016, 130 Stat. 1154; Pub. L. 115–52, title VI, §611(a), Aug. 18, 2017, 131 Stat. 1054; Pub. L. 117–9, §1(a)(3), Apr. 23, 2021, 135 Stat. 257.)

Editorial Notes

REFERENCES IN TEXT

Section 101(c) of the Food and Drug Administration Amendments Act of 2007, referred to in subsec. (a)(1), is section 101(c) of Pub. L. 110–85, which is set out as a note under section 379g of this title.

AMENDMENTS

2021—Subsec. (a)(4)(C). Pub. L. 117–9 amended subpar. (C) generally. Prior to amendment, subpar. (C) read as follows: ''is for a human drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under section 355(b)(1) of this title or section 262 of title 42.''

2017—Subsec. (a)(4)(A)(iii), (iv). Pub. L. 115–52 added cls. (iii) and (iv).

2016—Subsec. (a)(3)(Q). Pub. L. 114–146, §2(2), substituted ''Filovirus Diseases'' for ''Filoviruses''.

Subsec. (a)(3)(R), (S). Pub. L. 114–146, §2(1), (3), added subpar. (R) and redesignated former subpar. (R) as (S).

Subsec. (c)(4)(A). Pub. L. 114–255 made technical amendment to reference in original act which appears in text as reference to section 262 of title 42.

2014—Subsec. (a)(3)(Q), (R). Pub. L. 113–233, §2(1), added subpar. (Q), redesignated former subpar. (Q) as (R), and in subpar. (R) substituted ''order of'' for ''regulation by''.

Subsec. (b)(2). Pub. L. 113–233, §2(2)(A), inserted at end ''There is no limit on the number of times a priority review voucher may be transferred before such voucher is used.''

Subsec. (b)(4). Pub. L. 113–233, §2(2)(B), substituted ''90 days'' for ''365 days''.

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 2017 AMENDMENT

Pub. L. 115–52, title VI, §611(b), Aug. 18, 2017, 131 Stat. 1054, provided that: ''The amendments made by sub-

section (a) [amending this section] shall apply to human drug applications submitted after September 30, 2017.''

§ 360n–1. Priority review for qualified infectious disease products

(a) In general

If the Secretary designates a drug under section 355f(d) of this title as a qualified infectious disease product, then the Secretary shall give priority review to the first application submitted for approval for such drug under section 355(b) of this title, or section 262(a) of title 42, that requires clinical data (other than bioavailability studies) to demonstrate safety or effectiveness.

(b) Construction

Nothing in this section shall prohibit the Secretary from giving priority review to a human drug application or efficacy supplement submitted for approval under section 355(b) of this title that otherwise meets the criteria for the Secretary to grant priority review.

(June 25, 1938, ch. 675, § 524A, as added Pub. L. 112–144, title VIII, § 802(a), July 9, 2012, 126 Stat. 1079; amended Pub. L. 114–255, div. A, title III, § 3101(a)(2)(N), Dec. 13, 2016, 130 Stat. 1154; Pub. L. 117–328, div. FF, title III, § 3212(b), Dec. 29, 2022, 136 Stat. 5826.)

Editorial Notes

AMENDMENTS

2022—Subsec. (a). Pub. L. 117–328 inserted '', or section 262(a) of title 42, that requires clinical data (other than bioavailability studies) to demonstrate safety or effectiveness'' before period at end.

2016—Pub. L. 114–255 designated existing provisions as subsec. (a), inserted heading, substituted ''the first application'' for ''any application'', and added subsec. (b).

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE

Pub. L. 112–144, title VIII, § 802(b), July 9, 2012, 126 Stat. 1079, provided that: ''Section 524A of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360n–1], as added by subsection (a), applies only with respect to an application that is submitted under section 505(b) of such Act (21 U.S.C. 355(b)) on or after the date of the enactment of this Act [July 9, 2012].''

§ 360n–2. Ensuring cybersecurity of devices

(a) In general

A person who submits an application or submission under section 360(k), 360c, 360e(c), 360e(f), or 360j(m) of this title for a device that meets the definition of a cyber device under this section shall include such information as the Secretary may require to ensure that such cyber device meets the cybersecurity requirements under subsection (b).

(b) Cybersecurity requirements

The sponsor of an application or submission described in subsection (a) shall—

(1) submit to the Secretary a plan to monitor, identify, and address, as appropriate, in a reasonable time, postmarket cybersecurity vulnerabilities and exploits, including coordinated vulnerability disclosure and related procedures;

(2) design, develop, and maintain processes and procedures to provide a reasonable assurance that the device and related systems are cybersecure, and make available postmarket updates and patches to the device and related systems to address—

(A) on a reasonably justified regular cycle, known unacceptable vulnerabilities; and

(B) as soon as possible out of cycle, critical vulnerabilities that could cause uncontrolled risks;

(3) provide to the Secretary a software bill of materials, including commercial, open-source, and off-the-shelf software components; and

(4) comply with such other requirements as the Secretary may require through regulation to demonstrate reasonable assurance that the device and related systems are cybersecure.

(c) Definition

In this section, the term ''cyber device'' means a device that—

(1) includes software validated, installed, or authorized by the sponsor as a device or in a device;

(2) has the ability to connect to the internet; and

(3) contains any such technological characteristics validated, installed, or authorized by the sponsor that could be vulnerable to cybersecurity threats.

(d) Exemption

The Secretary may identify devices, or categories or types of devices, that are exempt from meeting the cybersecurity requirements established by this section and regulations promulgated pursuant to this section. The Secretary shall publish in the Federal Register, and update, as appropriate, a list of the devices, or categories or types of devices, so identified by the Secretary.

(June 25, 1938, ch. 675, § 524B, as added Pub. L. 117–328, div. FF, title III, § 3305(a), Dec. 29, 2022, 136 Stat. 5832.)

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE

Section effective 90 days after Dec. 29, 2022, see section 3305(d) of Pub. L. 117–328, set out as an Effective Date of 2022 Amendment note under section 331 of this title.

CONSTRUCTION

Nothing in section 3305(a) of Pub. L. 117–328, which enacted this section, to be construed to affect the Secretary's of Health and Human Services authority related to ensuring that there is a reasonable assurance of the safety and effectiveness of devices, which may include ensuring that there is a reasonable assurance of the cybersecurity of certain cyber devices, including for devices approved or cleared prior to Dec. 29, 2022, see section 3305(c) of Pub. L. 117–328, set out as a Construction of 2022 Amendment note under section 331 of this title.

GUIDANCE FOR INDUSTRY AND FDA STAFF ON DEVICE CYBERSECURITY

Pub. L. 117–328, div. FF, title III, § 3305(e), Dec. 29, 2022, 136 Stat. 5833, provided that: ''Not later than 2 years after the date of enactment of this Act [Dec. 29, 2022], and periodically thereafter as appropriate, the

Secretary [of Health and Human Services], in consultation with the Director of the Cybersecurity and Infrastructure Security Agency, shall review and, as appropriate and after soliciting and receiving feedback from device manufacturers, health care providers, third-party-device servicers, patient advocates, and other appropriate stakeholders, update the guidance entitled 'Content of Premarket Submissions for Management of Cybersecurity in Medical Devices' (or a successor document).''

[For definition of ''device'' as used in section 3305(e) of Pub. L. 117–328, set out above, see section 321(h) of this title, as made applicable by section 3305(h) of Pub. L. 117–328, which is set out below.]

RESOURCES REGARDING CYBERSECURITY OF DEVICES

Pub. L. 117–328, div. FF, title III, §3305(f), Dec. 29, 2022, 136 Stat. 5834, provided that: ''Not later than 180 days after the date of enactment of this Act [Dec. 29, 2022], and not less than annually thereafter, the Secretary [of Health and Human Services] shall update public information provided by the Food and Drug Administration, including on the website of the Food and Drug Administration, with information regarding improving cybersecurity of devices. Such information shall include information on identifying and addressing cyber vulnerabilities for health care providers, health systems, and device manufacturers, and how such entities may access support through the Cybersecurity and Infrastructure Security Agency and other Federal entities, including the Department of Health and Human Services, to improve the cybersecurity of devices.''

[For definition of ''device'' as used in section 3305(f) of Pub. L. 117–328, set out above, see section 321(h) of this title, as made applicable by section 3305(h) of Pub. L. 117–328, which is set out below.]

DEFINITION

Pub. L. 117–328, div. FF, title III, §3305(h), Dec. 29, 2022, 136 Stat. 5834, provided that: ''In this section [enacting this section, amending section 331 of this title, and enacting provisions set out as notes under this section and section 331 of this title], the term 'device' has the meaning given such term in section 201(h) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321(h)).''

PART B—DRUGS FOR RARE DISEASES OR CONDITIONS

§ 360aa. Recommendations for investigations of drugs for rare diseases or conditions

(a) Request by sponsor; response by Secretary

The sponsor of a drug for a disease or condition which is rare in the States may request the Secretary to provide written recommendations for the non-clinical and clinical investigations which must be conducted with the drug before—

(1) it may be approved for such disease or condition under section 355 of this title, or

(2) if the drug is a biological product, it may be licensed for such disease or condition under section 262 of title 42.

If the Secretary has reason to believe that a drug for which a request is made under this section is a drug for a disease or condition which is rare in the States, the Secretary shall provide the person making the request written recommendations for the non-clinical and clinical investigations which the Secretary believes, on the basis of information available to the Secretary at the time of the request under this section, would be necessary for approval of such drug for such disease or condition under section 355 of this title or licensing of such drug for such disease or condition under section 262 of title 42.

(b) Regulations

The Secretary shall by regulation promulgate procedures for the implementation of subsection (a).

(June 25, 1938, ch. 675, §525, as added Pub. L. 97–414, §2(a), Jan. 4, 1983, 96 Stat. 2049; amended Pub. L. 99–91, §3(a)(1), Aug. 15, 1985, 99 Stat. 387; Pub. L. 105–115, title I, §125(b)(2)(F), (G), Nov. 21, 1997, 111 Stat. 2325, 2326.)

Editorial Notes

AMENDMENTS

1997—Subsec. (a). Pub. L. 105–115, §125(b)(2)(G), struck out '', certification of such drug for such disease or condition under section 357 of this title,'' before ''or licensing of such drug'' in closing provisions.

Subsec. (a)(1) to (3). Pub. L. 105–115, §125(b)(2)(F), inserted ''or'' at end of par. (1), redesignated par. (3) as (2), and struck out former par. (2), which read as follows: ''if the drug is an antibiotic, it may be certified for such disease or condition under section 357 of this title, or''.

1985—Subsec. (a). Pub. L. 99–91 struck out ''or'' at end of par. (1), inserted par. (2), redesignated former par. (2) as (3) and struck out ''before'' after ''product,'', and in last sentence inserted provisions relating to certification of such drug for disease or condition under section 357 of this title and substituted ''licensing of such drug for such disease or condition under section 262 of title 42'' for ''licensing under section 262 of title 42 for such disease or condition''.

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 1985 AMENDMENT

Pub. L. 99–91, §8, Aug. 15, 1985, 99 Stat. 392, provided that:

''(a) GENERAL RULE.—Except as provided in subsection (b), this Act and the amendments made by this Act [amending this section, sections 360bb, 360cc, and 360ee of this title, and sections 295g–1 and 6022 of Title 42, The Public Health and Welfare, and enacting provisions set out as notes under section 301 of this title and section 236 of Title 42] shall take effect October 1, 1985.

''(b) EXCEPTION.—The amendments made by sections 2, 3, and 6(a) [amending this section and sections 360bb and 360cc of this title] shall take effect on the date of the enactment of this Act [Aug. 15, 1985]. The amendment made by section 6(b) [amending section 6022 of Title 42] shall take effect October 19, 1984. The amendments made by section 7 [amending section 295g–1 of Title 42] shall take effect October 1, 1984 and shall cease to be in effect after September 30, 1985.''

RARE DISEASE ENDPOINT ADVANCEMENT PILOT PROGRAM

Pub. L. 117–328, div. FF, title III, §3208, Dec. 29, 2022, 136 Stat. 5821, provided that:

''(a) IN GENERAL.—The Secretary [of Health and Human Services] shall establish a pilot program under which the Secretary establishes procedures to provide increased interaction with sponsors of rare disease drug development programs for purposes of advancing the development of efficacy endpoints, including surrogate and intermediate endpoints, for drugs intended to treat rare diseases, including through—

''(1) determining eligibility of participants for such program; and

''(2) developing and implementing a process for applying to, and participating in, such a program.

''(b) PUBLIC WORKSHOPS.—The Secretary shall conduct up to 3 public workshops, which shall be completed not later than September 30, 2026, to discuss topics relevant to the development of endpoints for rare diseases, which may include discussions about—

''(1) novel endpoints developed through the pilot program established under this section; and

''(2) as appropriate, the use of real world evidence and real world data to support the validation of efficacy endpoints, including surrogate and intermediate endpoints, for rare diseases.

''(c) REPORTS.—

''(1) INTERIM REPORT.—Not later than September 30, 2026, the Secretary shall submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives a report describing the completed and ongoing activities in the pilot program established under this section and public workshops described in subsection (b).

''(2) FINAL REPORT.—Not later than September 30, 2027, the Secretary shall submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives a report describing the outcomes of the pilot program established under this section.

''(d) GUIDANCE.—Not later than September 30, 2027, the Secretary shall issue guidance describing best practices and strategies for development of efficacy endpoints, including surrogate and intermediate endpoints, for rare diseases.

''(e) SUNSET.—The Secretary may not accept any new application or request to participate in the program established by this section on or after October 1, 2027.''

ALS AND OTHER RARE NEURODEGENERATIVE DISEASE ACTION PLAN

Pub. L. 117–79, § 4, Dec. 23, 2021, 135 Stat. 1536, provided that:

''(a) IN GENERAL.—Not later than 6 months after the date of enactment of this Act [Dec. 23, 2021], the Commissioner of Food and Drugs shall publish on the website of the Food and Drug Administration an action plan describing actions the Food and Drug Administration intends to take during the 5-year period following publication of the plan with respect to program enhancements, policy development, regulatory science initiatives, and other appropriate initiatives to—

''(1) foster the development of safe and effective drugs that improve or extend, or both, the lives of people living with amyotrophic lateral sclerosis and other rare neurodegenerative diseases; and

''(2) facilitate access to investigational drugs for amyotrophic lateral sclerosis and other rare neurodegenerative diseases.

''(b) CONTENTS.—The initial action plan published under subsection (a) shall—

''(1) identify appropriate representation from within the Food and Drug Administration to be responsible for implementation of such action plan;

''(2) include elements to facilitate—

''(A) interactions and collaboration between the Food and Drug Administration, including the review centers thereof, and stakeholders including patients, sponsors, and the external biomedical research community;

''(B) consideration of cross-cutting clinical and regulatory policy issues, including consistency of regulatory advice and decisionmaking;

''(C) identification of key regulatory science and policy issues critical to advancing development of safe and effective drugs; and

''(D) enhancement of collaboration and engagement of the relevant centers and offices of the Food and Drug Administration with other operating divisions within the Department of Health and Human Services, the Partnership, and the broader neurodegenerative disease community; and

''(3) be subject to revision, as determined appropriate by the Secretary of Health and Human Services.''

REVIEW GROUPS ON RARE DISEASES AND NEGLECTED DISEASES OF THE DEVELOPING WORLD; REPORT; GUIDANCE; STANDARDS

Pub. L. 111–80, title VII, § 740, Oct. 21, 2009, 123 Stat. 2127, provided that:

''(a) The Commissioner of Food and Drugs shall establish within the Food and Drug Administration a review group which shall recommend to the Commissioner of Food and Drugs appropriate preclinical, trial design, and regulatory paradigms and optimal solutions for the prevention, diagnosis, and treatment of rare diseases: *Provided*, That the Commissioner of Food and Drugs shall appoint individuals employed by the Food and Drug Administration to serve on the review group: *Provided further*, That members of the review group shall have specific expertise relating to the development of articles for use in the prevention, diagnosis, or treatment of rare diseases, including specific expertise in developing or carrying out clinical trials.

''(b) The Commissioner of Food and Drugs shall establish within the Food and Drug Administration a review group which shall recommend to the Commissioner of Food and Drugs appropriate preclinical, trial design, and regulatory paradigms and optimal solutions for the prevention, diagnosis, and treatment of neglected diseases of the developing world: *Provided*, That the Commissioner of Food and Drugs shall appoint individuals employed by the Food and Drug Administration to serve on the review group: *Provided further*, That members of the review group shall have specific expertise relating to the development of articles for use in the prevention, diagnosis, or treatment of neglected diseases of the developing world, including specific expertise in developing or carrying out clinical trials: *Provided further*, That for the purposes of this section the term 'neglected disease of the developing world' means a tropical disease, as defined in section 524(a)(3) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360n(a)(3)).

''(c) The Commissioner of Food and Drugs shall—

''(1) submit, not later than 1 year after the date of the establishment of review groups under subsections (a) and (b), a report to Congress that describes both the findings and recommendations made by the review groups under subsections (a) and (b);

''(2) issue, not later than 180 days after submission of the report to Congress under paragraph (1), guidance based on such recommendations for articles for use in the prevention, diagnosis, and treatment of rare diseases and for such uses in neglected diseases of the developing world; and

''(3) develop, not later than 180 days after submission of the report to Congress under paragraph (1), internal review standards based on such recommendations for articles for use in the prevention, diagnosis, and treatment of rare diseases and for such uses in neglected diseases of the developing world.''

STUDY

Pub. L. 100–290, § 3(d), Apr. 18, 1988, 102 Stat. 91, directed Secretary of Health and Human Services to conduct a study to determine whether the application of subchapter B of chapter V of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 360aa et seq. (relating to drugs for rare diseases and conditions), and 26 U.S.C. 28 (relating to tax credit) to medical devices or medical foods for rare diseases or conditions or to both was needed to encourage development of such devices and foods and report results of the study to Congress not later than one year after Apr. 18, 1988.

CONGRESSIONAL FINDINGS

Pub. L. 97–414, § 1(b), Jan. 4, 1983, 96 Stat. 2049, provided that: ''The Congress finds that—

''(1) there are many diseases and conditions, such as Huntington's disease, myoclonus, ALS (Lou Gehrig's disease), Tourette syndrome, and muscular dystrophy which affect such small numbers of individuals residing in the United States that the diseases and conditions are considered rare in the United States;

''(2) adequate drugs for many of such diseases and conditions have not been developed;

''(3) drugs for these diseases and conditions are commonly referred to as 'orphan drugs';

''(4) because so few individuals are affected by any one rare disease or condition, a pharmaceutical company which develops an orphan drug may reasonably expect the drug to generate relatively small sales in comparison to the cost of developing the drug and consequently to incur a financial loss;

''(5) there is reason to believe that some promising orphan drugs will not be developed unless changes are made in the applicable Federal laws to reduce the costs of developing such drugs and to provide financial incentives to develop such drugs; and

''(6) it is in the public interest to provide such changes and incentives for the development of orphan drugs.''

§ 360bb. Designation of drugs for rare diseases or conditions

(a) Request by sponsor; preconditions; "rare disease or condition" defined

(1) The manufacturer or the sponsor of a drug may request the Secretary to designate the drug as a drug for a rare disease or condition. A request for designation of a drug shall be made before the submission of an application under section 355(b) of this title for the drug, or the submission of an application for licensing of the drug under section 262 of title 42. If the Secretary finds that a drug for which a request is submitted under this subsection is being or will be investigated for a rare disease or condition and—

(A) if an application for such drug is approved under section 355 of this title, or

(B) if a license for such drug is issued under section 262 of title 42,

the approval, certification, or license would be for use for such disease or condition, the Secretary shall designate the drug as a drug for such disease or condition. A request for a designation of a drug under this subsection shall contain the consent of the applicant to notice being given by the Secretary under subsection (b)[1] respecting the designation of the drug.

(2) For purposes of paragraph (1), the term ''rare disease or condition'' means any disease or condition which (A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug. Determinations under the preceding sentence with respect to any drug shall be made on the basis of the facts and circumstances as of the date the request for designation of the drug under this subsection is made.

(b) Notification of discontinuance of drug or application as condition

A designation of a drug under subsection (a) shall be subject to the condition that—

(1) if an application was approved for the drug under section 355(b) of this title or a license was issued for the drug under section 262 of title 42, the manufacturer of the drug will notify the Secretary of any discontinuance of the production of the drug at least one year before discontinuance, and

(2) if an application has not been approved for the drug under section 355(b) of this title or a license has not been issued for the drug under section 262 of title 42 and if preclinical investigations or investigations under section 355(i) of this title are being conducted with the drug, the manufacturer or sponsor of the drug will notify the Secretary of any decision to discontinue active pursuit of approval of an application under section 355(b) of this title or approval of a license under section 262 of title 42.

(c) Notice to public

Notice respecting the designation of a drug under subsection (a) shall be made available to the public.

(d) Regulations

The Secretary shall by regulation promulgate procedures for the implementation of subsection (a).

(June 25, 1938, ch. 675, §526, as added Pub. L. 97–414, §2(a), Jan. 4, 1983, 96 Stat. 2050; amended Pub. L. 98–551, §4(a), Oct. 30, 1984, 98 Stat. 2817; Pub. L. 99–91, §3(a)(2), Aug. 15, 1985, 99 Stat. 387; Pub. L. 100–290, §2, Apr. 18, 1988, 102 Stat. 90; Pub. L. 105–115, title I, §125(b)(2)(H), (I), Nov. 21, 1997, 111 Stat. 2326.)

Editorial Notes

REFERENCES IN TEXT

Subsection (b), referred to in subsec. (a)(1), was redesignated as subsec. (c) of this section by Pub. L. 100–290, §2(b), Apr. 18, 1988, 102 Stat. 90.

AMENDMENTS

1997—Subsec. (a)(1). Pub. L. 105–115, §125(b)(2)(H), struck out ''the submission of an application for certification of the drug under section 357 of this title,'' before ''or the submission of an application for licensing of the drug'' in introductory provisions, inserted ''or'' at end of subpar. (A), redesignated subpar. (C) as (B), and struck out former subpar. (B) which read as follows: ''if a certification for such drug is issued under section 357 of this title, or''.

Subsec. (b)(1). Pub. L. 105–115, §125(b)(2)(I)(i), struck out '', a certificate was issued for the drug under section 357 of this title,'' before ''or a license was issued''.

Subsec. (b)(2). Pub. L. 105–115, §125(b)(2)(I)(ii), struck out '', a certificate has not been issued for the drug under section 357 of this title,'' before ''or a license has not been issued'' and '', approval of an application for certification under section 357 of this title,'' before ''or approval of a license''.

1988—Subsec. (a)(1). Pub. L. 100–290, §2(a), inserted after first sentence ''A request for designation of a drug shall be made before the submission of an application under section 355(b) of this title for the drug, the submission of an application for certification of the drug under section 357 of this title, or the submission of an application for licensing of the drug under section 262 of title 42.''

Subsecs. (b) to (d). Pub. L. 100–290, §2(b), added subsec. (b) and redesignated former subsecs. (b) and (c) as (c) and (d), respectively.

1985—Subsec. (a)(1). Pub. L. 99–91 struck out ''or'' at end of subpar. (A), struck out subpar. (B) and substituted subpars. (B) and (C), and inserted '', certification,'' after ''approval''.

1984—Subsec. (a)(2). Pub. L. 98–551 substituted ''which (A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which'' for ''which occurs so infrequently in the United States that''.

[1] See References in Text note below.

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 1985 AMENDMENT

Amendment by Pub. L. 99–91 effective Aug. 15, 1985, see section 8(b) of Pub. L. 99–91, set out as a note under section 360aa of this title.

§ 360cc. Protection for drugs for rare diseases or conditions

(a) Exclusive approval, certification, or license

Except as provided in subsection (b), if the Secretary—

(1) approves an application filed pursuant to section 355 of this title, or

(2) issues a license under section 262 of title 42

for a drug designated under section 360bb of this title for a rare disease or condition, the Secretary may not approve another application under section 355 of this title or issue another license under section 262 of title 42 for the same drug for the same disease or condition for a person who is not the holder of such approved application or of such license until the expiration of seven years from the date of the approval of the approved application or the issuance of the license. Section 355(c)(2)[1] of this title does not apply to the refusal to approve an application under the preceding sentence.

(b) Exceptions

During the 7-year period described in subsection (a) for an approved application under section 355 of this title or license under section 262 of title 42, the Secretary may approve an application or issue a license for a drug that is otherwise the same, as determined by the Secretary, as the already approved drug for the same rare disease or condition if—

(1) the Secretary finds, after providing the holder of exclusive approval or licensure notice and opportunity for the submission of views, that during such period the holder of the exclusive approval or licensure cannot ensure the availability of sufficient quantities of the drug to meet the needs of persons with the disease or condition for which the drug was designated; or

(2) the holder provides the Secretary in writing the consent of such holder for the approval of other applications or the issuance of other licenses before the expiration of such seven-year period.

(c) Condition of clinical superiority

(1) In general

If a sponsor of a drug that is designated under section 360bb of this title and is otherwise the same, as determined by the Secretary, as an already approved or licensed drug is seeking exclusive approval or exclusive licensure described in subsection (a) for the same rare disease or condition as the already approved drug, the Secretary shall require such sponsor, as a condition of such exclusive approval or licensure, to demonstrate that such drug is clinically superior to any already approved or licensed drug that is the same drug.

(2) Definition

For purposes of paragraph (1), the term ''clinically superior'' with respect to a drug means that the drug provides a significant therapeutic advantage over and above an already approved or licensed drug in terms of greater efficacy, greater safety, or by providing a major contribution to patient care.

(3) Applicability

This subsection applies to any drug designated under section 360bb of this title for which an application was approved under section 355 of this title or licensed under section 262 of title 42 after August 18, 2017, regardless of the date on which such drug was designated under section 360bb of this title.

(d) Regulations

The Secretary may promulgate regulations for the implementation of subsection (c). Beginning on August 18, 2017, until such time as the Secretary promulgates regulations in accordance with this subsection, the Secretary may apply any definitions set forth in regulations that were promulgated prior to such date, to the extent such definitions are not inconsistent with the terms of this section, as amended by such Act.

(e) Demonstration of clinical superiority standard

To assist sponsors in demonstrating clinical superiority as described in subsection (c), the Secretary—

(1) upon the designation of any drug under section 360bb of this title, shall notify the sponsor of such drug in writing of the basis for the designation, including, as applicable, any plausible hypothesis offered by the sponsor and relied upon by the Secretary that the drug is clinically superior to a previously approved drug; and

(2) upon granting exclusive approval or licensure under subsection (a) on the basis of a demonstration of clinical superiority as described in subsection (c), shall publish a summary of the clinical superiority findings.

(June 25, 1938, ch. 675, § 527, as added Pub. L. 97–414, § 2(a), Jan. 4, 1983, 96 Stat. 2050; amended Pub. L. 98–417, title I, § 102(b)(6), Sept. 24, 1984, 98 Stat. 1593; Pub. L. 99–91, §§ 2, 3(a)(3), Aug. 15, 1985, 99 Stat. 387, 388; Pub. L. 103–80, § 3(v), Aug. 13, 1993, 107 Stat. 778; Pub. L. 105–115, title I, § 125(b)(2)(J), (K), Nov. 21, 1997, 111 Stat. 2326; Pub. L. 107–281, § 4, Nov. 6, 2002, 116 Stat. 1993; Pub. L. 115–52, title VI, § 607(a), Aug. 18, 2017, 131 Stat. 1049; Pub. L. 116–260, div. BB, title III, § 323, Dec. 27, 2020, 134 Stat. 2933.)

Editorial Notes

REFERENCES IN TEXT

Section 355(c)(2) of this title, referred to in subsec. (a), was redesignated as section 355(c)(1)(B) of this title by Pub. L. 98–417, title I, § 102(a)(2), Sept. 24, 1984, 98 Stat. 1592.

This section, as amended by such Act, referred to in subsec. (d), means this section as amended by the FDA Reauthorization Act of 2017, Pub. L. 115–52.

AMENDMENTS

2020—Subsec. (c)(3). Pub. L. 116–260 added par. (3).

[1] See References in Text note below.

2017—Subsec. (a). Pub. L. 115–52, § 607(a)(1), substituted ''the same drug for the same disease or condition'' for ''such drug for such disease or condition'' in concluding provisions.

Subsec. (b). Pub. L. 115–52, § 607(a)(2)(A), in introductory provisions, substituted ''During the 7-year period described in subsection (a) for an approved application under section 355 of this title or license under section 262 of title 42, the Secretary may approve an application or issue a license for a drug that is otherwise the same, as determined by the Secretary, as the already approved drug for the same rare disease or condition if'' for ''If an application filed pursuant to section 355 of this title is approved for a drug designated under section 360bb of this title for a rare disease or condition or if a license is issued under section 262 of title 42 for such a drug, the Secretary may, during the seven-year period beginning on the date of the application approval or of the issuance of the license, approve another application under section 355 of this title or issue a license under section 262 of title 42, for such drug for such disease or condition for a person who is not the holder of such approved application or of such license if''.

Subsec. (b)(1). Pub. L. 115–52, § 607(a)(2)(B), substituted ''of exclusive approval or licensure notice and opportunity for the submission of views, that during such period the holder of the exclusive approval or licensure cannot ensure'' for ''notice and opportunity for the submission of views, that in such period the holder of the approved application or of the license cannot assure''.

Subsec. (b)(2). Pub. L. 115–52, § 607(a)(2)(C), substituted ''the holder provides'' for ''such holder provides''.

Subsecs. (c) to (e). Pub. L. 115–52, § 607(a)(3), added subsecs. (c) to (e).

2002—Subsec. (a). Pub. L. 107–281, in concluding provisions, struck out '', of such certification,'' after ''such approved application'' and '', the issuance of the certification,'' after ''approval of the approved application''.

1997—Subsec. (a). Pub. L. 105–115, § 125(b)(2)(J), struck out '', issue another certification under section 357 of this title,'' before ''or issue another license'' in closing provisions, inserted ''or'' at end of par. (1), redesignated par. (3) as (2), and struck out former par. (2) which read as follows: ''issues a certification under section 357 of this title, or''.

Subsec. (b). Pub. L. 105–115, § 125(b)(2)(K), in introductory provisions, struck out '', if a certification is issued under section 357 of this title for such a drug,'' after ''rare disease or condition'', '', of the issuance of the certification under section 357 of this title,'' after ''application approval'', '', issue another certification under section 357 of this title,'' after ''application under section 355 of this title'', and '', of such certification,'' after ''approved application''.

Subsec. (b)(1). Pub. L. 105–115, § 125(b)(2)(K), struck out '', of the certification,'' after ''holder of the approved application''.

Subsec. (b)(2). Pub. L. 105–115, § 125(b)(2)(K), struck out '', issuance of other certifications,'' after ''approval of other applications''.

1993—Subsec. (b). Pub. L. 103–80 struck out extraneous comma before ''or issue a license under section 262'' in introductory provisions and substituted ''the'' for ''The'' at beginning of par. (1).

1985—Pub. L. 99–91, § 2(3), struck out ''unpatented'' before ''drugs'' in section catchline.

Subsec. (a). Pub. L. 99–91, §§ 2(1), 3(a)(3)(A)–(D), struck out ''or'' at end of par. (1), added par. (2), redesignated former par. (2) as (3), struck out ''and for which a United States Letter of Patent may not be issued'' after ''rare disease or condition'', inserted in first sentence '', issue another certification under section 357 of this title,'' after ''section 355 of this title'' the second time it appeared, inserted '', of such certification,'' after ''holder of such approved application'', and inserted '', the issuance of the certification,'' after ''approval of the approved application''.

Subsec. (b). Pub. L. 99–91, §§ 2(2), 3(a)(3)(E)–(K), struck out ''and if a United States Letter of Patent may not be issued for the drug'' after ''such a drug'', substituted '', if a certification is issued under section 357 of this title for such a drug, or if a license'' for ''or a license'', inserted '', of the issuance of the certification under section 357 of this title,'' after ''application approval'', struck out '', if the drug is a biological product,'' before ''issue a license'', inserted '', issue another certification under section 357 of this title,'' after ''section 355 of this title'', inserted '', of such certification,'' after ''holder of such approved application'', inserted '', of such certification,'' after ''application'' in par. (1), and inserted '', issuance of other certifications,'' after ''other applications'' in par. (2).

1984—Subsecs. (a), (b). Pub. L. 98–417 substituted ''section 355'' for ''section 355(b)'' wherever appearing.

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 1985 AMENDMENT

Amendment by Pub. L. 99–91 effective Aug. 15, 1985, see section 8(b) of Pub. L. 99–91, set out as a note under section 360aa of this title.

CONSTRUCTION

Pub. L. 115–52, title VI, § 607(b), Aug. 18, 2017, 131 Stat. 1050, provided that: ''Nothing in the amendments made by subsection (a) [amending this section] shall affect any determination under sections 526 and 527 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bb, 360cc) made prior to the date of enactment of the FDA Reauthorization Act of 2017 [Aug. 18, 2017].''

§ 360dd. Open protocols for investigations of drugs for rare diseases or conditions

If a drug is designated under section 360bb of this title as a drug for a rare disease or condition and if notice of a claimed exemption under section 355(i) of this title or regulations issued thereunder is filed for such drug, the Secretary shall encourage the sponsor of such drug to design protocols for clinical investigations of the drug which may be conducted under the exemption to permit the addition to the investigations of persons with the disease or condition who need the drug to treat the disease or condition and who cannot be satisfactorily treated by available alternative drugs.

(June 25, 1938, ch. 675, § 528, as added Pub. L. 97–414, § 2(a), Jan. 4, 1983, 96 Stat. 2051.)

§ 360ee. Grants and contracts for development of drugs for rare diseases and conditions

(a) Authority of Secretary

The Secretary may make grants to and enter into contracts with public and private entities and individuals to assist in (1) defraying the costs of developing drugs for rare diseases or conditions, including qualified testing expenses, (2) defraying the costs of developing medical devices for rare diseases or conditions, (3) defraying the costs of developing medical foods for rare diseases or conditions, and (4) developing regulatory science pertaining to the chemistry, manufacturing, and controls of individualized medical products to treat individuals with rare diseases or conditions.

(b) Definitions

For purposes of subsection (a):

(1) The term ''qualified testing'' means—

(A) human clinical testing—

(i) which is carried out under an exemption for a drug for a rare disease or condi-

tion under section 355(i) of this title (or regulations issued under such section); and

(ii) which occurs before the date on which an application with respect to such drug is submitted under section 355(b) of this title or under section 262 of title 42;

(B) preclinical testing involving a drug for a rare disease or condition which occurs after the date such drug is designated under section 360bb of this title and before the date on which an application with respect to such drug is submitted under section 355(b) of this title or under section 262 of title 42; and

(C) prospectively planned and designed observational studies and other analyses conducted to assist in the understanding of the natural history of a rare disease or condition and in the development of a therapy, including studies and analyses to—

(i) develop or validate a drug development tool related to a rare disease or condition; or

(ii) understand the full spectrum of the disease manifestations, including describing genotypic and phenotypic variability and identifying and defining distinct subpopulations affected by a rare disease or condition.

(2) The term ''rare disease or condition'' means (1) in the case of a drug, any disease or condition which (A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug, (2) in the case of a medical device, any disease or condition that occurs so infrequently in the United States that there is no reasonable expectation that a medical device for such disease or condition will be developed without assistance under subsection (a), and (3) in the case of a medical food, any disease or condition that occurs so infrequently in the United States that there is no reasonable expectation that a medical food for such disease or condition will be developed without assistance under subsection (a). Determinations under the preceding sentence with respect to any drug shall be made on the basis of the facts and circumstances as of the date the request for designation of the drug under section 360bb of this title is made.

(3) The term ''medical food'' means a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation.

(c) Authorization of appropriations

For grants and contracts under subsection (a), there is authorized to be appropriated $6,904,110 for the period beginning on October 1, 2022 and ending on December 23, 2022.[1]

[1] See 2022 Amendment notes below.

(Pub. L. 97–414, § 5, Jan. 4, 1983, 96 Stat. 2056; Pub. L. 98–551, § 4(b), Oct. 30, 1984, 98 Stat. 2817; Pub. L. 99–91, § 5, Aug. 15, 1985, 99 Stat. 391; Pub. L. 100–290, § 3(a)–(c), Apr. 18, 1988, 102 Stat. 90, 91; Pub. L. 105–115, title I, § 125(b)(2)(N), Nov. 21, 1997, 111 Stat. 2326; Pub. L. 107–281, § 3, Nov. 6, 2002, 116 Stat. 1993; Pub. L. 110–85, title XI, § 1112(b), Sept. 27, 2007, 121 Stat. 976; Pub. L. 112–144, title IX, § 906, July 9, 2012, 126 Stat. 1092; Pub. L. 114–255, div. A, title III, § 3015, Dec. 13, 2016, 130 Stat. 1094; Pub. L. 115–52, title VI, § 603, Aug. 18, 2017, 131 Stat. 1048; Pub. L. 117–180, div. F, title V, § 5006, Sept. 30, 2022, 136 Stat. 2167; Pub. L. 117–229, div. C, title III, § 307, Dec. 16, 2022, 136 Stat. 2312; Pub. L. 117–328, div. FF, title III, § 3107, Dec. 29, 2022, 136 Stat. 5808.)

Editorial Notes

CODIFICATION

Section was enacted as part of the Orphan Drug Act, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

AMENDMENTS

2022—Subsec. (a)(4). Pub. L. 117–328, § 3107(1), added par. (4).

Subsec. (c). Pub. L. 117–328, § 3107(2), which directed the substitution of ''$30,000,000 for each of fiscal years 2023 through 2027'' for ''$6,328,767 for the period beginning on October 1, 2022, and ending on December 23, 2022'', could not be executed because ''$6,328,767'' did not appear after the intervening amendment by Pub. L. 117–229. See below.

Pub. L. 117–229 substituted ''$6,904,110 for the period beginning on October 1, 2022 and ending on December 23, 2022'' for ''$6,328,767 for the period beginning on October 1, 2022, and ending on December 16, 2022''.

Pub. L. 117–180 substituted ''$6,328,767 for the period beginning on October 1, 2022, and ending on December 16, 2022'' for ''$30,000,000 for each of fiscal years 2018 through 2022''.

2017—Subsec. (c). Pub. L. 115–52 substituted ''2018 through 2022'' for ''2013 through 2017''.

2016—Subsec. (a)(1). Pub. L. 114–255, § 3015(1), added par. (1) and struck out former par. (1) which read as follows: ''defraying the costs of qualified testing expenses incurred in connection with the development of drugs for rare diseases and conditions,''.

Subsec. (b)(1)(C). Pub. L. 114–255, § 3015(2), added subpar. (C).

2012—Subsec. (b)(1)(A)(ii). Pub. L. 112–144, § 906(a), struck out ''after the date such drug is designated under section 360bb of this title and'' after ''which occurs''.

Subsec. (c). Pub. L. 112–144, § 906(b), amended subsec. (c) generally. Prior to amendment, text read as follows: ''For grants and contracts under subsection (a), there is authorized to be appropriated $30,000,000 for each of fiscal years 2008 through 2012.''

2007—Subsec. (c). Pub. L. 110–85 amended subsec. (c) generally. Prior to amendment, subsec. (c) read as follows: ''For grants and contracts under subsection (a) of this section, there are authorized to be appropriated such sums as already have been appropriated for fiscal year 2002, and $25,000,000 for each of the fiscal years 2003 through 2006.''

2002—Subsec. (c). Pub. L. 107–281 amended subsec. (c) generally. Prior to amendment, subsec. (c) read as follows: ''For grants and contracts under subsection (a) of this section there are authorized to be appropriated $10,000,000 for fiscal year 1988, $12,000,000 for fiscal year 1989, $14,000,000 for fiscal year 1990.''

1997—Subsec. (b)(1)(A)(ii), (B). Pub. L. 105–115 struck out ''or 357'' after ''355(b)''.

1988—Subsec. (a). Pub. L. 100–290, § 3(a)(1), (b)(1), inserted ''(1)'' after ''assist in'' and added pars. (2) and (3).

Subsec. (b)(2). Pub. L. 100–290, §3(a)(2), (b)(2), inserted ''(1) in the case of a drug,'' after ''means'', added cls. (2) and (3), and substituted ''under section 360bb of this title'' for ''under this subsection'' in last sentence.

Subsec. (b)(3). Pub. L. 100–290, §3(b)(3), added par. (3).

Subsec. (c). Pub. L. 100–290, §3(c), amended subsec. (c) generally. Prior to amendment, subsec. (c) read as follows: ''For grants and contracts under subsection (a) of this section there are authorized to be appropriated $4,000,000 for fiscal year 1986, $4,000,000 for fiscal year 1987, and $4,000,000 for fiscal year 1988.''

1985—Subsec. (a). Pub. L. 99–91, §5(a)(1), struck out ''clinical'' before ''testing''.

Subsec. (b)(1). Pub. L. 99–91, §5(a)(2), substituted provisions defining ''qualified testing'' for provisions defining ''qualified clinical testing''.

Subsec. (c). Pub. L. 99–91, §5(b), substituted provisions authorizing appropriations for fiscal years 1986 to 1988, for provisions authorizing appropriations for fiscal years 1983 and the two succeeding fiscal years.

1984—Subsec. (b)(2). Pub. L. 98–551 substituted ''which (A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which'' for ''which occurs so infrequently in the United States that''.

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 1985 AMENDMENT

Amendment by Pub. L. 99–91 effective Oct. 1, 1985, see section 8(a) of Pub. L. 99–91, set out as a note under section 360aa of this title.

GRANTS FOR RESEARCH ON THERAPIES FOR ALS

Pub. L. 117–79, §2, Dec. 23, 2021, 135 Stat. 1533, provided that:

''(a) IN GENERAL.—The Secretary of Health and Human Services (referred to in this section as the 'Secretary') shall award grants to participating entities for purposes of scientific research utilizing data from expanded access to investigational drugs for individuals who are not otherwise eligible for clinical trials for the prevention, diagnosis, mitigation, treatment, or cure of amyotrophic lateral sclerosis. In the case of a participating entity seeking such a grant, an expanded access request must be submitted, and allowed to proceed by the Secretary, under section 561 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb) and part 312 of title 21, Code of Federal Regulations (or any successor regulations), before the application for such grant is submitted.

''(b) APPLICATION.—

''(1) IN GENERAL.—A participating entity seeking a grant under this section shall submit to the Secretary an application at such time, in such manner, and containing such information as the Secretary shall specify.

''(2) USE OF DATA.—An application submitted under paragraph (1) shall include a description of how data generated through an expanded access request under section 561 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb) with respect to the investigational drug involved will be used to support research or development related to the prevention, diagnosis, mitigation, treatment, or cure of amyotrophic lateral sclerosis.

''(3) NONINTERFERENCE WITH CLINICAL TRIALS.—An application submitted under paragraph (1) shall include a description of how the proposed expanded access program will be designed so as not to interfere with patient enrollment in ongoing clinical trials for investigational therapies for the prevention, diagnosis, mitigation, treatment, or cure of amyotrophic lateral sclerosis.

''(c) SELECTION.—Consistent with sections 406 and 492 of the Public Health Service Act (42 U.S.C. 284a, 289a), the Secretary shall, in determining whether to award a grant under this section, confirm that—

''(1) such grant will be used to support a scientific research objective relating to the prevention, diagnosis, mitigation, treatment, or cure of amyotrophic lateral sclerosis (as described in subsection (a));

''(2) such grant shall not have the effect of diminishing eligibility for, or impeding enrollment of, ongoing clinical trials for the prevention, diagnosis, mitigation, treatment, or cure of amyotrophic lateral sclerosis by determining that individuals who receive expanded access to investigational drugs through such a grant are not eligible for enrollment in—

''(A) ongoing clinical trials that are registered on ClinicalTrials.gov (or successor website), with respect to a drug for the prevention, diagnosis, mitigation, treatment, or cure of amyotrophic lateral sclerosis; or

''(B) clinical trials for the prevention, diagnosis, mitigation, treatment, or cure of amyotrophic lateral sclerosis for which an exemption under section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)) has been granted by the Food and Drug Administration and which are expected to begin enrollment within one year; and

''(3) the resulting project funded by such grant will allow for equitable access to investigational drugs by minority and underserved populations.

''(d) USE OF FUNDS.—A participating entity shall use funds received through the grant—

''(1) to pay the manufacturer or sponsor for the direct costs of the investigational drug, as authorized under section 312.8(d) of title 21, Code of Federal Regulations (or successor regulations), to prevent, diagnose, mitigate, treat, or cure amyotrophic lateral sclerosis that is the subject of an expanded access request described in subsection (a), if such costs are justified as part of peer review of the grant;

''(2) for the entity's direct costs incurred in providing such drug consistent with the research mission of the grant; or

''(3) for the direct and indirect costs of the entity in conducting research with respect to such drug.

''(e) DEFINITIONS.—In this section:

''(1) The term 'participating entity' means a participating clinical trial site or sites sponsored by a small business concern (as defined in section 3(a) of the Small Business Act (15 U.S.C. 632(a))) that is the sponsor of a drug that is the subject of an investigational new drug application under section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)) to prevent, diagnose, mitigate, treat, or cure amyotrophic lateral sclerosis.

''(2) The term 'participating clinical trial' means a phase 3 clinical trial conducted pursuant to an exemption under section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)) or section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)) to investigate a drug intended to prevent, diagnose, mitigate, treat, or cure amyotrophic lateral sclerosis.

''(3) The term 'participating clinical trial site' means a health care facility, or network of facilities, at which patients participating in a participating clinical trial receive an investigational drug through such trial.

''(f) SUNSET.—The Secretary may not award grants under this section on or after September 30, 2026.''

FINDINGS AND PURPOSES

Pub. L. 107–281, §2, Nov. 6, 2002, 116 Stat. 1992, provided that:

''(a) FINDINGS.—Congress makes the following findings:

''(1) Rare diseases and disorders are those which affect small patient populations, typically populations smaller than 200,000 individuals in the United States. Such diseases and conditions include Huntington's disease, amyotrophic lateral sclerosis (Lou Gehrig's disease), Tourette syndrome, Crohn's disease, cystic fibrosis, cystinosis, and Duchenne muscular dystrophy.

''(2) For many years, the 25,000,000 Americans suffering from the over 6,000 rare diseases and disorders

were denied access to effective medicines because prescription drug manufacturers could rarely make a profit from marketing drugs for such small groups of patients. The prescription drug industry did not adequately fund research into such treatments. Despite the urgent health need for these medicines, they came to be known as 'orphan drugs' because no companies would commercialize them.

''(3) During the 1970s, an organization called the National Organization for Rare Disorders (NORD) was founded to provide services and to lobby on behalf of patients with rare diseases and disorders. NORD was instrumental in pressing Congress for legislation to encourage the development of orphan drugs.

''(4) The Orphan Drug Act [see Short Title of 1983 Amendments note set out under section 301 of this title] created financial incentives for the research and production of such orphan drugs. New Federal programs at the National Institutes of Health and the Food and Drug Administration encouraged clinical research and commercial product development for products that target rare diseases. An Orphan Products Board was established to promote the development of drugs and devices for rare diseases or disorders.

''(5) Before 1983, some 38 orphan drugs had been developed. Since the enactment of the Orphan Drug Act [Jan. 4, 1983], more than 220 new orphan drugs have been approved and marketed in the United States and more than 800 additional drugs are in the research pipeline.

''(6) Despite the tremendous success of the Orphan Drug Act, rare diseases and disorders deserve greater emphasis in the national biomedical research enterprise.

''(7) The Food and Drug Administration supports small clinical trials through Orphan Products Research Grants. Such grants embody successful partnerships of government and industry, and have led to the development of at least 23 drugs and four medical devices for rare diseases and disorders. Yet the appropriations in fiscal year 2001 for such grants were less than in fiscal year 1995.

''(b) PURPOSES.—The purpose of this Act [see Short Title of 2002 Amendments note set out under section 301 of this title] is to increase the national investment in the development of diagnostics and treatments for patients with rare diseases and disorders.''

§ 360ee–1. FDA rare neurodegenerative disease grant program

The Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs, shall award grants and contracts to public and private entities to cover the costs of research on, and development of interventions intended to prevent, diagnose, mitigate, treat, or cure, amyotrophic lateral sclerosis and other rare neurodegenerative diseases in adults and children, including costs incurred with respect to the development and critical evaluation of tools, methods, and processes—

(1) to characterize such neurodegenerative diseases and their natural history;

(2) to identify molecular targets for such neurodegenerative diseases; and

(3) to increase efficiency and productivity of clinical development of therapies, including through—

(A) the use of master protocols and adaptive and add-on clinical trial designs; and

(B) efforts to establish new or leverage existing clinical trial networks.

(Pub. L. 117–79, § 5, Dec. 23, 2021, 135 Stat. 1537.)

Editorial Notes

CODIFICATION

Section was enacted as part of the Accelerating Access to Critical Therapies for ALS Act, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

§ 360ff. Priority review to encourage treatments for rare pediatric diseases

(a) Definitions

In this section:

(1) Priority review

The term ''priority review'', with respect to a human drug application as defined in section 379g(1) of this title, means review and action by the Secretary on such application not later than 6 months after receipt by the Secretary of such application, as described in the Manual of Policies and Procedures of the Food and Drug Administration and goals identified in the letters described in section 101(b) of the Prescription Drug User Fee Amendments of 2012.

(2) Priority review voucher

The term ''priority review voucher'' means a voucher issued by the Secretary to the sponsor of a rare pediatric disease product application that entitles the holder of such voucher to priority review of a single human drug application submitted under section 355(b)(1) of this title or section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)] after the date of approval of the rare pediatric disease product application.

(3) Rare pediatric disease

The term ''rare pediatric disease'' means a disease that meets each of the following criteria:

(A) The disease is a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents.

(B) The disease is a rare disease or condition, within the meaning of section 360bb of this title.

(4) Rare pediatric disease product application

The term ''rare pediatric disease product application'' means a human drug application, as defined in section 379g(1) of this title, that—

(A) is for a drug or biological product that is for the prevention or treatment of a rare pediatric disease;

(B)(i) is for such a drug—

(I) that contains no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) that has been previously approved in any other application under subsection (b)(1), (b)(2), or (j) of section 355 of this title; and

(II) that is the subject of an application submitted under section 355(b)(1) of this title; or

(ii) is for such a biological product—

(I) that contains no active ingredient that has been previously approved in any

other application under section 351(a) or 351(k) of the Public Health Service Act [42 U.S.C. 262(a), 262(k)]; and

(II) that is the subject of an application submitted under section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)];

(C) the Secretary deems eligible for priority review;

(D) that[1] relies on clinical data derived from studies examining a pediatric population and dosages of the drug intended for that population;

(E) that[1] does not seek approval for an adult indication in the original rare pediatric disease product application; and

(F) is approved after September 30, 2016.

(b) Priority review voucher

(1) In general

The Secretary shall award a priority review voucher to the sponsor of a rare pediatric disease product application upon approval by the Secretary of such rare pediatric disease product application.

(2) Transferability

(A) In general

The sponsor of a rare pediatric disease product application that receives a priority review voucher under this section may transfer (including by sale) the entitlement to such voucher. There is no limit on the number of times a priority review voucher may be transferred before such voucher is used.

(B) Notification of transfer

Each person to whom a voucher is transferred shall notify the Secretary of such change in ownership of the voucher not later than 30 days after such transfer.

(3) Limitation

A sponsor of a rare pediatric disease product application may not receive a priority review voucher under this section if the rare pediatric disease product application was submitted to the Secretary prior to the date that is 90 days after July 9, 2012.

(4) Notification

(A) Sponsor of a rare pediatric disease product

(i) In general

Beginning on the date that is 90 days after September 30, 2016, the sponsor of a rare pediatric disease product application that intends to request a priority review voucher under this section shall notify the Secretary of such intent upon submission of the rare pediatric disease product application that is the basis of the request for a priority review voucher.

(ii) Applications submitted but not yet approved

The sponsor of a rare pediatric disease product application that was submitted and that has not been approved as of September 30, 2016, shall be considered eligible for a priority review voucher, if—

(I) such sponsor has submitted such rare pediatric disease product application—

(aa) on or after the date that is 90 days after July 9, 2012; and

(bb) on or before September 30, 2016; and

(II) such application otherwise meets the criteria for a priority review voucher under this section.

(B) Sponsor of a drug application using a priority review voucher

(i) In general

The sponsor of a human drug application shall notify the Secretary not later than 90 days prior to submission of the human drug application that is the subject of a priority review voucher of an intent to submit the human drug application, including the date on which the sponsor intends to submit the application. Such notification shall be a legally binding commitment to pay the user fee to be assessed in accordance with this section.

(ii) Transfer after notice

The sponsor of a human drug application that provides notification of the intent of such sponsor to use the voucher for the human drug application under clause (i) may transfer the voucher after such notification is provided, if such sponsor has not yet submitted the human drug application described in the notification.

(5) Termination of authority

The Secretary may not award any priority review vouchers under paragraph (1) after December 20, 2024, unless the rare pediatric disease product application—

(A) is for a drug that, not later than December 20, 2024, is designated under subsection (d) as a drug for a rare pediatric disease; and

(B) is, not later than September 30, 2026, approved under section 355(b)(1) of this title or section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)].

(c) Priority review user fee

(1) In general

The Secretary shall establish a user fee program under which a sponsor of a human drug application that is the subject of a priority review voucher shall pay to the Secretary a fee determined under paragraph (2). Such fee shall be in addition to any fee required to be submitted by the sponsor under subchapter VII.

(2) Fee amount

The amount of the priority review user fee shall be determined each fiscal year by the Secretary, based on the difference between—

(A) the average cost incurred by the Food and Drug Administration in the review of a human drug application subject to priority review in the previous fiscal year; and

(B) the average cost incurred by the Food and Drug Administration in the review of a

[1] So in original. The word ''that'' probably should not appear.

human drug application that is not subject to priority review in the previous fiscal year.

(3) Annual fee setting

The Secretary shall establish, before the beginning of each fiscal year beginning after September 30, 2012, the amount of the priority review user fee for that fiscal year.

(4) Payment

(A) In general

The priority review user fee required by this subsection shall be due upon the notification by a sponsor of the intent of such sponsor to use the voucher, as specified in subsection (b)(4)(A).[2] All other user fees associated with the human drug application shall be due as required by the Secretary or under applicable law.

(B) Complete application

An application described under subparagraph (A) for which the sponsor requests the use of a priority review voucher shall be considered incomplete if the fee required by this subsection and all other applicable user fees are not paid in accordance with the Secretary's procedures for paying such fees.

(C) No waivers, exemptions, reductions, or refunds

The Secretary may not grant a waiver, exemption, reduction, or refund of any fees due and payable under this section.

(5) Offsetting collections

Fees collected pursuant to this subsection for any fiscal year—

(A) shall be deposited and credited as offsetting collections to the account providing appropriations to the Food and Drug Administration; and

(B) shall not be collected for any fiscal year except to the extent provided in advance in appropriations Acts.

(d) Designation process

(1) In general

Upon the request of the manufacturer or the sponsor of a new drug, the Secretary may designate—

(A) the new drug as a drug for a rare pediatric disease; and

(B) the application for the new drug as a rare pediatric disease product application.

(2) Request for designation

The request for a designation under paragraph (1) shall be made at the same time a request for designation of orphan disease status under section 360bb of this title or fast-track designation under section 356 of this title is made. Requesting designation under this subsection is not a prerequisite to receiving a priority review voucher under this section.

(3) Determination by Secretary

Not later than 60 days after a request is submitted under paragraph (1), the Secretary shall determine whether—

(A) the disease or condition that is the subject of such request is a rare pediatric disease; and

(B) the application for the new drug is a rare pediatric disease product application.

(e) Marketing of rare pediatric disease products

(1) Revocation

The Secretary may revoke any priority review voucher awarded under subsection (b) if the rare pediatric disease product for which such voucher was awarded is not marketed in the United States within the 365-day period beginning on the date of the approval of such drug under section 355 of this title or section 351 of the Public Health Service Act [42 U.S.C. 262].

(2) Postapproval production report

The sponsor of an approved rare pediatric disease product shall submit a report to the Secretary not later than 5 years after the approval of the applicable rare pediatric disease product application. Such report shall provide the following information, with respect to each of the first 4 years after approval of such product:

(A) The estimated population in the United States suffering from the rare pediatric disease.

(B) The estimated demand in the United States for such rare pediatric disease product.

(C) The actual amount of such rare pediatric disease product distributed in the United States.

(f) Notice and report

(1) Notice of issuance of voucher and approval of products under voucher

The Secretary shall publish a notice in the Federal Register and on the Internet Web site of the Food and Drug Administration not later than 30 days after the occurrence of each of the following:

(A) The Secretary issues a priority review voucher under this section.

(B) The Secretary approves a drug pursuant to an application submitted under section 355(b) of this title or section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)] for which the sponsor of the application used a priority review voucher under this section.

(2) Notification

If, after the last day of the 1-year period that begins on the date that the Secretary awards the third rare pediatric disease priority voucher under this section, a sponsor of an application submitted under section 355(b) of this title or section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)] for a drug uses a priority review voucher under this section for such application, the Secretary shall submit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate a document—

(A) notifying such Committees of the use of such voucher; and

(B) identifying the drug for which such priority review voucher is used.

[2] See References in Text note below.

(g) Eligibility for other programs

Nothing in this section precludes a sponsor who seeks a priority review voucher under this section from participating in any other incentive program, including under this chapter, except that no sponsor of a rare pediatric disease product application may receive more than one priority review voucher issued under any section of this chapter with respect to the drug for which the application is made..[3]

(h) Relation to other provisions

The provisions of this section shall supplement, not supplant, any other provisions of this chapter or the Public Health Service Act [42 U.S.C. 201 et seq.] that encourage the development of drugs for tropical diseases and rare pediatric diseases.

(i) GAO study and report

(1) Study

(A) In general

Beginning on the date that the Secretary awards the third rare pediatric disease priority voucher under this section, the Comptroller General of the United States shall conduct a study of the effectiveness of awarding rare pediatric disease priority vouchers under this section in the development of human drug products that treat or prevent such diseases.

(B) Contents of study

In conducting the study under subparagraph (A), the Comptroller General shall examine the following:

(i) The indications for which each rare disease product for which a priority review voucher was awarded was approved under section 355 of this title or section 351 of the Public Health Service Act [42 U.S.C. 262].

(ii) Whether, and to what extent, an unmet need related to the treatment or prevention of a rare pediatric disease was met through the approval of such a rare disease product.

(iii) The value of the priority review voucher if transferred.

(iv) Identification of each drug for which a priority review voucher was used.

(v) The length of the period of time between the date on which a priority review voucher was awarded and the date on which it was used.

(2) Report

Not later than 1 year after the date under paragraph (1)(A), the Comptroller General shall submit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate, a report containing the results of the study under paragraph (1).

(June 25, 1938, ch. 675, §529, as added Pub. L. 112–144, title IX, §908, July 9, 2012, 126 Stat. 1094; amended Pub. L. 114–113, div. A, title VII, §765, Dec. 18, 2015, 129 Stat. 2286; Pub. L. 114–229, §2(a), Sept. 30, 2016, 130 Stat. 943; Pub. L. 114–255, div. A, title III, §3013(a), Dec. 13, 2016, 130 Stat. 1093; Pub. L. 116–159, div. C, title I, §2105, Oct. 1, 2020, 134 Stat. 729; Pub. L. 116–215, div. B, title II, §1211, Dec. 11, 2020, 134 Stat. 1045; Pub. L. 116–260, div. BB, title III, §321, Dec. 27, 2020, 134 Stat. 2932; Pub. L. 117–9, §1(a)(4), Apr. 23, 2021, 135 Stat. 257; Pub. L. 118–83, div. B, title II, §202, Sept. 26, 2024, 138 Stat. 1538.)

[3] So in original.

Editorial Notes

REFERENCES IN TEXT

Section 101(b) of the Prescription Drug User Fee Amendments of 2012, referred to in subsec. (a)(1), is section 101(b) of Pub. L. 112–144, which is set out as a note under section 379g of this title.

Subsection (b)(4)(A), referred to in subsec. (c)(4)(A), was part of subsec. (b)(4) of this section that was struck out by Pub. L. 114–229, §2(a)(2)(A), Sept. 30, 2016, 130 Stat. 943, which provision also added a new subsec. (b)(4) in which former subsec. (b)(4)(A) was restated as subsec. (b)(4)(B)(i).

The Public Health Service Act, referred to in subsec. (h), is act July 1, 1944, ch. 373, 58 Stat. 682, which is classified generally to chapter 6A (§201 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 201 of Title 42 and Tables.

AMENDMENTS

2024—Subsec. (b)(5). Pub. L. 118–83 substituted ''December 20, 2024'' for ''September 30, 2024'' in introductory provisions and in subpar. (A).

2021—Subsec. (a)(4)(A), (B). Pub. L. 117–9 added subpars. (A) and (B) and struck out former subpars. (A) and (B) which read as follows:

''(A) is for a drug or biological product—

''(i) that is for the prevention or treatment of a rare pediatric disease; and

''(ii) that contains no active ingredient (including any ester or salt of the active ingredient) that has been previously approved in any other application under section 355(b)(1), 355(b)(2), or 355(j) of this title or section 351(a) or 351(k) of the Public Health Service Act;

''(B) is submitted under section 355(b)(1) of this title or section 351(a) of the Public Health Service Act;''.

2020—Subsec. (b)(5). Pub. L. 116–260 substituted ''September 30, 2024'' for ''December 18, 2020'' in introductory provisions and in subpar. (A) and substituted ''September 30, 2026'' for ''December 18, 2022'' in subpar. (B).

Pub. L. 116–215 substituted ''December 18, 2020'' for ''December 11, 2020'' in introductory provisions and in subpar. (A) and substituted ''December 18, 2022'' for ''December 11, 2022'' in subpar. (B).

Pub. L. 116–159 substituted ''December 11, 2020'' for ''September 30, 2020'' in introductory provisions and in subpar. (A) and substituted ''December 11, 2022'' for ''September 30, 2022'' in subpar. (B).

2016—Subsec. (a)(3)(A). Pub. L. 114–229, §2(a)(1)(A), amended subpar. (A) generally. Prior to amendment, subpar. (A) read as follows: ''The disease primarily affects individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents.''

Subsec. (a)(4)(F). Pub. L. 114–229, §2(a)(1)(B), substituted ''September 30, 2016'' for ''July 9, 2012''.

Subsec. (b)(4). Pub. L. 114–229, §2(a)(2)(A), added par. (4) and struck out former par. (4). Prior to amendment, text read as follows:

''(A) IN GENERAL.—The sponsor of a human drug application shall notify the Secretary not later than 90 days prior to submission of the human drug application that is the subject of a priority review voucher of an intent to submit the human drug application, including the date on which the sponsor intends to submit the application. Such notification shall be a legally binding

commitment to pay for the user fee to be assessed in accordance with this section.

''(B) TRANSFER AFTER NOTICE.—The sponsor of a human drug application that provides notification of the intent of such sponsor to use the voucher for the human drug application under subparagraph (A) may transfer the voucher after such notification is provided, if such sponsor has not yet submitted the human drug application described in the notification.''

Subsec. (b)(5). Pub. L. 114–255 added par. (5) and struck out former par. (5). Prior to amendment, text read as follows: ''The Secretary may not award any priority review vouchers under paragraph (1) after December 31, 2016.''

Pub. L. 114–229, § 2(a)(2)(B), added par. (5) and struck out former par. (5). Prior to amendment, text read as follows: ''The Secretary may not award any priority review vouchers under paragraph (1) after September 30, 2016.''

Subsec. (g). Pub. L. 114–229, § 2(a)(3), inserted before period at end '', except that no sponsor of a rare pediatric disease product application may receive more than one priority review voucher issued under any section of this chapter with respect to the drug for which the application is made.''

2015—Subsec. (b)(5). Pub. L. 114–113 substituted ''September 30, 2016.'' for ''the last day of the 1-year period that begins on the date that the Secretary awards the third rare pediatric disease priority voucher under this section.''

Statutory Notes and Related Subsidiaries

CONSTRUCTION

Pub. L. 114–229, § 2(b), Sept. 30, 2016, 130 Stat. 944, provided that: ''Nothing in this Act [amending this section and enacting provisions set out as a note under section 301 of this title], or the amendments made by this Act, shall be construed to affect the validity of a priority review voucher that was issued under section 529 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360ff) before the date of enactment of this Act [Sept. 30, 2016].''

§ 360ff–1. Targeted drugs for rare diseases

(a) Purpose

The purpose of this section, through the approach provided for in subsection (b), is to—

(1) facilitate the development, review, and approval of genetically targeted drugs and variant protein targeted drugs to address an unmet medical need in one or more patient subgroups, including subgroups of patients with different mutations of a gene, with respect to rare diseases or conditions that are serious or life-threatening; and

(2) maximize the use of scientific tools or methods, including surrogate endpoints and other biomarkers, for such purposes.

(b) Leveraging of data from previously approved drug application or applications

The Secretary may, consistent with applicable standards for approval under this chapter or section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)], allow the sponsor of an application under section 355(b)(1) of this title or section 351(a) of the Public Health Service Act for a genetically targeted drug or a variant protein targeted drug to rely upon data and information—

(1) previously developed by the same sponsor (or another sponsor that has provided the sponsor with a contractual right of reference to such data and information); and

(2) submitted by a sponsor described in paragraph (1) in support of one or more previously approved applications that were submitted under section 355(b)(1) of this title or section 351(a) of the Public Health Service Act,

for a drug that incorporates or utilizes the same or similar genetically targeted technology as the drug or drugs that are the subject of an application or applications described in paragraph (2) or for a variant protein targeted drug that is the same or incorporates or utilizes the same variant protein targeted drug, as the drug or drugs that are the subject of an application or applications described in paragraph (2).

(c) Definitions

For purposes of this section—

(1) the term ''genetically targeted drug'' means a drug that—

(A) is the subject of an application under section 355(b)(1) of this title or section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)] for the treatment of a rare disease or condition (as such term is defined in section 360bb of this title) that is serious or life-threatening;

(B) may result in the modulation (including suppression, up-regulation, or activation) of the function of a gene or its associated gene product; and

(C) incorporates or utilizes a genetically targeted technology;

(2) the term ''genetically targeted technology'' means a technology comprising non-replicating nucleic acid or analogous compounds with a common or similar chemistry that is intended to treat one or more patient subgroups, including subgroups of patients with different mutations of a gene, with the same disease or condition, including a disease or condition due to other variants in the same gene; and

(3) the term ''variant protein targeted drug'' means a drug that—

(A) is the subject of an application under section 355(b)(1) of this title or section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)] for the treatment of a rare disease or condition (as such term is defined in section 360bb of this title) that is serious or life-threatening;

(B) modulates the function of a product of a mutated gene where such mutation is responsible in whole or in part for a given disease or condition; and

(C) is intended to treat one or more patient subgroups, including subgroups of patients with different mutations of a gene, with the same disease or condition.

(d) Rule of construction

Nothing in this section shall be construed to—

(1) alter the authority of the Secretary to approve drugs pursuant to this chapter or section 351 of the Public Health Service Act [42 U.S.C. 262] (as authorized prior to December 13, 2016), including the standards of evidence, and applicable conditions, for approval under such applicable chapter or Act; or

(2) confer any new rights, beyond those authorized under this chapter or the Public

Health Service Act [42 U.S.C. 201 et seq.] prior to December 13, 2016, with respect to the permissibility of a sponsor referencing information contained in another application submitted under section 355(b)(1) of this title or section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)].

(June 25, 1938, ch. 675, § 529A, as added Pub. L. 114–255, div. A, title III, § 3012, Dec. 13, 2016, 130 Stat. 1091.)

Editorial Notes

REFERENCES IN TEXT

The Public Health Service Act, referred to in subsec. (d)(2), is act July 1, 1944, ch. 373, 58 Stat. 682, which is classified generally to chapter 6A (§ 201 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 201 of Title 42 and Tables.

PART C—ELECTRONIC PRODUCT RADIATION CONTROL

Editorial Notes

CODIFICATION

This part was classified to subpart 3 (§ 263c et seq.) of part F of subchapter II of chapter 6A of Title 42, The Public Health and Welfare, prior to its renumbering by Pub. L. 101–629, § 19(a)(4), Nov. 28, 1990, 104 Stat. 4530, as amended by Pub. L. 103–80, § 4(a)(2), Aug. 13, 1993, 107 Stat. 779.

§ 360hh. Definitions

As used in this part—

(1) the term ''electronic product radiation'' means—

(A) any ionizing or non-ionizing electromagnetic or particulate radiation, or

(B) any sonic, infrasonic, or ultrasonic wave, which is emitted from an electronic product as the result of the operation of an electronic circuit in such product;

(2) the term ''electronic product'' means (A) any manufactured or assembled product which, when in operation, (i) contains or acts as part of an electronic circuit and (ii) emits (or in the absence of effective shielding or other controls would emit) electronic product radiation, or (B) any manufactured or assembled article which is intended for use as a component, part, or accessory of a product described in clause (A) and which when in operation emits (or in the absence of effective shielding or other controls would emit) such radiation;

(3) the term ''manufacturer'' means any person engaged in the business of manufacturing, assembling, or importing of electronic products;

(4) the term ''commerce'' means (A) commerce between any place in any State and any place outside thereof; and (B) commerce wholly within the District of Columbia; and

(5) the term ''State'' includes the District of Columbia, the Commonwealth of Puerto Rico, the Northern Mariana Islands, the Virgin Islands, Guam, and American Samoa.

(June 25, 1938, ch. 675, § 531, formerly act July 1, 1944, ch. 373, title III, § 531, formerly § 355, as added Pub. L. 90–602, § 2(3), Oct. 18, 1968, 82 Stat. 1174; amended Pub. L. 94–484, title IX, § 905(b)(1), Oct. 12, 1976, 90 Stat. 2325; renumbered § 531 and amended Pub. L. 101–629, § 19(a)(1)(B), (3), (4), Nov. 28, 1990, 104 Stat. 4529, 4530; Pub. L. 103–80, § 4(a)(2), Aug. 13, 1993, 107 Stat. 779.)

Editorial Notes

CODIFICATION

Section was classified to section 263c of Title 42, The Public Health and Welfare, prior to renumbering by Pub. L. 101–629.

AMENDMENTS

1993—Pub. L. 103–80 amended directory language of Pub. L. 101–629, § 19(a)(4), which renumbered section 263c of Title 42, The Public Health and Welfare, as this section.

1990—Pub. L. 101–629, § 19(a)(1)(B), substituted ''this part'' for ''this subpart'' in introductory provisions.

1976—Par. (5). Pub. L. 94–484 defined ''State'' to include Northern Mariana Islands.

Statutory Notes and Related Subsidiaries

SHORT TITLE

For short title of Pub. L. 90–602, which enacted provisions now comprising this part (§§ 360hh to 360ss), as the ''Radiation Control for Health and Safety Act of 1968'', see section 1 of Pub. L. 90–602, set out as a Short Title of 1968 Amendments note under section 301 of this title.

TRANSFER OF SUBPART; CONSTRUCTION

Pub. L. 101–629, § 19(c), Nov. 28, 1990, 104 Stat. 4530, provided that: ''The transfer of subpart 3 of part F of title III of the Public Health Service Act [42 U.S.C. 263b et seq.] to the Federal Food, Drug, and Cosmetic Act [this chapter] does not change the application of the requirements of such subpart and such Act to electronic products which were in effect on the date of the enactment of this Act [Nov. 28, 1990].''

DEFINITION OF ''SECRETARY'' AND ''DEPARTMENT''

Pub. L. 90–602, § 3, Oct. 18, 1968, 82 Stat. 1186, as amended by Pub. L. 96–88, title V, § 509(b), Oct. 17, 1979, 93 Stat. 695, provided that: ''As used in the amendments made by section 2 of this Act [enacting provisions now comprising sections 360hh to 360ss of this title], except when otherwise specified, the term 'Secretary' means the Secretary of Health and Human Services, and the term 'Department' means the Department of Health and Human Services.''

NONINTERFERENCE WITH OTHER FEDERAL AGENCIES

Pub. L. 90–602, § 4, Oct. 18, 1968, 82 Stat. 1187, provided that: ''The amendments made by section 2 of this Act [enacting provisions now comprising sections 360hh to 360ss of this title] shall not be construed as superseding or limiting the functions, under any other provision of law, of any officer or agency of the United States.''

§ 360ii. Program of control

(a) Establishment

The Secretary shall establish and carry out an electronic product radiation control program designed to protect the public health and safety from electronic product radiation. As a part of such program, he shall—

(1) pursuant to section 360kk of this title, develop and administer performance standards for electronic products;

(2) plan, conduct, coordinate, and support research, development, training, and operational activities to minimize the emissions of and

the exposure of people to, unnecessary electronic product radiation;

(3) maintain liaison with and receive information from other Federal and State departments and agencies with related interests, professional organizations, industry, industry and labor associations, and other organizations on present and future potential electronic product radiation;

(4) study and evaluate emissions of, and conditions of exposure to, electronic product radiation and intense magnetic fields;

(5) develop, test, and evaluate the effectiveness of procedures and techniques for minimizing exposure to electronic product radiation; and

(6) consult and maintain liaison with the Secretary of Commerce, the Secretary of Defense, the Secretary of Labor, the Atomic Energy Commission, and other appropriate Federal departments and agencies on (A) techniques, equipment, and programs for testing and evaluating electronic product radiation, and (B) the development of performance standards pursuant to section 360kk of this title to control such radiation emissions.

(b) Powers of Secretary

In carrying out the purposes of subsection (a), the Secretary is authorized to—

(1)(A) collect and make available, through publications and other appropriate means, the results of, and other information concerning, research and studies relating to the nature and extent of the hazards and control of electronic product radiation; and (B) make such recommendations relating to such hazards and control as he considers appropriate;

(2) make grants to public and private agencies, organizations, and institutions, and to individuals for the purposes stated in paragraphs (2), (4), and (5) of subsection (a) of this section;

(3) contract with public or private agencies, institutions, and organizations, and with individuals, without regard to section 3324 of title 31 and section 6101 of title 41; and

(4) procure (by negotiation or otherwise) electronic products for research and testing purposes, and sell or otherwise dispose of such products.

(c) Record keeping

(1) Each recipient of assistance under this part pursuant to grants or contracts entered into under other than competitive bidding procedures shall keep such records as the Secretary shall prescribe, including records which fully disclose the amount and disposition by such recipient of the proceeds of such assistance, the total cost of the project or undertaking in connection with which such assistance is given or used, and the amount of that portion of the cost of the project or undertaking supplied by other sources, and such other records as will facilitate an effective audit.

(2) The Secretary and the Comptroller General of the United States, or any of their duly authorized representatives, shall have access for the purpose of audit and examination to any books, documents, papers, and records of the recipients that are pertinent to the grants or contracts entered into under this part under other than competitive bidding procedures.

(June 25, 1938, ch. 675, § 532, formerly act July 1, 1944, ch. 373, title III, § 532, formerly § 356, as added Pub. L. 90–602, § 2(3), Oct. 18, 1968, 82 Stat. 1174; renumbered § 532 and amended Pub. L. 101–629, § 19(a)(1)(B), (2)(A), (3), (4), Nov. 28, 1990, 104 Stat. 4529, 4530; Pub. L. 103–80, § 4(a)(2), Aug. 13, 1993, 107 Stat. 779.)

Editorial Notes

CODIFICATION

In subsec. (b)(3), ''section 6101 of title 41'' substituted for ''section 3709 of the Revised Statutes of the United States (41 U.S.C. 5)'' on authority of Pub. L. 111–350, § 6(c), Jan. 4, 2011, 124 Stat. 3854, which Act enacted Title 41, Public Contracts.

Section was classified to section 263d of Title 42, The Public Health and Welfare, prior to renumbering by Pub. L. 101–629.

AMENDMENTS

1993—Pub. L. 103–80 amended directory language of Pub. L. 101–629, § 19(a)(4), which renumbered section 263d of Title 42, The Public Health and Welfare, as this section.

1990—Subsec. (a)(1), (6). Pub. L. 101–629, § 19(a)(2)(A)(i), substituted ''section 360kk'' for ''section 263f''.

Subsec. (b)(3). Pub. L. 101–629, § 19(a)(2)(A)(ii), substituted reference to section 3324 of title 31 for reference to section 3648 of the Revised Statutes (31 U.S.C. 529).

Subsec. (c)(1), (2). Pub. L. 101–629, § 19(a)(1)(B), substituted ''this part'' for ''this subpart''.

Statutory Notes and Related Subsidiaries

TRANSFER OF FUNCTIONS

Atomic Energy Commission abolished and functions transferred by sections 5814 and 5841 of Title 42, The Public Health and Welfare. See also Transfer of Functions notes set out under those sections.

NONINTERFERENCE WITH OTHER FEDERAL AGENCIES

Enactment of this section not to be construed to supersede or limit the functions under any other provision of law or any officer or agency of the United States, see section 4 of Pub. L. 90–602, set out as a note under section 360hh of this title.

§ 360jj. Studies by Secretary

(a) Report to Congress

The Secretary shall conduct the following studies, and shall make a report or reports of the results of such studies to the Congress on or before January 1, 1970, and from time to time thereafter as he may find necessary, together with such recommendations for legislation as he may deem appropriate:

(1) A study of present State and Federal control of health hazards from electronic product radiation and other types of ionizing radiation, which study shall include, but not be limited to—

(A) control of health hazards from radioactive materials other than materials regulated under the Atomic Energy Act of 1954 [42 U.S.C. 2011 et seq.];

(B) any gaps and inconsistencies in present controls;

(C) the need for controlling the sale of certain used electronic products, particularly antiquated X-ray equipment, without upgrading such products to meet the standards for new products or separate standards for used products;

(D) measures to assure consistent and effective control of the aforementioned health hazards;

(E) measures to strengthen radiological health programs of State governments; and

(F) the feasibility of authorizing the Secretary to enter into arrangements with individual States or groups of States to define their respective functions and responsibilities for the control of electronic product radiation and other ionizing radiation;

(2) A study to determine the necessity for the development of standards for the use of nonmedical electronic products for commercial and industrial purposes; and

(3) A study of the development of practicable procedures for the detection and measurement of electronic product radiation which may be emitted from electronic products manufactured or imported prior to the effective date of any applicable standard established pursuant to this part.

(b) Participation of other Federal agencies

In carrying out these studies, the Secretary shall invite the participation of other Federal departments and agencies having related responsibilities and interests, State governments—particularly those of States which regulate radioactive materials under section 274 of the Atomic Energy Act of 1954, as amended [42 U.S.C. 2021], and interested professional, labor, and industrial organizations. Upon request from congressional committees interested in these studies, the Secretary shall keep these committees currently informed as to the progress of the studies and shall permit the committees to send observers to meetings of the study groups.

(c) Organization of studies and participation

The Secretary or his designee shall organize the studies and the participation of the invited participants as he deems best. Any dissent from the findings and recommendations of the Secretary shall be included in the report if so requested by the dissenter.

(June 25, 1938, ch. 675, §533, formerly act July 1, 1944, ch. 373, title III, §533, formerly §357, as added Pub. L. 90–602, §2(3), Oct. 18, 1968, 82 Stat. 1176; renumbered §533 and amended Pub. L. 101–629, §19(a)(1)(B), (3), (4), Nov. 28, 1990, 104 Stat. 4529, 4530; Pub. L. 103–80, §4(a)(2), Aug. 13, 1993, 107 Stat. 779.)

Editorial Notes

REFERENCES IN TEXT

The Atomic Energy Act of 1954, referred to in subsec. (a)(1)(A), is act Aug. 1, 1946, ch. 724, as added by act Aug. 30, 1954, ch. 1073, §1, 68 Stat. 919, which is classified principally to chapter 23 (§2011 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 2011 of Title 42 and Tables.

CODIFICATION

Section was classified to section 263e of Title 42, The Public Health and Welfare, prior to renumbering by Pub. L. 101–629.

AMENDMENTS

1993—Pub. L. 103–80 amended directory language of Pub. L. 101–629, §19(a)(4), which renumbered section 263e of Title 42, The Public Health and Welfare, as this section.

1990—Subsec. (a)(3). Pub. L. 101–629, §19(a)(1)(B), substituted ''this part'' for ''this subpart''.

Statutory Notes and Related Subsidiaries

NONINTERFERENCE WITH OTHER FEDERAL AGENCIES

Enactment of this section not to be construed to supersede or limit the functions under any other provision of law of any officer or agency of the United States, see section 4 of Pub. L. 90–602, set out as a note under section 360hh of this title.

§360kk. Performance standards for electronic products

(a) Promulgation of regulations

(1) The Secretary shall by regulation prescribe performance standards for electronic products to control the emission of electronic product radiation from such products if he determines that such standards are necessary for the protection of the public health and safety. Such standards may include provisions for the testing of such products and the measurement of their electronic product radiation emissions, may require the attachment of warning signs and labels, and may require the provision of instructions for the installation, operation, and use of such products. Such standards may be prescribed from time to time whenever such determinations are made, but the first of such standards shall be prescribed prior to January 1, 1970. In the development of such standards, the Secretary shall consult with Federal and State departments and agencies having related responsibilities or interests and with appropriate professional organizations and interested persons, including representatives of industries and labor organizations which would be affected by such standards, and shall give consideration to—

(A) the latest available scientific and medical data in the field of electronic product radiation;

(B) the standards currently recommended by (i) other Federal agencies having responsibilities relating to the control and measurement of electronic product radiation, and (ii) public or private groups having an expertise in the field of electronic product radiation;

(C) the reasonableness and technical feasibility of such standards as applied to a particular electronic product;

(D) the adaptability of such standards to the need for uniformity and reliability of testing and measuring procedures and equipment; and

(E) in the case of a component, or accessory described in paragraph (2)(B) of section 360hh of this title, the performance of such article in the manufactured or assembled product for which it is designed.

(2) The Secretary may prescribe different and individual performance standards, to the extent appropriate and feasible, for different electronic products so as to recognize their different operating characteristics and uses.

(3) The performance standards prescribed under this section shall not apply to any electronic product which is intended solely for export if (A) such product and the outside of any shipping container used in the export of such

product are labeled or tagged to show that such product is intended for export, and (B) such product meets all the applicable requirements of the country to which such product is intended for export.

(4) The Secretary may by regulation amend or revoke any performance standard prescribed under this section.

(5) The Secretary may exempt from the provisions of this section any electronic product intended for use by departments or agencies of the United States provided such department or agency has prescribed procurement specifications governing emissions of electronic product radiation and provided further that such product is of a type used solely or predominantly by departments or agencies of the United States.

(b) Administrative procedure

The provisions of subchapter II of chapter 5 of title 5 (relating to the administrative procedure for rulemaking), and of chapter 7 of title 5 (relating to judicial review), shall apply with respect to any regulation prescribing, amending, or revoking any standard prescribed under this section.

(c) Publication in Federal Register

Each regulation prescribing, amending, or revoking a standard shall specify the date on which it shall take effect which, in the case of any regulation prescribing, or amending any standard, may not be sooner than one year or not later than two years after the date on which such regulation is issued, unless the Secretary finds, for good cause shown, that an earlier or later effective date is in the public interest and publishes in the Federal Register his reason for such finding, in which case such earlier or later date shall apply.

(d) Judicial review

(1) In a case of actual controversy as to the validity of any regulation issued under this section prescribing, amending, or revoking a performance standard, any person who will be adversely affected by such regulation when it is effective may at any time prior to the sixtieth day after such regulation is issued file a petition with the United States court of appeals for the circuit wherein such person resides or has his principal place of business, for a judicial review of such regulation. A copy of the petition shall be forthwith transmitted by the clerk of the court to the Secretary or other officer designated by him for that purpose. The Secretary thereupon shall file in the court the record of the proceedings on which the Secretary based the regulation, as provided in section 2112 of title 28.

(2) If the petitioner applies to the court for leave to adduce additional evidence, and shows to the satisfaction of the court that such additional evidence is material and that there were reasonable grounds for the failure to adduce such evidence in the proceeding before the Secretary, the court may order such additional evidence (and evidence in rebuttal thereof) to be taken before the Secretary, and to be adduced upon the hearing, in such manner and upon such terms and conditions as to the court may seem proper. The Secretary may modify his findings, or make new findings, by reason of the additional evidence so taken, and he shall file such modified or new findings, and his recommendations, if any, for the modification or setting aside of his original regulation, with the return of such additional evidence.

(3) Upon the filing of the petition referred to in paragraph (1) of this subsection, the court shall have jurisdiction to review the regulation in accordance with chapter 7 of title 5 and to grant appropriate relief as provided in such chapter.

(4) The judgment of the court affirming or setting aside, in whole or in part, any such regulation of the Secretary shall be final, subject to review by the Supreme Court of the United States upon certiorari or certification as provided in section 1254 of title 28.

(5) Any action instituted under this subsection shall survive, notwithstanding any change in the person occupying the office of Secretary or any vacancy in such office.

(6) The remedies provided for in this subsection shall be in addition to and not in substitution for any other remedies provided by law.

(e) Availability of record

A certified copy of the transcript of the record and administrative proceedings under this section shall be furnished by the Secretary to any interested party at his request, and payment of the costs thereof, and shall be admissible in any criminal, exclusion of imports, or other proceeding arising under or in respect of this part irrespective of whether proceedings with respect to the regulation have previously been initiated or become final under this section.

(f) Technical Electronic Product Radiation Safety Standards Committee

(1)(A) The Secretary shall establish a Technical Electronic Product Radiation Safety Standards Committee (hereafter in this part referred to as the ''Committee'') which he shall consult before prescribing any standard under this section. The Committee shall be appointed by the Secretary, after consultation with public and private agencies concerned with the technical aspect of electronic product radiation safety, and shall be composed of fifteen members each of whom shall be technically qualified by training and experience in one or more fields of science or engineering applicable to electronic product radiation safety, as follows:

(i) Five members shall be selected from governmental agencies, including State and Federal Governments;

(ii) Five members shall be selected from the affected industries after consultation with industry representatives; and

(iii) Five members shall be selected from the general public, of which at least one shall be a representative of organized labor.

(B) The Committee may propose electronic product radiation safety standards to the Secretary for his consideration. All proceedings of the Committee shall be recorded and the record of each such proceeding shall be available for public inspection.

(2) Payments to members of the Committee who are not officers or employees of the United

States pursuant to subsection (c) of section 210 of title 42 shall not render members of the Committee officers or employees of the United States for any purpose.

(g) Review and evaluation

The Secretary shall review and evaluate on a continuing basis testing programs carried out by industry to assure the adequacy of safeguards against hazardous electronic product radiation and to assure that electronic products comply with standards prescribed under this section.

(h) Product certification

Every manufacturer of an electronic product to which is applicable a standard in effect under this section shall furnish to the distributor or dealer at the time of delivery of such product, in the form of a label or tag permanently affixed to such product or in such manner as approved by the Secretary, the certification that such product conforms to all applicable standards under this section. Such certification shall be based upon a test, in accordance with such standard, of the individual article to which it is attached or upon a testing program which is in accord with good manufacturing practice and which has not been disapproved by the Secretary (in such manner as he shall prescribe by regulation) on the grounds that it does not assure the adequacy of safeguards against hazardous electronic product radiation or that it does not assure that electronic products comply with the standards prescribed under this section.

(June 25, 1938, ch. 675, §534, formerly act July 1, 1944, ch. 373, title III, §534, formerly §358, as added Pub. L. 90–602, §2(3), Oct. 18, 1968, 82 Stat. 1177; amended Pub. L. 91–515, title VI, §601(b)(2), (3), Oct. 30, 1970, 84 Stat. 1311; renumbered §534 and amended Pub. L. 101–629, §19(a)(1)(B), (2)(B), (3), (4), Nov. 28, 1990, 104 Stat. 4529, 4530; Pub. L. 103–80, §§3(w), 4(a)(2), Aug. 13, 1993, 107 Stat. 778, 779.)

Editorial Notes

CODIFICATION

Section was classified to section 263f of Title 42, The Public Health and Welfare, prior to renumbering by Pub. L. 101–629.

AMENDMENTS

1993—Pub. L. 103–80, §4(a)(2), amended directory language of Pub. L. 101–629, §19(a)(4), which renumbered section 263f of Title 42, The Public Health and Welfare, as this section.

Subsec. (f)(2). Pub. L. 103–80, §3(w), made technical amendment to reference to section 210 of title 42 to reflect correction of corresponding provision of original act.

1990—Subsec. (a)(1)(E). Pub. L. 101–629, §19(a)(2)(B), substituted ''section 360hh'' for ''section 263c''.

Subsecs. (e), (f)(1)(A). Pub. L. 101–629, §19(a)(1)(B), substituted ''this part'' for ''this subpart''.

1970—Subsec. (f)(2). Pub. L. 91–515 struck out provisions related to payment of compensation and travel expenses of members of the Committee who are not officers or employees of the United States, and substituted ''to members of the Committee who are not officers or employees of the United States pursuant to subsection (c) of section 210 of title 42'' for ''under this subsection''.

Statutory Notes and Related Subsidiaries

NONINTERFERENCE WITH OTHER FEDERAL AGENCIES

Enactment of this section not to be construed to supersede or limit the functions under any other provision of law of any officer or agency of the United States, see section 4 of Pub. L. 90–602, set out as a note under section 360hh of this title.

§ 360*ll*. Notification of defects in and repair or replacement of electronic products

(a) Notification; exemption

(1) Every manufacturer of electronic products who discovers that an electronic product produced, assembled, or imported by him has a defect which relates to the safety of use of such product by reason of the emission of electronic product radiation, or that an electronic product produced, assembled, or imported by him on or after the effective date of an applicable standard prescribed pursuant to section 360kk of this title fails to comply with such standard, shall immediately notify the Secretary of such defect or failure to comply if such product has left the place of manufacture and shall (except as authorized by paragraph (2)) with reasonable promptness furnish notification of such defect or failure to the persons (where known to the manufacturer) specified in subsection (b) of this section.

(2) If, in the opinion of such manufacturer, the defect or failure to comply is not such as to create a significant risk of injury, including genetic injury, to any person, he may, at the time of giving notice to the Secretary of such defect or failure to comply, apply to the Secretary for an exemption from the requirement of notice to the persons specified in subsection (b). If such application states reasonable grounds for such exemption, the Secretary shall afford such manufacturer an opportunity to present his views and evidence in support of the application, the burden of proof being on the manufacturer. If, after such presentation, the Secretary is satisfied that such defect or failure to comply is not such as to create a significant risk of injury, including genetic injury, to any person, he shall exempt such manufacturer from the requirement of notice to the persons specified in subsection (b) of this section and from the requirements of repair or replacement imposed by subsection (f) of this section.

(b) Method of notification

The notification (other than to the Secretary) required by paragraph (1) of subsection (a) of this section shall be accomplished—

(1) by certified mail to the first purchaser of such product for purposes other than resale, and to any subsequent transferee of such product; and

(2) by certified mail or other more expeditious means to the dealers or distributors of such manufacturer to whom such product was delivered.

(c) Requisite elements of notification

The notifications required by paragraph (1) of subsection (a) of this section shall contain a clear description of such defect or failure to comply with an applicable standard, an evaluation of the hazard reasonably related to such de-

fect or failure to comply, and a statement of the measures to be taken to repair such defect. In the case of a notification to a person referred to in subsection (b) of this section, the notification shall also advise the person of his rights under subsection (f) of this section.

(d) Copies to Secretary of communications by manufacturers to dealers or distributors regarding defects

Every manufacturer of electronic products shall furnish to the Secretary a true or representative copy of all notices, bulletins, and other communications to the dealers or distributors of such manufacturer or to purchasers (or subsequent transferees) of electronic products of such manufacturer regarding any such defect in such product or any such failure to comply with a standard applicable to such product. The Secretary shall disclose to the public so much of the information contained in such notice or other information obtained under section 360nn of this title as he deems will assist in carrying out the purposes of this part, but he shall not disclose any information which contains or relates to a trade secret or other matter referred to in section 1905 of title 18 unless he determines that it is necessary to carry out the purposes of this part.

(e) Notice from Secretary to manufacturer of defects or failure to comply with standards

If through testing, inspection, investigation, or research carried out pursuant to this part, or examination of reports submitted pursuant to section 360nn of this title, or otherwise, the Secretary determines that any electronic product—

(1) does not comply with an applicable standard prescribed pursuant to section 360kk of this title; or

(2) contains a defect which relates to the safety of use of such product by reason of the emission of electronic product radiation;

he shall immediately notify the manufacturer of such product of such defect or failure to comply. The notice shall contain the findings of the Secretary and shall include all information upon which the findings are based. The Secretary shall afford such manufacturer an opportunity to present his views and evidence in support thereof, to establish that there is no failure of compliance or that the alleged defect does not exist or does not relate to safety of use of the product by reason of the emission of such radiation hazard. If after such presentation by the manufacturer the Secretary determines that such product does not comply with an applicable standard prescribed pursuant to section 360kk of this title, or that it contains a defect which relates to the safety of use of such product by reason of the emission of electronic product radiation, the Secretary shall direct the manufacturer to furnish the notification specified in subsection (c) of this section to the persons specified in paragraphs (1) and (2) of subsection (b) of this section (where known to the manufacturer), unless the manufacturer has applied for an exemption from the requirement of such notification on the ground specified in paragraph (2) of subsection (a) and the Secretary is satisfied that such noncompliance or defect is not such as to create a significant risk of injury, including genetic injury, to any person.

(f) Correction of defects

If any electronic product is found under subsection (a) or (e) to fail to comply with an applicable standard prescribed under this part or to have a defect which relates to the safety of use of such product, and the notification specified in subsection (c) is required to be furnished on account of such failure or defect, the manufacturer of such product shall (1) without charge, bring such product into conformity with such standard or remedy such defect and provide reimbursement for any expenses for transportation of such product incurred in connection with having such product brought into conformity or having such defect remedied, (2) replace such product with a like or equivalent product which complies with each applicable standard prescribed under this part and which has no defect relating to the safety of its use, or (3) make a refund of the cost of such product. The manufacturer shall take the action required by this subsection in such manner, and with respect to such persons, as the Secretary by regulations shall prescribe.

(g) Effective date

This section shall not apply to any electronic product that was manufactured before October 18, 1968.

(June 25, 1938, ch. 675, § 535, formerly act July 1, 1944, ch. 373, title III, § 535, formerly § 359, as added Pub. L. 90–602, § 2(3), Oct. 18, 1968, 82 Stat. 1180; renumbered § 535 and amended Pub. L. 101–629, § 19(a)(1)(B), (2)(C), (3), (4), Nov. 28, 1990, 104 Stat. 4529, 4530; Pub. L. 103–80, § 4(a)(2), Aug. 13, 1993, 107 Stat. 779.)

Editorial Notes

CODIFICATION

Section was classified to section 263g of Title 42, The Public Health and Welfare, prior to renumbering by Pub. L. 101–629.

AMENDMENTS

1993—Pub. L. 103–80 amended directory language of Pub. L. 101–629, § 19(a)(4), which renumbered section 263g of Title 42, The Public Health and Welfare, as this section.

1990—Subsec. (a)(1). Pub. L. 101–629, § 19(a)(2)(C)(i), substituted ''section 360kk'' for ''section 263f''.

Subsec. (d). Pub. L. 101–629, § 19(a)(1)(B), (2)(C)(ii), substituted ''section 360nn'' for ''section 263i'' and ''this part'' for ''this subpart'' in two places.

Subsec. (e). Pub. L. 101–629, § 19(a)(1)(B), (2)(C), substituted ''this part'' for ''this subpart'' and ''section 360nn'' for ''section 263i'' in introductory provisions and ''section 360kk'' for ''section 263f'' in par. (1) and concluding provisions.

Subsec. (f). Pub. L. 101–629, § 19(a)(1)(B), substituted ''this part'' for ''this subpart'' in two places.

Statutory Notes and Related Subsidiaries

NONINTERFERENCE WITH OTHER FEDERAL AGENCIES

Enactment of this section not to be construed to supersede or limit the functions under any other provision of law of any officer or agency of the United States, see section 4 of Pub. L. 90–602, set out as a note under section 360hh of this title.

§ 360mm. Imports

(a) Refusal of admission to noncomplying electronic products

Any electronic product offered for importation into the United States which fails to comply with an applicable standard prescribed under this part, or to which is not affixed a certification in the form of a label or tag in conformity with section 360kk(h) of this title shall be refused admission into the United States. The Secretary of the Treasury shall deliver to the Secretary of Health and Human Services, upon the latter's request, samples of electronic products which are being imported or offered for import into the United States, giving notice thereof to the owner or consignee, who may have a hearing before the Secretary of Health and Human Services. If it appears from an examination of such samples or otherwise that any electronic product fails to comply with applicable standards prescribed pursuant to section 360kk of this title, then, unless subsection (b) of this section applies and is complied with, (1) such electronic product shall be refused admission, and (2) the Secretary of the Treasury shall cause the destruction of such electronic product unless such article is exported, under regulations prescribed by the Secretary of the Treasury, within 90 days after the date of notice of refusal of admission or within such additional time as may be permitted by such regulations.

(b) Bond

If it appears to the Secretary of Health and Human Services that any electronic product refused admission pursuant to subsection (a) of this section can be brought into compliance with applicable standards prescribed pursuant to section 360kk of this title, final determination as to admission of such electronic product may be deferred upon filing of timely written application by the owner or consignee and the execution by him of a good and sufficient bond providing for the payment of such liquidated damages in the event of default as the Secretary of Health and Human Services may by regulation prescribe. If such application is filed and such bond is executed the Secretary of Health and Human Services may, in accordance with rules prescribed by him, permit the applicant to perform such operations with respect to such electronic product as may be specified in the notice of permission.

(c) Liability of owner or consignee for expenses connected with refusal of admission

All expenses (including travel, per diem or subsistence, and salaries of officers or employees of the United States) in connection with the destruction provided for in subsection (a) of this section and the supervision of operations provided for in subsection (b) of this section, and all expenses in connection with the storage, cartage, or labor with respect to any electronic product refused admission pursuant to subsection (a) of this section, shall be paid by the owner or consignee, and, in event of default, shall constitute a lien against any future importations made by such owner or consignee.

(d) Designation of agent for purposes of service

It shall be the duty of every manufacturer offering an electronic product for importation into the United States to designate in writing an agent upon whom service of all administrative and judicial processes, notices, orders, decisions, and requirements may be made for and on behalf of said manufacturer, and to file such designation with the Secretary, which designation may from time to time be changed by like writing, similarly filed. Service of all administrative and judicial processes, notices, orders, decisions, and requirements may be made upon said manufacturer by service upon such designated agent at his office or usual place of residence with like effect as if made personally upon said manufacturer, and in default of such designation of such agent, service of process, notice, order, requirement, or decision in any proceeding before the Secretary or in any judicial proceeding for enforcement of this part or any standards prescribed pursuant to this part may be made by posting such process, notice, order, requirement, or decision in the Office of the Secretary or in a place designated by him by regulation.

(June 25, 1938, ch. 675, § 536, formerly act July 1, 1944, ch. 373, title III, § 536, formerly § 360, as added Pub. L. 90–602, § 2(3), Oct. 18, 1968, 82 Stat. 1181; renumbered § 536 and amended Pub. L. 101–629, § 19(a)(1)(B), (2)(D), (3), (4), Nov. 28, 1990, 104 Stat. 4529, 4530; Pub. L. 102–300, § 6(b)(1), June 16, 1992, 106 Stat. 240; Pub. L. 103–80, § 4(a)(2), Aug. 13, 1993, 107 Stat. 779.)

Editorial Notes

CODIFICATION

Section was classified to section 263h of Title 42, The Public Health and Welfare, prior to renumbering by Pub. L. 101–629.

AMENDMENTS

1993—Pub. L. 103–80 amended directory language of Pub. L. 101–629, § 19(a)(4), which renumbered section 263h of Title 42, The Public Health and Welfare, as this section.

1992—Subsecs. (a), (b). Pub. L. 102–300 substituted ''Health and Human Services'' for ''Health, Education, and Welfare'' wherever appearing.

1990—Subsec. (a). Pub. L. 101–629, § 19(a)(1)(B), (2)(D), substituted ''this part'' for ''this subpart'', ''section 360kk(h)'' for ''section 263f(h)'', and ''section 360kk'' for ''section 263f''.

Subsec. (b). Pub. L. 101–629, § 19(a)(2)(D), substituted ''section 360kk'' for ''section 263f''.

Subsec. (d). Pub. L. 101–629, § 19(a)(1)(B), substituted ''this part'' for ''this subpart'' in two places.

Statutory Notes and Related Subsidiaries

NONINTERFERENCE WITH OTHER FEDERAL AGENCIES

Enactment of this section not to be construed to supersede or limit the functions under any other provision of law of any officer or agency of the United States, see section 4 of Pub. L. 90–602, set out as a note under section 360hh of this title.

§ 360nn. Inspection, records, and reports

(a) Inspection of premises

If the Secretary finds for good cause that the methods, tests, or programs related to electronic product radiation safety in a particular factory, warehouse, or establishment in which electronic products are manufactured or held, may not be adequate or reliable, officers or em-

ployees duly designated by the Secretary, upon presenting appropriate credentials and a written notice to the owner, operator, or agent in charge, are thereafter authorized (1) to enter, at reasonable times, any area in such factory, warehouse, or establishment in which the manufacturer's tests (or testing programs) required by section 360kk(h) of this title are carried out, and (2) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, the facilities and procedures within such area which are related to electronic product radiation safety. Each such inspection shall be commenced and completed with reasonable promptness. In addition to other grounds upon which good cause may be found for purposes of this subsection, good cause will be considered to exist in any case where the manufacturer has introduced into commerce any electronic product which does not comply with an applicable standard prescribed under this part and with respect to which no exemption from the notification requirements has been granted by the Secretary under section 360*ll*(a)(2) or 360*ll*(e) of this title.

(b) Record keeping

Every manufacturer of electronic products shall establish and maintain such records (including testing records), make such reports, and provide such information, as the Secretary may reasonably require to enable him to determine whether such manufacturer has acted or is acting in compliance with this part and standards prescribed pursuant to this part and shall, upon request of an officer or employee duly designated by the Secretary, permit such officer or employee to inspect appropriate books, papers, records, and documents relevant to determining whether such manufacturer has acted or is acting in compliance with standards prescribed pursuant to this part.

(c) Disclosure of technical data

Every manufacturer of electronic products shall provide to the Secretary such performance data and other technical data related to safety as may be required to carry out the purposes of this part. The Secretary is authorized to require the manufacturer to give such notification of such performance and technical data at the time of original purchase to the ultimate purchaser of the electronic product, as he determines necessary to carry out the purposes of this part after consulting with the affected industry.

(d) Public nature of reports

Accident and investigation reports made under this part by any officer, employee, or agent of the Secretary shall be available for use in any civil, criminal, or other judicial proceeding arising out of such accident. Any such officer, employee, or agent may be required to testify in such proceedings as to the facts developed in such investigations. Any such report shall be made available to the public in a manner which need not identify individuals. All reports on research projects, demonstration projects, and other related activities shall be public information.

(e) Trade secrets

The Secretary or his representative shall not disclose any information reported to or otherwise obtained by him, pursuant to subsection (a) or (b) of this section, which concerns any information which contains or relates to a trade secret or other matter referred to in section 1905 of title 18, except that such information may be disclosed to other officers or employees of the Department and of other agencies concerned with carrying out this part or when relevant in any proceeding under this part. Nothing in this section shall authorize the withholding of information by the Secretary, or by any officers or employees under his control, from the duly authorized committees of the Congress.

(f) Information required to identify and locate first purchasers of electronic products

The Secretary may by regulation (1) require dealers and distributors of electronic products, to which there are applicable standards prescribed under this part and the retail prices of which is not less than $50, to furnish manufacturers of such products such information as may be necessary to identify and locate, for purposes of section 360*ll* of this title, the first purchasers of such products for purposes other than resale, and (2) require manufacturers to preserve such information. Any regulation establishing a requirement pursuant to clause (1) of the preceding sentence shall (A) authorize such dealers and distributors to elect, in lieu of immediately furnishing such information to the manufacturer, to hold and preserve such information until advised by the manufacturer or Secretary that such information is needed by the manufacturer for purposes of section 360*ll* of this title, and (B) provide that the dealer or distributor shall, upon making such election, give prompt notice of such election (together with information identifying the notifier and the product) to the manufacturer and shall, when advised by the manufacturer or Secretary, of the need therefor for the purposes of section 360*ll* of this title, immediately furnish the manufacturer with the required information. If a dealer or distributor discontinues the dealing in or distribution of electronic products, he shall turn the information over to the manufacturer. Any manufacturer receiving information pursuant to this subsection concerning first purchasers of products for purposes other than resale shall treat it as confidential and may use it only if necessary for the purpose of notifying persons pursuant to section 360*ll*(a) of this title.

(June 25, 1938, ch. 675, § 537, formerly act July 1, 1944, ch. 373, title III, § 537, formerly § 360A, as added Pub. L. 90–602, § 2(3), Oct. 18, 1968, 82 Stat. 1182; renumbered § 537 and amended Pub. L. 101–629, § 19(a)(1)(B), (2)(E), (3), (4), Nov. 28, 1990, 104 Stat. 4529, 4530; Pub. L. 103–80, § 4(a)(2), Aug. 13, 1993, 107 Stat. 779.)

Editorial Notes

CODIFICATION

Section was classified to section 263i of Title 42, The Public Health and Welfare, prior to renumbering by Pub. L. 101–629.

AMENDMENTS

1993—Pub. L. 103–80 amended directory language of Pub. L. 101–629, § 19(a)(4), which renumbered section 263i

of Title 42, The Public Health and Welfare, as this section.

1990—Subsec. (a). Pub. L. 101–629, §19(a)(1)(B), (2)(E), substituted ''section 360kk(h)'' for ''section 263f(h)'', ''this part'' for ''this subpart'', and ''section 360*ll*(a)(2) or 360*ll*(e)'' for ''section 263g(a)(2) or 263g(e)''.

Subsecs. (b) to (e). Pub. L. 101–629, §19(a)(1)(B), substituted ''this part'' for ''this subpart'' wherever appearing.

Subsec. (f). Pub. L. 101–629, §19(a)(1)(B), (2)(E)(ii), substituted ''this part'' for ''this subpart'', ''section 360*ll*'' for ''section 263g'' in three places, and ''section 360*ll*(a)'' for ''section 263g(a)''.

Statutory Notes and Related Subsidiaries

NONINTERFERENCE WITH OTHER FEDERAL AGENCIES

Enactment of this section not to be construed to supersede or limit the functions under any other provision of law of any officer or agency of the United States, see section 4 of Pub. L. 90–602, set out as a note under section 360hh of this title.

§ 360*oo*. Prohibited acts

(a) It shall be unlawful—

(1) for any manufacturer to introduce, or to deliver for introduction, into commerce, or to import into the United States, any electronic product which does not comply with an applicable standard prescribed pursuant to section 360kk of this title;

(2) for any person to fail to furnish any notification or other material or information required by section 360*ll* or 360nn of this title; or to fail to comply with the requirements of section 360*ll*(f) of this title;

(3) for any person to fail or to refuse to establish or maintain records required by this part or to permit access by the Secretary or any of his duly authorized representatives to, or the copying of, such records, or to permit entry or inspection, as required by or pursuant to section 360nn of this title;

(4) for any person to fail or to refuse to make any report required pursuant to section 360nn(b) of this title or to furnish or preserve any information required pursuant to section 360nn(f) of this title; or

(5) for any person (A) to fail to issue a certification as required by section 360kk(h) of this title, or (B) to issue such a certification when such certification is not based upon a test or testing program meeting the requirements of section 360kk(h) of this title or when the issuer, in the exercise of due care, would have reason to know that such certification is false or misleading in a material respect.

(b) The Secretary may exempt any electronic product, or class thereof, from all or part of subsection (a), upon such conditions as he may find necessary to protect the public health or welfare, for the purpose of research, investigations, studies, demonstrations, or training, or for reasons of national security.

(June 25, 1938, ch. 675, §538, formerly act July 1, 1944, ch. 373, title III, §538, formerly §360B, as added Pub. L. 90–602, §2(3), Oct. 18, 1968, 82 Stat. 1184; renumbered §538 and amended Pub. L. 101–629, §19(a)(1)(B), (2)(F), (3), (4), Nov. 28, 1990, 104 Stat. 4529, 4530; Pub. L. 103–80, §4(a)(2), Aug. 13, 1993, 107 Stat. 779.)

Editorial Notes

CODIFICATION

Section was classified to section 263j of Title 42, The Public Health and Welfare, prior to renumbering by Pub. L. 101–629.

AMENDMENTS

1993—Pub. L. 103–80 amended directory language of Pub. L. 101–629, §19(a)(4), which renumbered section 263j of Title 42, The Public Health and Welfare, as this section.

1990—Subsec. (a)(1). Pub. L. 101–629, §19(a)(2)(F)(i), substituted ''section 360kk'' for ''section 263f''.

Subsec. (a)(2). Pub. L. 101–629, §19(a)(2)(F)(ii), (iii), substituted ''section 360*ll* or 360nn'' for ''section 263g or 263i'' and ''section 360*ll*(f)'' for ''section 263g(f)''.

Subsec. (a)(3). Pub. L. 101–629, §19(a)(1)(B), (2)(F)(iii), substituted ''this part'' for ''this subpart'' and ''section 360nn'' for ''section 263i''.

Subsec. (a)(4). Pub. L. 101–629, §19(a)(2)(F)(iii), substituted ''section 360nn(b)'' for ''section 263i(b)'' and ''section 360nn(f)'' for ''section 263i(f)''.

Subsec. (a)(5). Pub. L. 101–629, §19(a)(2)(F)(i), substituted ''section 360kk(h)'' for ''section 263f(h)'' in two places.

Statutory Notes and Related Subsidiaries

NONINTERFERENCE WITH OTHER FEDERAL AGENCIES

Enactment of this section not to be construed to supersede or limit the functions under any other provision of law of any officer or agency of the United States, see section 4 of Pub. L. 90–602, set out as a note under section 360hh of this title.

§ 360pp. Enforcement

(a) Jurisdiction of courts

The district courts of the United States shall have jurisdiction, for cause shown, to restrain violations of section 360*oo* of this title and to restrain dealers and distributors of electronic products from selling or otherwise disposing of electronic products which do not conform to an applicable standard prescribed pursuant to section 360kk of this title except when such products are disposed of by returning them to the distributor or manufacturer from whom they were obtained. The district courts of the United States shall also have jurisdiction in accordance with section 1355 of title 28 to enforce the provisions of subsection (b) of this section.

(b) Penalties

(1) Any person who violates section 360*oo* of this title shall be subject to a civil penalty of not more than $1,000. For purposes of this subsection, any such violation shall with respect to each electronic product involved, or with respect to each act or omission made unlawful by section 360*oo* of this title, constitute a separate violation, except that the maximum civil penalty imposed on any person under this subsection for any related series of violations shall not exceed $300,000.

(2) Any such civil penalty may on application be remitted or mitigated by the Secretary. In determining the amount of such penalty, or whether it should be remitted or mitigated and in what amount, the appropriateness of such penalty to the size of the business of the person charged and the gravity of the violation shall be considered. The amount of such penalty, when finally determined, may be deducted from any

sums owing by the United States to the person charged.

(c) Venue; process

Actions under subsections (a) and (b) of this section may be brought in the district court of the United States for the district wherein any act or omission or transaction constituting the violation occurred, or in such court for the district where the defendant is found or transacts business, and process in such cases may be served in any other district of which the defendant is an inhabitant or wherever the defendant may be found.

(d) Warnings

Nothing in this part shall be construed as requiring the Secretary to report for the institution of proceedings minor violations of this part whenever he believes that the public interest will be adequately served by a suitable written notice or warning.

(e) Compliance with regulations

Except as provided in the first sentence of section 360ss of this title, compliance with this part or any regulations issued thereunder shall not relieve any person from liability at common law or under statutory law.

(f) Additional remedies

The remedies provided for in this part shall be in addition to and not in substitution for any other remedies provided by law.

(June 25, 1938, ch. 675, § 539, formerly act July 1, 1944, ch. 373, title III, § 539, formerly § 360C, as added Pub. L. 90–602, § 2(3), Oct. 18, 1968, 82 Stat. 1184; renumbered § 539 and amended Pub. L. 101–629, § 19(a)(1)(B), (2)(G), (3), (4), Nov. 28, 1990, 104 Stat. 4529, 4530; Pub. L. 103–80, § 4(a)(2), Aug. 13, 1993, 107 Stat. 779.)

Editorial Notes

CODIFICATION

Section was classified to section 263k of Title 42, The Public Health and Welfare, prior to renumbering by Pub. L. 101–629.

AMENDMENTS

1993—Pub. L. 103–80 amended directory language of Pub. L. 101–629, § 19(a)(4), which renumbered section 263k of Title 42, The Public Health and Welfare, as this section.

1990—Subsec. (a). Pub. L. 101–629, § 19(a)(2)(G)(i), (ii), substituted ''section 360*oo*'' for ''section 263j'' and ''section 360kk'' for ''section 263f''.

Subsec. (b)(1). Pub. L. 101–629, § 19(a)(2)(G)(ii), substituted ''section 360*oo*'' for ''section 263j'' in two places.

Subsec. (d). Pub. L. 101–629, § 19(a)(1)(B), substituted ''this part'' for ''this subpart'' in two places.

Subsec. (e). Pub. L. 101–629, § 19(a)(1)(B), (2)(G)(iii), substituted ''section 360ss'' for ''section 263n'' and ''this part'' for ''this subpart''.

Subsec. (f). Pub. L. 101–629, § 19(a)(1)(B), substituted ''this part'' for ''this subpart''.

Statutory Notes and Related Subsidiaries

NONINTERFERENCE WITH OTHER FEDERAL AGENCIES

Enactment of this section not to be construed to supersede or limit the functions under any other provision of law of any officer or agency of the United States, see section 4 of Pub. L. 90–602, set out as a note under section 360hh of this title.

§ 360qq. Repealed. Pub. L. 105–362, title VI, § 601(a)(2)(A), Nov. 10, 1998, 112 Stat. 3285

Section, act June 25, 1938, ch. 675, § 540, formerly act July 1, 1944, ch. 373, title III, § 540, formerly § 360D, as added Pub. L. 90–602, § 2(3), Oct. 18, 1968, 82 Stat. 1185; renumbered § 540 and amended Pub. L. 101–629, § 19(a)(1)(B), (3), (4), Nov. 28, 1990, 104 Stat. 4529, 4530; Pub. L. 103–80, § 4(a)(2), Aug. 13, 1993, 107 Stat. 779, related to annual report on administration of electronic product radiation control program.

§ 360rr. Federal-State cooperation

The Secretary is authorized (1) to accept from State and local authorities engaged in activities related to health or safety or consumer protection, on a reimbursable basis or otherwise, any assistance in the administration and enforcement of this part which he may request and which they may be able and willing to provide and, if so agreed, may pay in advance or otherwise for the reasonable cost of such assistance, and (2) he may, for the purpose of conducting examinations, investigations, and inspections, commission any officer or employee of any such authority as an officer of the Department.

(June 25, 1938, ch. 675, § 541, formerly act July 1, 1944, ch. 373, title III, § 541, formerly § 360E, as added Pub. L. 90–602, § 2(3), Oct. 18, 1968, 82 Stat. 1186; renumbered § 541 and amended Pub. L. 101–629, § 19(a)(1)(B), (3), (4), Nov. 28, 1990, 104 Stat. 4529, 4530; Pub. L. 103–80, § 4(a)(2), Aug. 13, 1993, 107 Stat. 779.)

Editorial Notes

CODIFICATION

Section was classified to section 263m of Title 42, The Public Health and Welfare, prior to renumbering by Pub. L. 101–629.

AMENDMENTS

1993—Pub. L. 103–80 amended directory language of Pub. L. 101–629, § 19(a)(4), which renumbered section 263m of Title 42, The Public Health and Welfare, as this section.

1990—Pub. L. 101–629, § 19(a)(1)(B), substituted ''this part'' for ''this subpart''.

Statutory Notes and Related Subsidiaries

NONINTERFERENCE WITH OTHER FEDERAL AGENCIES

Enactment of this section not to be construed to supersede or limit the functions under any other provision of law of any officer or agency of the United States, see section 4 of Pub. L. 90–602, set out as a note under section 360hh of this title.

§ 360ss. State standards

Whenever any standard prescribed pursuant to section 360kk of this title with respect to an aspect of performance of an electronic product is in effect, no State or political subdivision of a State shall have any authority either to establish, or to continue in effect, any standard which is applicable to the same aspect of performance of such product and which is not identical to the Federal standard. Nothing in this part shall be construed to prevent the Federal Government or the government of any State or political sub-

division thereof from establishing a requirement with respect to emission of radiation from electronic products procured for its own use if such requirement imposes a more restrictive standard than that required to comply with the otherwise applicable Federal standard.

(June 25, 1938, ch. 675, §542, formerly act July 1, 1944, ch. 373, title III, §542, formerly §360F, as added Pub. L. 90–602, §2(3), Oct. 18, 1968, 82 Stat. 1186; renumbered §542 and amended Pub. L. 101–629, §19(a)(1)(B), (2)(H), (3), (4), Nov. 28, 1990, 104 Stat. 4529, 4530; Pub. L. 103–80, §4(a)(2), Aug. 13, 1993, 107 Stat. 779.)

Editorial Notes

CODIFICATION

Section was classified to section 263n of Title 42, The Public Health and Welfare, prior to renumbering by Pub. L. 101–629.

AMENDMENTS

1993—Pub. L. 103–80 amended directory language of Pub. L. 101–629, §19(a)(4), which renumbered section 263n of Title 42, The Public Health and Welfare, as this section.

1990—Pub. L. 101–629, §19(a)(1)(B), (2)(H), substituted ''section 360kk'' for ''section 263f'' and ''this part'' for ''this subpart''.

Statutory Notes and Related Subsidiaries

NONINTERFERENCE WITH OTHER FEDERAL AGENCIES

Enactment of this section not to be construed to supersede or limit the functions under any other provision of law of any officer or agency of the United States, see section 4 of Pub. L. 90–602, set out as a note under section 360hh of this title.

PART D—DISSEMINATION OF TREATMENT INFORMATION

§§ 360aaa to 360aaa–6. Omitted

Editorial Notes

CODIFICATION

Sections 360aaa to 360aaa–6 ceased to be effective pursuant to section 401(e) of Pub. L. 105–115, set out as an Effective and Termination Dates note below.

Section 360aaa, act June 25, 1938, ch. 675, §551, as added Pub. L. 105–115, title IV, §401(a), Nov. 21, 1997, 111 Stat. 2356, related to requirements for dissemination of treatment information on drugs or devices.

Section 360aaa–1, act June 25, 1938, ch. 675, §552, as added Pub. L. 105–115, title IV, §401(a), Nov. 21, 1997, 111 Stat. 2358, related to information authorized to be disseminated under section 360aaa.

Section 360aaa–2, act June 25, 1938, ch. 675, §553, as added Pub. L. 105–115, title IV, §401(a), Nov. 21, 1997, 111 Stat. 2359, related to establishment of list of articles and publications disseminated and list of providers that received articles and reference publications.

Section 360aaa–3, act June 25, 1938, ch. 675, §554, as added Pub. L. 105–115, title IV, §401(a), Nov. 21, 1997, 111 Stat. 2359, related to requirement regarding submission of supplemental application for new use and an exemption from that requirement.

Section 360aaa–4, act June 25, 1938, ch. 675, §555, as added Pub. L. 105–115, title IV, §401(a), Nov. 21, 1997, 111 Stat. 2361, related to corrective actions and cessation of dissemination.

Section 360aaa–5, act June 25, 1938, ch. 675, §556, as added Pub. L. 105–115, title IV, §401(a), Nov. 21, 1997, 111 Stat. 2362, related to definitions.

Section 360aaa–6, act June 25, 1938, ch. 675, §557, as added Pub. L. 105–115, title IV, §401(a), Nov. 21, 1997, 111 Stat. 2363, related to rules of construction.

Statutory Notes and Related Subsidiaries

EFFECTIVE AND TERMINATION DATES

Pub. L. 105–115, title IV, §401(d), Nov. 21, 1997, 111 Stat. 2364, provided that: ''The amendments made by this section [enacting this part and amending section 331 of this title] shall take effect 1 year after the date of enactment of this Act [Nov. 21, 1997], or upon the Secretary's issuance of final regulations pursuant to subsection (c) [section 401(c) of Pub. L. 105–115 set out below] [Such regulations were issued effective Nov. 20, 1998. See 63 F.R. 64556.], whichever is sooner.''

Pub. L. 105–115, title IV, §401(e), Nov. 21, 1997, 111 Stat. 2364, provided that: ''The amendments made by this section [enacting this part and amending section 331 of this title] cease to be effective September 30, 2006, or 7 years after the date on which the Secretary promulgates the regulations described in subsection (c) [section 401(c) of Pub. L. 105–115 set out below] [Such regulations were issued effective Nov. 20, 1998. See 63 F.R. 64556.], whichever is later.''

REGULATIONS

Pub. L. 105–115, title IV, §401(c), Nov. 21, 1997, 111 Stat. 2364, provided that: ''Not later than 1 year after the date of enactment of this Act [Nov. 21, 1997], the Secretary of Health and Human Services shall promulgate regulations to implement the amendments made by this section [enacting this part and amending section 331 of this title].''

PART E—GENERAL PROVISIONS RELATING TO DRUGS AND DEVICES

§360bbb. Expanded access to unapproved therapies and diagnostics

(a) Emergency situations

The Secretary may, under appropriate conditions determined by the Secretary, authorize the shipment of investigational drugs or investigational devices for the diagnosis, monitoring, or treatment of a serious disease or condition in emergency situations.

(b) Individual patient access to investigational products intended for serious diseases

Any person, acting through a physician licensed in accordance with State law, may request from a manufacturer or distributor, and any manufacturer or distributor may, after complying with the provisions of this subsection, provide to such physician an investigational drug or investigational device for the diagnosis, monitoring, or treatment of a serious disease or condition if—

(1) the licensed physician determines that the person has no comparable or satisfactory alternative therapy available to diagnose, monitor, or treat the disease or condition involved, and that the probable risk to the person from the investigational drug or investigational device is not greater than the probable risk from the disease or condition;

(2) the Secretary determines that there is sufficient evidence of safety and effectiveness to support the use of the investigational drug or investigational device in the case described in paragraph (1);

(3) the Secretary determines that provision of the investigational drug or investigational device will not interfere with the initiation, conduct, or completion of clinical investigations to support marketing approval; and

(4) the sponsor, or clinical investigator, of the investigational drug or investigational de-

vice submits to the Secretary a clinical protocol consistent with the provisions of section 355(i) or 360j(g) of this title, including any regulations promulgated under section 355(i) or 360j(g) of this title, describing the use of the investigational drug or investigational device in a single patient or a small group of patients.

(c) Treatment investigational new drug applications and treatment investigational device exemptions

Upon submission by a sponsor or a physician of a protocol intended to provide widespread access to an investigational drug or investigational device for eligible patients (referred to in this subsection as an ''expanded access protocol''), the Secretary shall permit such investigational drug or investigational device to be made available for expanded access under a treatment investigational new drug application or treatment investigational device exemption if the Secretary determines that—

(1) under the treatment investigational new drug application or treatment investigational device exemption, the investigational drug or investigational device is intended for use in the diagnosis, monitoring, or treatment of a serious or immediately life-threatening disease or condition;

(2) there is no comparable or satisfactory alternative therapy available to diagnose, monitor, or treat that stage of disease or condition in the population of patients to which the investigational drug or investigational device is intended to be administered;

(3)(A) the investigational drug or investigational device is under investigation in a controlled clinical trial for the use described in paragraph (1) under an investigational drug application in effect under section 355(i) of this title or investigational device exemption in effect under section 360j(g) of this title; or

(B) all clinical trials necessary for approval of that use of the investigational drug or investigational device have been completed;

(4) the sponsor of the controlled clinical trials is actively pursuing marketing approval of the investigational drug or investigational device for the use described in paragraph (1) with due diligence;

(5) in the case of an investigational drug or investigational device described in paragraph (3)(A), the provision of the investigational drug or investigational device will not interfere with the enrollment of patients in ongoing clinical investigations under section 355(i) or 360j(g) of this title;

(6) in the case of serious diseases, there is sufficient evidence of safety and effectiveness to support the use described in paragraph (1); and

(7) in the case of immediately life-threatening diseases, the available scientific evidence, taken as a whole, provides a reasonable basis to conclude that the investigational drug or investigational device may be effective for its intended use and would not expose patients to an unreasonable and significant risk of illness or injury.

A protocol submitted under this subsection shall be subject to the provisions of section 355(i) or 360j(g) of this title, including regulations promulgated under section 355(i) or 360j(g) of this title. The Secretary may inform national, State, and local medical associations and societies, voluntary health associations, and other appropriate persons about the availability of an investigational drug or investigational device under expanded access protocols submitted under this subsection. The information provided by the Secretary, in accordance with the preceding sentence, shall be the same type of information that is required by section 282(i)(3) of title 42.

(d) Termination

The Secretary may, at any time, with respect to a sponsor, physician, manufacturer, or distributor described in this section, terminate expanded access provided under this section for an investigational drug or investigational device if the requirements under this section are no longer met.

(e) Definitions

In this section, the terms ''investigational drug'', ''investigational device'', ''treatment investigational new drug application'', and ''treatment investigational device exemption'' shall have the meanings given the terms in regulations prescribed by the Secretary.

(June 25, 1938, ch. 675, § 561, as added Pub. L. 105–115, title IV, § 402, Nov. 21, 1997, 111 Stat. 2365; amended Pub. L. 109–482, title I, § 102(f)(2), Jan. 15, 2007, 120 Stat. 3685.)

Editorial Notes

AMENDMENTS

2007—Subsec. (c). Pub. L. 109–482 substituted ''section 282(i)(3)'' for ''section 282(j)(3)'' in concluding provisions.

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 2007 AMENDMENT

Amendment by Pub. L. 109–482 applicable only with respect to amounts appropriated for fiscal year 2007 or subsequent fiscal years, see section 109 of Pub. L. 109–482, set out as a note under section 281 of Title 42, The Public Health and Welfare.

EFFECTIVE DATE

Section effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as an Effective Date of 1997 Amendment note under section 321 of this title.

INVESTIGATIONAL DRUGS

Pub. L. 115–52, title VI, § 610(a), (b), Aug. 18, 2017, 131 Stat. 1051, 1053, provided that:

''(a) PATIENT ACCESS TO INVESTIGATIONAL DRUGS.—

''(1) PUBLIC MEETING.—

''(A) IN GENERAL.—The Secretary of Health and Human Services (referred to in this section as the 'Secretary'), acting through the Commissioner of Food and Drugs, in coordination with the Director of the National Institutes of Health, and in consultation with patients, health care providers, drug sponsors, bioethicists, and other stakeholders, shall, not later than 270 days after the date of enactment of this Act [Aug. 18, 2007], convene a public meeting to discuss clinical trial inclusion and exclusion criteria to inform the guidance under paragraph (3). The Secretary shall inform the Comptroller General of the United States of the date when the public meeting will take place.

''(B) TOPICS.—The Secretary shall make available on the internet website of the Food and Drug Administration a report on the topics discussed at the meeting described in subparagraph (A) within 90 days of such meeting. Such topics shall include discussion of—

''(i) the rationale for, and potential barriers for patients created by, research clinical trial inclusion and exclusion criteria;

''(ii) how appropriate patient populations can benefit from the results of trials that employ alternative designs;

''(iii) barriers to participation in clinical trials, including—

''(I) information regarding any potential risks and benefits of participation;

''(II) regulatory, geographical, and socioeconomic barriers; and

''(III) the impact of exclusion criteria on the enrollment in clinical trials of particular populations, including infants and children, pregnant and lactating women, seniors, individuals with advanced disease, and individuals with comorbid conditions;

''(iv) clinical trial designs and methods, including expanded access trials, that increase enrollment of more diverse patient populations, when appropriate, while facilitating the collection of data to establish safe use and support substantial evidence of effectiveness, including data obtained from expanded access trials; and

''(v) how changes to clinical trial inclusion and exclusion criteria may impact the complexity and length of clinical trials, the data necessary to demonstrate safety and effectiveness, and potential approaches to mitigating those impacts.

''(2) REPORT.—Not later than 1 year after the Secretary issues the report under paragraph (1)(B), the Comptroller General of the United States shall report to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives on individual access to investigational drugs through the expanded access program under section 561(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb(b)). The report shall include—

''(A) a description of actions taken by manufacturers and distributors under section 561A of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb–0);

''(B) consideration of whether Form FDA 3926 and the guidance documents titled 'Expanded Access to Investigational Drugs for Treatment Use—Questions and Answers' and 'Individual Patient Expanded Access Applications: Form FDA 3926', issued by the Food and Drug Administration in June 2016, have reduced application burden with respect to individuals and physicians seeking access to investigational new drugs pursuant to section 561(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb) and improved clarity for patients, physicians, and drug manufacturers about such process;

''(C) consideration of whether the guidance or regulations issued to implement section 561 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb) have improved access for individual patients to investigational drugs who do not qualify for clinical trials of such investigational drugs, and what barriers to such access remain;

''(D) an assessment of methods patients and health care providers use to engage with the Food and Drug Administration or drug sponsors on expanded access; and

''(E) an analysis of the Secretary's report under paragraph (1)(B).

''(3) GUIDANCE.—

''(A) IN GENERAL.—Not later than 1 year after the publication of the report under paragraph (1)(B), the Secretary, acting through the Commissioner of Food and Drugs, shall issue one or more draft guidances regarding eligibility criteria for clinical trials. Not later than 1 year after the public comment period on each such draft guidance ends, the Secretary shall issue a revised draft guidance or final guidance.

''(B) CONTENTS.—The guidance documents described in subparagraph (A) shall address methodological approaches that a manufacturer or sponsor of an investigation of a new drug may take to—

''(i) broaden eligibility criteria for clinical trials and expanded access trials, especially with respect to drugs for the treatment of serious and life-threatening conditions or diseases for which there is an unmet medical need;

''(ii) develop eligibility criteria for, and increase trial recruitment to, clinical trials so that enrollment in such trials more accurately reflects the patients most likely to receive the drug, as applicable and as appropriate, while establishing safe use and supporting findings of substantial evidence of effectiveness; and

''(iii) use the criteria described in clauses (i) and (ii) in a manner that is appropriate for drugs intended for the treatment of rare diseases or conditions.

''(b) IMPROVING INSTITUTIONAL REVIEW BOARD REVIEW OF SINGLE PATIENT EXPANDED ACCESS PROTOCOL.—Not later than 1 year after the date of enactment of this Act [Aug. 18, 2017], the Secretary, acting through the Commissioner of Food and Drugs, shall issue guidance or regulations, or revise existing guidance or regulations, to streamline the institutional review board review of individual patient expanded access protocols submitted under [section] 561(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb(b)). To facilitate the use of expanded access protocols, any guidance or regulations so issued or revised may include a description of the process for any person acting through a physician licensed in accordance with State law to request that an institutional review board chair (or designated member of the institutional review board) review a single patient expanded access protocol submitted under such section 561(b) for a drug. The Secretary shall update any relevant forms associated with individual patient expanded access requests under such section 561(b) as necessary.''

§ 360bbb–0. Expanded access policy required for investigational drugs

(a) In general

The manufacturer or distributor of one or more investigational drugs for the diagnosis, monitoring, or treatment of one or more serious diseases or conditions shall make available the policy of the manufacturer or distributor on evaluating and responding to requests submitted under section 360bbb(b) of this title for provision of such a drug.

(b) Public availability of expanded access policy

The policies under subsection (a) shall be made public and readily available, such as by posting such policies on a publicly available Internet website. Such policies may be generally applicable to all investigational drugs of such manufacturer or distributor.

(c) Content of policy

A policy described in subsection (a) shall include—

(1) contact information for the manufacturer or distributor to facilitate communication about requests described in subsection (a);

(2) procedures for making such requests;

(3) the general criteria the manufacturer or distributor will use to evaluate such requests

for individual patients, and for responses to such requests;

(4) the length of time the manufacturer or distributor anticipates will be necessary to acknowledge receipt of such requests; and

(5) a hyperlink or other reference to the clinical trial record containing information about the expanded access for such drug that is required under section 282(j)(2)(A)(ii)(II)(gg) of title 42.

(d) No guarantee of access

The posting of policies by manufacturers and distributors under subsection (a) shall not serve as a guarantee of access to any specific investigational drug by any individual patient.

(e) Revised policy

Nothing in this section shall prevent a manufacturer or distributor from revising a policy required under this section at any time.

(f) Application

This section shall apply to a manufacturer or distributor with respect to an investigational drug beginning on the earlier of—

(1) the first initiation of a phase 2 or phase 3 study (as such terms are defined in section 312.21(b) and (c) of title 21, Code of Federal Regulations (or any successor regulations)) with respect to such investigational drug; or

(2) as applicable, 15 days after the drug receives a designation as a breakthrough therapy, fast track product, or regenerative advanced therapy under subsection (a), (b), or (g), respectively, of section 356 of this title.

(June 25, 1938, ch. 675, § 561A, as added Pub. L. 114–255, div. A, title III, § 3032, Dec. 13, 2016, 130 Stat. 1100; amended Pub. L. 115–52, title VI, § 610(c), Aug. 18, 2017, 131 Stat. 1053.)

Editorial Notes

AMENDMENTS

2017—Subsec. (f). Pub. L. 115–52 substituted ''earlier'' for ''later'' in introductory provisions, added par. (2), redesignated former par. (2) as (1), and struck out former par. (1) which read as follows: ''the date that is 60 calendar days after December 13, 2016; or''.

§ 360bbb–0a. Investigational drugs for use by eligible patients

(a) Definitions

For purposes of this section—

(1) the term ''eligible patient'' means a patient—

(A) who has been diagnosed with a life-threatening disease or condition (as defined in section 312.81 of title 21, Code of Federal Regulations (or any successor regulations));

(B) who has exhausted approved treatment options and is unable to participate in a clinical trial involving the eligible investigational drug, as certified by a physician, who—

(i) is in good standing with the physician's licensing organization or board; and

(ii) will not be compensated directly by the manufacturer for so certifying; and

(C) who has provided to the treating physician written informed consent regarding the eligible investigational drug, or, as applicable, on whose behalf a legally authorized representative of the patient has provided such consent;

(2) the term ''eligible investigational drug'' means an investigational drug (as such term is used in section 360bbb of this title)—

(A) for which a Phase 1 clinical trial has been completed;

(B) that has not been approved or licensed for any use under section 355 of this title or section 351 of the Public Health Service Act [42 U.S.C. 262];

(C)(i) for which an application has been filed under section 355(b) of this title or section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)]; or

(ii) that is under investigation in a clinical trial that—

(I) is intended to form the primary basis of a claim of effectiveness in support of approval or licensure under section 355 of this title or section 351 of the Public Health Service Act [42 U.S.C. 262]; and

(II) is the subject of an active investigational new drug application under section 355(i) of this title or section 351(a)(3) of the Public Health Service Act [42 U.S.C. 262(a)(3)], as applicable; and

(D) the active development or production of which is ongoing and has not been discontinued by the manufacturer or placed on clinical hold under section 355(i) of this title; and

(3) the term ''phase 1 trial'' means a phase 1 clinical investigation of a drug as described in section 312.21 of title 21, Code of Federal Regulations (or any successor regulations).

(b) Exemptions

Eligible investigational drugs provided to eligible patients in compliance with this section are exempt from sections 352(f), 353(b)(4), 355(a), and 355(i) of this title, section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)], and parts 50, 56, and 312 of title 21, Code of Federal Regulations (or any successor regulations), provided that the sponsor of such eligible investigational drug or any person who manufactures, distributes, prescribes, dispenses, introduces or delivers for introduction into interstate commerce, or provides to an eligible patient an eligible investigational drug pursuant to this section is in compliance with the applicable requirements set forth in sections 312.6, 312.7, and 312.8(d)(1) of title 21, Code of Federal Regulations (or any successor regulations) that apply to investigational drugs.

(c) Use of clinical outcomes

(1) In general

Notwithstanding any other provision of this chapter, the Public Health Service Act [42 U.S.C. 201 et seq.], or any other provision of Federal law, the Secretary may not use a clinical outcome associated with the use of an eligible investigational drug pursuant to this section to delay or adversely affect the review or approval of such drug under section 355 of this title or section 351 of the Public Health Service Act [42 U.S.C. 262] unless—

(A) the Secretary makes a determination, in accordance with paragraph (2), that use of such clinical outcome is critical to determining the safety of the eligible investigational drug; or

(B) the sponsor requests use of such outcomes.

(2) Limitation

If the Secretary makes a determination under paragraph (1)(A), the Secretary shall provide written notice of such determination to the sponsor, including a public health justification for such determination, and such notice shall be made part of the administrative record. Such determination shall not be delegated below the director of the agency center that is charged with the premarket review of the eligible investigational drug.

(d) Reporting

(1) In general

The manufacturer or sponsor of an eligible investigational drug shall submit to the Secretary an annual summary of any use of such drug under this section. The summary shall include the number of doses supplied, the number of patients treated, the uses for which the drug was made available, and any known serious adverse events. The Secretary shall specify by regulation the deadline of submission of such annual summary and may amend section 312.33 of title 21, Code of Federal Regulations (or any successor regulations) to require the submission of such annual summary in conjunction with the annual report for an applicable investigational new drug application for such drug.

(2) Posting of information

The Secretary shall post an annual summary report of the use of this section on the internet website of the Food and Drug Administration, including the number of drugs for which clinical outcomes associated with the use of an eligible investigational drug pursuant to this section was—

(A) used in accordance with subsection (c)(1)(A);

(B) used in accordance with subsection (c)(1)(B); and

(C) not used in the review of an application under section 355 of this title or section 351 of the Public Health Service Act [42 U.S.C. 262].

(June 25, 1938, ch. 675, §561B, as added Pub. L. 115–176, §2(a), May 30, 2018, 132 Stat. 1372.)

Editorial Notes

REFERENCES IN TEXT

The Public Health Service Act, referred to in subsec. (c)(1), is act July 1, 1944, ch. 373, 58 Stat. 682, which is classified generally to chapter 6A (§201 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 201 of Title 42 and Tables.

Statutory Notes and Related Subsidiaries

LIMITATION OF LIABILITY

Pub. L. 115–176, §2(b), May 30, 2018, 132 Stat. 1374, provided that:

''(1) ALLEGED ACTS OR OMISSIONS.—With respect to any alleged act or omission with respect to an eligible investigational drug provided to an eligible patient pursuant to section 561B of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360bbb–0a] and in compliance with such section, no liability in a cause of action shall lie against—

''(A) a sponsor or manufacturer; or

''(B) a prescriber, dispenser, or other individual entity (other than a sponsor or manufacturer), unless the relevant conduct constitutes reckless or willful misconduct, gross negligence, or an intentional tort under any applicable State law.

''(2) DETERMINATION NOT TO PROVIDE DRUG.—No liability shall lie against a sponsor manufacturer, prescriber, dispenser or other individual entity for its determination not to provide access to an eligible investigational drug under section 561B of the Federal Food, Drug, and Cosmetic Act.

''(3) LIMITATION.—Except as set forth in paragraphs (1) and (2), nothing in this section shall be construed to modify or otherwise affect the right of any person to bring a private action under any State or Federal product liability, tort, consumer protection, or warranty law.''

§ 360bbb–1. Dispute resolution

If, regarding an obligation concerning drugs or devices under this Act or section 351 of the Public Health Service Act [42 U.S.C. 262], there is a scientific controversy between the Secretary and a person who is a sponsor, applicant, or manufacturer and no specific provision of the Act involved, including a regulation promulgated under such Act, provides a right of review of the matter in controversy, the Secretary shall, by regulation, establish a procedure under which such sponsor, applicant, or manufacturer may request a review of such controversy, including a review by an appropriate scientific advisory panel described in section 355(n) of this title or an advisory committee described in section 360e(g)(2)(B) of this title. Any such review shall take place in a timely manner. The Secretary shall promulgate such regulations within 1 year after November 21, 1997.

(June 25, 1938, ch. 675, §562, as added Pub. L. 105–115, title IV, §404, Nov. 21, 1997, 111 Stat. 2368.)

Editorial Notes

REFERENCES IN TEXT

This Act, referred to in text, is the Federal Food, Drug, and Cosmetic Act, act June 25, 1938, ch. 675, 52 Stat. 1040, which is classified generally to this chapter. For complete classification of this Act to the Code, see section 301 of this title and Tables.

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE

Section effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as an Effective Date of 1997 Amendment note under section 321 of this title.

§ 360bbb–2. Classification of products

(a) Request

A person who submits an application or submission (including a petition, notification, and any other similar form of request) under this chapter for a product, may submit a request to

the Secretary respecting the classification of the product as a drug, biological product, device, or a combination product subject to section 353(g) of this title or respecting the component of the Food and Drug Administration that will regulate the product. In submitting the request, the person shall recommend a classification for the product, or a component to regulate the product, as appropriate.

(b) Statement

Not later than 60 days after the receipt of the request described in subsection (a), the Secretary shall determine the classification of the product under subsection (a), or the component of the Food and Drug Administration that will regulate the product, and shall provide to the person a written statement that identifies such classification or such component, and the reasons for such determination. The Secretary may not modify such statement except with the written consent of the person, or for public health reasons based on scientific evidence.

(c) Inaction of Secretary

If the Secretary does not provide the statement within the 60-day period described in subsection (b), the recommendation made by the person under subsection (a) shall be considered to be a final determination by the Secretary of such classification of the product, or the component of the Food and Drug Administration that will regulate the product, as applicable, and may not be modified by the Secretary except with the written consent of the person, or for public health reasons based on scientific evidence.

(June 25, 1938, ch. 675, §563, as added Pub. L. 105–115, title IV, §416, Nov. 21, 1997, 111 Stat. 2378.)

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE

Section effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as an Effective Date of 1997 Amendment note under section 321 of this title.

§ 360bbb–3. Authorization for medical products for use in emergencies

(a) In general

(1) Emergency uses

Notwithstanding any provision of this chapter and section 351 of the Public Health Service Act [42 U.S.C. 262], and subject to the provisions of this section, the Secretary may authorize the introduction into interstate commerce, during the effective period of a declaration under subsection (b), of a drug, device, or biological product intended for use in an actual or potential emergency (referred to in this section as an ''emergency use'').

(2) Approval status of product

An authorization under paragraph (1) may authorize an emergency use of a product that—

(A) is not approved, licensed, or cleared for commercial distribution under section 355, 360(k), 360b, or 360e of this title or section 351 of the Public Health Service Act [42 U.S.C. 262] or conditionally approved under section 360ccc of this title (referred to in this section as an ''unapproved product''); or

(B) is approved, conditionally approved under section 360ccc of this title, licensed, or cleared under such a provision, but which use is not under such provision an approved, conditionally approved under section 360ccc of this title, licensed, or cleared use of the product (referred to in this section as an ''unapproved use of an approved product'').

(3) Relation to other uses

An emergency use authorized under paragraph (1) for a product is in addition to any other use that is authorized for the product under a section of this chapter or the Public Health Service Act [42 U.S.C. 201 et seq.] referred to in paragraph (2)(A).

(4) Definitions

For purposes of this section:

(A) The term ''biological product'' has the meaning given such term in section 351 of the Public Health Service Act [42 U.S.C. 262].

(B) The term ''emergency use'' has the meaning indicated for such term in paragraph (1).

(C) The term ''product'' means a drug, device, or biological product.

(D) The term ''unapproved product'' has the meaning indicated for such term in paragraph (2)(A).

(E) The term ''unapproved use of an approved product'' has the meaning indicated for such term in paragraph (2)(B).

(b) Declaration of emergency or threat justifying emergency authorized use

(1) In general

The Secretary may make a declaration that the circumstances exist justifying the authorization under this subsection for a product on the basis of—

(A) a determination by the Secretary of Homeland Security that there is a domestic emergency, or a significant potential for a domestic emergency, involving a heightened risk of attack with a biological, chemical, radiological, or nuclear agent or agents;

(B) a determination by the Secretary of Defense that there is a military emergency, or a significant potential for a military emergency, involving a heightened risk to United States military forces, including personnel operating under the authority of title 10 or title 50, of attack with—

(i) a biological, chemical, radiological, or nuclear agent or agents; or

(ii) an agent or agents that may cause, or are otherwise associated with, an imminently life-threatening and specific risk to United States military forces;

(C) a determination by the Secretary that there is a public health emergency, or a significant potential for a public health emergency, that affects, or has a significant potential to affect, national security or the health and security of United States citizens living abroad, and that involves a biological,

chemical, radiological, or nuclear agent or agents, or a disease or condition that may be attributable to such agent or agents; or

(D) the identification of a material threat pursuant to section 319F–2 of the Public Health Service Act [42 U.S.C. 247d–6b] sufficient to affect national security or the health and security of United States citizens living abroad.

(2) Termination of declaration

(A) In general

A declaration under this subsection shall terminate upon the earlier of—

(i) a determination by the Secretary, in consultation as appropriate with the Secretary of Homeland Security or the Secretary of Defense, that the circumstances described in paragraph (1) have ceased to exist; or

(ii) a change in the approval status of the product such that the circumstances described in subsection (a)(2) have ceased to exist.

(B) Disposition of product

If an authorization under this section with respect to an unapproved product ceases to be effective as a result of a termination under subparagraph (A) of this paragraph, the Secretary shall consult with the manufacturer of such product with respect to the appropriate disposition of the product.

(3) Advance notice of termination

The Secretary shall provide advance notice that a declaration under this subsection will be terminated. The period of advance notice shall be a period reasonably determined to provide—

(A) in the case of an unapproved product, a sufficient period for disposition of the product, including the return of such product (except such quantities of product as are necessary to provide for continued use consistent with subsection (f)(2)) to the manufacturer (in the case of a manufacturer that chooses to have such product returned); and

(B) in the case of an unapproved use of an approved product, a sufficient period for the disposition of any labeling, or any information under subsection (e)(2)(B)(ii), as the case may be, that was provided with respect to the emergency use involved.

(4) Publication

The Secretary shall promptly publish in the Federal Register each declaration, determination, and advance notice of termination under this subsection.

(5) Explanation by Secretary

If an authorization under this section with respect to an unapproved product or an unapproved use of an approved product has been in effect for more than 1 year, the Secretary shall provide in writing to the sponsor of such product an explanation of the scientific, regulatory, or other obstacles to approval, licensure, or clearance of such product or use, including specific actions to be taken by the Secretary and the sponsor to overcome such obstacles.

(6) Military emergencies

In the case of a determination described in paragraph (1)(B), the Secretary shall determine, within 45 calendar days of such determination, whether to make a declaration under paragraph (1), and, if appropriate, shall promptly make such a declaration.

(c) Criteria for issuance of authorization

The Secretary may issue an authorization under this section with respect to the emergency use of a product only if, after consultation with the Assistant Secretary for Preparedness and Response, the Director of the National Institutes of Health, and the Director of the Centers for Disease Control and Prevention (to the extent feasible and appropriate given the applicable circumstances described in subsection (b)(1)), the Secretary concludes—

(1) that an agent referred to in a declaration under subsection (b) can cause a serious or life-threatening disease or condition;

(2) that, based on the totality of scientific evidence available to the Secretary, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that—

(A) the product may be effective in diagnosing, treating, or preventing—

(i) such disease or condition; or

(ii) a serious or life-threatening disease or condition caused by a product authorized under this section, approved or cleared under this chapter, or licensed under section 351 of the Public Health Service Act [42 U.S.C. 262], for diagnosing, treating, or preventing such a disease or condition caused by such an agent; and

(B) the known and potential benefits of the product, when used to diagnose, prevent, or treat such disease or condition, outweigh the known and potential risks of the product, taking into consideration the material threat posed by the agent or agents identified in a declaration under subsection (b)(1)(D), if applicable;

(3) that there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating such disease or condition;

(4) in the case of a determination described in subsection (b)(1)(B)(ii), that the request for emergency use is made by the Secretary of Defense; and

(5) that such other criteria as the Secretary may by regulation prescribe are satisfied.

(d) Scope of authorization

An authorization of a product under this section shall state—

(1) each disease or condition that the product may be used to diagnose, prevent, or treat within the scope of the authorization;

(2) the Secretary's conclusions, made under subsection (c)(2)(B), that the known and potential benefits of the product, when used to diagnose, prevent, or treat such disease or condition, outweigh the known and potential risks of the product; and

(3) the Secretary's conclusions, made under subsection (c), concerning the safety and po-

tential effectiveness of the product in diagnosing, preventing, or treating such diseases or conditions, including, to the extent practicable given the circumstances of the emergency, an assessment of the available scientific evidence.

(e) Conditions of authorization

(1) Unapproved product

(A) Required conditions

With respect to the emergency use of an unapproved product, the Secretary, to the extent practicable given the applicable circumstances described in subsection (b)(1), shall, for a person who carries out any activity for which the authorization is issued, establish such conditions on an authorization under this section as the Secretary finds necessary or appropriate to protect the public health, including the following:

(i) Appropriate conditions designed to ensure that health care professionals administering the product are informed—

(I) that the Secretary has authorized the emergency use of the product;

(II) of the significant known and potential benefits and risks of the emergency use of the product, and of the extent to which such benefits and risks are unknown; and

(III) of the alternatives to the product that are available, and of their benefits and risks.

(ii) Appropriate conditions designed to ensure that individuals to whom the product is administered are informed—

(I) that the Secretary has authorized the emergency use of the product;

(II) of the significant known and potential benefits and risks of such use, and of the extent to which such benefits and risks are unknown; and

(III) of the option to accept or refuse administration of the product, of the consequences, if any, of refusing administration of the product, and of the alternatives to the product that are available and of their benefits and risks.

(iii) Appropriate conditions for the monitoring and reporting of adverse events associated with the emergency use of the product.

(iv) For manufacturers of the product, appropriate conditions concerning recordkeeping and reporting, including records access by the Secretary, with respect to the emergency use of the product.

(B) Authority for additional conditions

With respect to the emergency use of an unapproved product, the Secretary may, for a person who carries out any activity for which the authorization is issued, establish such conditions on an authorization under this section as the Secretary finds necessary or appropriate to protect the public health, including the following:

(i) Appropriate conditions on which entities may distribute the product with respect to the emergency use of the product (including limitation to distribution by government entities), and on how distribution is to be performed.

(ii) Appropriate conditions on who may administer the product with respect to the emergency use of the product, and on the categories of individuals to whom, and the circumstances under which, the product may be administered with respect to such use.

(iii) Appropriate conditions with respect to collection and analysis of information concerning the safety and effectiveness of the product with respect to the use of such product during the period when the authorization is in effect and a reasonable time following such period.

(iv) For persons other than manufacturers of the product, appropriate conditions concerning recordkeeping and reporting, including records access by the Secretary, with respect to the emergency use of the product.

(2) Unapproved use

With respect to the emergency use of a product that is an unapproved use of an approved product:

(A) For a person who carries out any activity for which the authorization is issued, the Secretary shall, to the extent practicable given the applicable circumstances described in subsection (b)(1), establish conditions described in clauses (i) and (ii) of paragraph (1)(A), and may establish conditions described in clauses (iii) and (iv) of such paragraph or in paragraph (1)(B).

(B)(i) If the authorization under this section regarding the emergency use authorizes a change in the labeling of the product, but the manufacturer of the product chooses not to make such change, such authorization may not authorize distributors of the product or any other person to alter or obscure the labeling provided by the manufacturer, except as provided in section 360bbb–3a of this title with respect to authorized changes to the product expiration date.

(ii) In the circumstances described in clause (i), for a person who does not manufacture the product and who chooses to act under this clause, an authorization under this section regarding the emergency use shall, to the extent practicable given the circumstances of the emergency, authorize such person to provide appropriate information with respect to such product in addition to the labeling provided by the manufacturer, subject to compliance with clause (i). While the authorization under this section is effective, such additional information shall not be considered labeling for purposes of section 352 of this title.

(C) In establishing conditions under this paragraph with respect to the distribution and administration of the product for the unapproved use, the Secretary shall not impose conditions that would restrict distribution or administration of the product when distributed or administered for the approved use.

(3) Good manufacturing practice; prescription

With respect to the emergency use of a product for which an authorization under this section is issued (whether an unapproved product or an unapproved use of an approved product), the Secretary may waive or limit, to the extent appropriate given the applicable circumstances described in subsection (b)(1)—

(A) requirements regarding current good manufacturing practice otherwise applicable to the manufacture, processing, packing, or holding of products subject to regulation under this chapter, including such requirements established under section 351 or 360j(f)(1) of this title, and including relevant conditions prescribed with respect to the product by an order under section 360j(f)(2) of this title;

(B) requirements established under subsection (b) or (f) of section 353 of this title or under section 354 of this title; and

(C) requirements established under section 360j(e) of this title.

(4) Advertising

The Secretary may establish conditions on advertisements and other promotional descriptive printed matter that relate to the emergency use of a product for which an authorization under this section is issued (whether an unapproved product or an unapproved use of an approved product), including, as appropriate—

(A) with respect to drugs and biological products, requirements applicable to prescription drugs pursuant to section 352(n) of this title; or

(B) with respect to devices, requirements applicable to restricted devices pursuant to section 352(r) of this title.

(f) Duration of authorization

(1) In general

Except as provided in paragraph (2), an authorization under this section shall be effective until the earlier of the termination of the declaration under subsection (b) or a revocation under subsection (g).

(2) Continued use after end of effective period

Notwithstanding the termination of the declaration under subsection (b) or a revocation under subsection (g), an authorization shall continue to be effective to provide for continued use of an unapproved product with respect to a patient to whom, or an animal to which, it was administered during the period described by paragraph (1), to the extent found necessary by such patient's attending physician or by the veterinarian caring for such animal, as applicable.

(g) Review and revocation of authorization

(1) Review

The Secretary shall periodically review the circumstances and the appropriateness of an authorization under this section. As part of such review, the Secretary shall regularly review the progress made with respect to the approval, conditional approval under section 360ccc of this title, licensure, or clearance of—

(A) an unapproved product for which an authorization was issued under this section; or

(B) an unapproved use of an approved product for which an authorization was issued under this section.

(2) Revision and revocation

The Secretary may revise or revoke an authorization under this section if—

(A) the circumstances described under subsection (b)(1) no longer exist;

(B) the criteria under subsection (c) for issuance of such authorization are no longer met; or

(C) other circumstances make such revision or revocation appropriate to protect the public health or safety.

(h) Publication; confidential information

(1) Publication

The Secretary shall promptly publish on the internet website of the Food and Drug Administration and in the Federal Register a notice of each authorization, and each termination or revocation of an authorization under this section, and an explanation of the reasons therefor (which may include a summary of data or information that has been submitted to the Secretary in an application, request, or submission under this section or section 355(b), 355(i), 355(j), 360b(b), 360b(j), 360b(n), 360e, 360(k), 360c(f)(2), 360j(g), 360j(m), 360ccc, or 360ccc–1 of this title, or section 351(a) or 351(k) of the Public Health Service Act [42 U.S.C. 262(a), (k)], even if such summary may reveal the existence of such an application, request, or submission, or data contained in such application, request, or submission). The Secretary shall make any revisions to an authorization under this section available on the Internet Web site of the Food and Drug Administration, which may include a summary of the data and information supporting such revisions.

(2) Confidential information

Nothing in this section alters or amends section 1905 of title 18 or section 552(b)(4) of title 5. Information made publicly available by the Secretary in accordance with paragraph (1) shall be considered a disclosure authorized by law for purposes of section 1905 of title 18[1]

(i) Actions committed to agency discretion

Actions under the authority of this section by the Secretary, by the Secretary of Defense, or by the Secretary of Homeland Security are committed to agency discretion.

(j) Rules of construction

The following applies with respect to this section:

(1) Nothing in this section impairs the authority of the President as Commander in Chief of the Armed Forces of the United States under article II, section 2 of the United States Constitution.

(2) Nothing in this section impairs the authority of the Secretary of Defense with respect to the Department of Defense, including

[1] So in original. Probably should be followed by a period.

the armed forces, under other provisions of Federal law.

(3) Nothing in this section (including any exercise of authority by a manufacturer under subsection (e)(2)) impairs the authority of the United States to use or manage quantities of a product that are owned or controlled by the United States (including quantities in the stockpile maintained under section 319F–2 of the Public Health Service Act [42 U.S.C. 247d–6b]).

(4) Nothing in this section shall be construed as authorizing a delay in the review or other consideration by the Secretary of any application or submission pending before the Food and Drug Administration for a product for which an authorization under this section is issued.

(k) Relation to other provisions

If a product is the subject of an authorization under this section, the use of such product within the scope of the authorization shall not be considered to constitute a clinical investigation for purposes of section 355(i), 360b(j), or 360j(g) of this title or any other provision of this chapter or section 351 of the Public Health Service Act [42 U.S.C. 262].

(*l*) Option to carry out authorized activities

Nothing in this section provides the Secretary any authority to require any person to carry out any activity that becomes lawful pursuant to an authorization under this section, and no person is required to inform the Secretary that the person will not be carrying out such activity, except that a manufacturer of a sole-source unapproved product authorized for emergency use shall report to the Secretary within a reasonable period of time after the issuance by the Secretary of such authorization if such manufacturer does not intend to carry out any activity under the authorization. This section only has legal effect on a person who carries out an activity for which an authorization under this section is issued. This section does not modify or affect activities carried out pursuant to other provisions of this chapter or section 351 of the Public Health Service Act [42 U.S.C. 262]. Nothing in this subsection may be construed as restricting the Secretary from imposing conditions on persons who carry out any activity pursuant to an authorization under this section.

(m) Categorization of laboratory tests associated with devices subject to authorization

(1) In general

In issuing an authorization under this section with respect to a device, the Secretary may, subject to the provisions of this section, determine that a laboratory examination or procedure associated with such device shall be deemed, for purposes of section 353 of the Public Health Service Act [42 U.S.C. 263a], to be in a particular category of examinations and procedures (including the category described by subsection (d)(3) of such section) if, based on the totality of scientific evidence available to the Secretary—

(A) such categorization would be beneficial to protecting the public health; and

(B) the known and potential benefits of such categorization under the circumstances of the authorization outweigh the known and potential risks of the categorization.

(2) Conditions of determination

The Secretary may establish appropriate conditions on the performance of the examination or procedure pursuant to such determination.

(3) Effective period

A determination under this subsection shall be effective for purposes of section 353 of the Public Health Service Act [42 U.S.C. 263a] notwithstanding any other provision of that section during the effective period of the relevant declaration under subsection (b).

(June 25, 1938, ch. 675, § 564, as added Pub. L. 108–136, div. A, title XVI, § 1603(a), Nov. 24, 2003, 117 Stat. 1684; amended Pub. L. 108–276, § 4(a), July 21, 2004, 118 Stat. 853; Pub. L. 113–5, title III, § 302(a), Mar. 13, 2013, 127 Stat. 179; Pub. L. 114–255, div. A, title III, § 3088(a), Dec. 13, 2016, 130 Stat. 1148; Pub. L. 115–92, § 1(a), Dec. 12, 2017, 131 Stat. 2023; Pub. L. 117–328, div. FF, title II, § 2504, Dec. 29, 2022, 136 Stat. 5802.)

Editorial Notes

REFERENCES IN TEXT

The Public Health Service Act, referred to in subsec. (a)(3), is act July 1, 1944, ch. 373, 58 Stat. 682, which is classified generally to chapter 6A (§ 201 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 201 of Title 42 and Tables.

AMENDMENTS

2022—Subsec. (h)(1). Pub. L. 117–328, § 2504(1)(A), (C), inserted ''on the internet website of the Food and Drug Administration and'' after ''promptly publish'' and '', which may include a summary of the data and information supporting such revisions'' before period at end of second sentence.

Pub. L. 117–328, § 2504(1)(B), which directed substitution of ''application, request, or submission under this section or section 355(b), 355(i), 355(j), 360b(b), 360b(j), 360b(n), 360e, 360(k), 360c(f)(2), 360j(g), 360j(m), 360ccc, or 360ccc–1 of this title, or section 351(a) or 351(k) of the Public Health Service Act, even if such summary may reveal the existence of such an application, request, or submission, or data contained in such application, request, or submission'' for ''application under section 355(i), 360b(j), or 360j(g) of this title, even if such summary may indirectly reveal the existence of such application'', was executed by making the substitution for ''application under section 355(i) 360b(j), or 360j(g) of this title, even if such summary may indirectly reveal the existence of such application'', to reflect the probable intent of Congress.

Subsec. (h)(2). Pub. L. 117–328, § 2504(2), inserted at end ''Information made publicly available by the Secretary in accordance with paragraph (1) shall be considered a disclosure authorized by law for purposes of section 1905 of title 18''.

2017—Subsec. (b)(1)(B). Pub. L. 115–92, § 1(a)(1)(A), amended subpar. (B) generally. Prior to amendment, subpar. (B) read as follows: ''a determination by the Secretary of Defense that there is a military emergency, or a significant potential for a military emergency, involving a heightened risk to United States military forces of attack with a biological, chemical, radiological, or nuclear agent or agents;''.

Subsec. (b)(6). Pub. L. 115–92, § 1(a)(1)(B), added par. (6).

Subsec. (c)(4), (5). Pub. L. 115–92, § 1(a)(2), added par. (4) and redesignated former par. (4) as (5).

2016—Subsec. (a)(2)(A). Pub. L. 114–255, § 3088(a)(1)(A), substituted ''360b, or 360e'' for ''or 360e'' and inserted ''or conditionally approved under section 360ccc of this title'' after ''Public Health Service Act''.

Subsec. (a)(2)(B). Pub. L. 114–255, § 3088(a)(1)(B), inserted ''conditionally approved under section 360ccc of this title,'' after ''approved,'' in two places.

Subsec. (b)(4). Pub. L. 114–255, § 3088(a)(2), struck out second comma after ''determination''.

Subsec. (e)(3)(B). Pub. L. 114–255, § 3088(a)(3), substituted ''subsection (b) or (f) of section 353 of this title or under section 354 of this title'' for ''section 353(b) of this title''.

Subsec. (f)(2). Pub. L. 114–255, § 3088(a)(4), inserted '', or an animal to which,'' after ''to a patient to whom'' and ''or by the veterinarian caring for such animal, as applicable'' after ''attending physician''.

Subsec. (g)(1). Pub. L. 114–255, § 3088(a)(5), inserted ''conditional approval under section 360ccc of this title,'' after ''approval,''.

Subsec. (h)(1). Pub. L. 114–255, § 3088(a)(6), substituted ''360b(j), or 360j(g) of this title'' for ''or section 360j(g) of this title''.

Subsec. (k). Pub. L. 114–255, § 3088(a)(7), substituted ''360b(j), or 360j(g) of this title'' for ''section 360j(g) of this title,''.

2013—Subsec. (a)(1). Pub. L. 113–5, § 302(a)(1)(A), substituted ''any provision of this chapter'' for ''sections 355, 360(k), and 360e of this title''.

Subsec. (a)(2)(A). Pub. L. 113–5, § 302(a)(1)(B), substituted ''under section 355, 360(k), or 360e of this title or section 351 of the Public Health Service Act'' for ''under a provision of law referred to in such paragraph''.

Subsec. (a)(3). Pub. L. 113–5, § 302(a)(1)(C), substituted ''a section of this chapter or the Public Health Service Act referred to in paragraph (2)(A)'' for ''a provision of law referred to in such paragraph''.

Subsec. (b). Pub. L. 113–5, § 302(a)(2)(A), inserted ''or threat justifying emergency authorized use'' after ''emergency'' in heading.

Subsec. (b)(1). Pub. L. 113–5, § 302(a)(2)(B), substituted ''may make a declaration that the circumstances exist'' for ''may declare an emergency'' in introductory provisions, struck out ''specified'' before ''biological'' in subpars. (A) and (B), added subpar. (D), and amended subpar. (C) generally. Prior to amendment, subpar. (C) read as follows: ''a determination by the Secretary of a public health emergency under section 319 of the Public Health Service Act that affects, or has a significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such agent or agents.''

Subsec. (b)(2)(A)(ii). Pub. L. 113–5, § 302(a)(2)(C)(i), amended cl. (ii) generally. Prior to amendment, cl. (ii) read as follows: ''the expiration of the one-year period beginning on the date on which the declaration is made.''

Subsec. (b)(2)(B), (C). Pub. L. 113–5, § 302(a)(2)(C)(ii), (iii), redesignated subpar. (C) as (B) and struck out former subpar. (B). Prior to amendment, text of subpar. (B) read as follows: ''Notwithstanding subparagraph (A), the Secretary may renew a declaration under this subsection, and this paragraph shall apply to any such renewal.''

Subsec. (b)(4). Pub. L. 113–5, § 302(a)(2)(D), substituted '', and advance notice of termination under this subsection'' for ''advance notice of termination, and renewal under this subsection''.

Subsec. (b)(5). Pub. L. 113–5, § 302(a)(2)(E), added par. (5).

Subsec. (c). Pub. L. 113–5, § 302(a)(3)(A), in introductory provisions, inserted ''the Assistant Secretary for Preparedness and Response,'' after ''consultation with'' and substituted ''Director of the National Institutes of Health, and'' for ''Director of the National Institutes of Health and'' and ''applicable circumstances described in subsection (b)(1)'' for ''circumstances of the emergency involved''.

Subsec. (c)(1). Pub. L. 113–5, § 302(a)(3)(B), substituted ''referred to'' for ''specified''.

Subsec. (c)(2)(B). Pub. L. 113–5, § 302(a)(3)(C), inserted '', taking into consideration the material threat posed by the agent or agents identified in a declaration under subsection (b)(1)(D), if applicable'' after ''risks of the product''.

Subsec. (d)(3). Pub. L. 113–5, § 302(a)(4), inserted '', to the extent practicable given the circumstances of the emergency,'' after ''including''.

Subsec. (e)(1)(A). Pub. L. 113–5, § 302(a)(5)(A), substituted ''applicable circumstances described in subsection (b)(1)'' for ''circumstances of the emergency'' in introductory provisions.

Subsec. (e)(1)(B)(iii). Pub. L. 113–5, § 302(a)(5)(B), amended cl. (iii) generally. Prior to amendment, cl. (iii) read as follows: ''Appropriate conditions with respect to the collection and analysis of information, during the period when the authorization is in effect, concerning the safety and effectiveness of the product with respect to the emergency use of such product.''

Subsec. (e)(2)(A). Pub. L. 113–5, § 302(a)(5)(C)(i), substituted ''person'' for ''manufacturer of the product'' and ''applicable circumstances described in subsection (b)(1)'' for ''circumstances of the emergency'' and inserted ''or in paragraph (1)(B)'' before period at end.

Subsec. (e)(2)(B)(i). Pub. L. 113–5, § 302(a)(5)(C)(ii), inserted '', except as provided in section 360bbb–3a of this title with respect to authorized changes to the product expiration date'' before period at end.

Subsec. (e)(2)(C). Pub. L. 113–5, § 302(a)(5)(C)(iii), amended subpar. (C) generally. Prior to amendment, subpar. (C) read as follows: ''The Secretary may establish with respect to the distribution and administration of the product for the unapproved use conditions no more restrictive than those established by the Secretary with respect to the distribution and administration of the product for the approved use.''

Subsec. (e)(3). Pub. L. 113–5, § 302(a)(5)(D), amended par. (3) generally. Prior to amendment, text read as follows: ''With respect to the emergency use of a product for which an authorization under this section is issued (whether an unapproved product or an unapproved use of an approved product), the Secretary may waive or limit, to the extent appropriate given the circumstances of the emergency, requirements regarding current good manufacturing practice otherwise applicable to the manufacture, processing, packing, or holding of products subject to regulation under this chapter, including such requirements established under section 351 of this title.''

Subsec. (g). Pub. L. 113–5, § 302(a)(6)(A), substituted ''Review and revocation'' for ''Revocation'' in heading.

Subsec. (g)(1). Pub. L. 113–5, § 302(a)(6)(B), inserted at end ''As part of such review, the Secretary shall regularly review the progress made with respect to the approval, licensure, or clearance of—

''(A) an unapproved product for which an authorization was issued under this section; or

''(B) an unapproved use of an approved product for which an authorization was issued under this section.''

Subsec. (g)(2). Pub. L. 113–5, § 302(a)(6)(C), amended par. (2) generally. Prior to amendment, text read as follows: ''The Secretary may revoke an authorization under this section if the criteria under subsection (c) of this section for issuance of such authorization are no longer met or other circumstances make such revocation appropriate to protect the public health or safety.''

Subsec. (h)(1). Pub. L. 113–5, § 302(a)(7), inserted at end ''The Secretary shall make any revisions to an authorization under this section available on the Internet Web site of the Food and Drug Administration.''

Subsec. (j)(4). Pub. L. 113–5, § 302(a)(8), added par. (4).

Subsec. (m). Pub. L. 113–5, § 302(a)(9), added subsec. (m).

2004—Pub. L. 108–276 amended section generally, substituting provisions of subsecs. (a) to (*l*) for similar former provisions, except for additional provisions in

subsec. (b)(1) allowing Secretary to authorize use of medical products in actual or potential domestic and public health emergencies in addition to actual or potential military emergencies.

Executive Documents

MAKING GENERAL USE RESPIRATORS AVAILABLE

Memorandum of President of the United States, Mar. 11, 2020, 85 F.R. 15049, provided:

Memorandum for the Secretary of Health and Human Services [and] the Secretary of Labor

By the authority vested in me as President by the Constitution and the laws of the United States of America, it is hereby ordered as follows:

It is the policy of the United States to take proactive measures to prepare for and respond to public health threats, including the public health emergency involving Coronavirus Disease 2019 (COVID–19), which was declared by the Secretary of Health and Human Services on February 4, 2020, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb–3). We must ensure that our healthcare providers have full access to the products they need. On March 10, 2020, the Secretary of Health and Human Services took action by issuing a declaration pursuant to section 319F–3 of the Public Health Service Act (42 U.S.C. 247d–6d), which will help bring products necessary for addressing the epidemic to healthcare providers across the Nation. Unfortunately, at present, public health experts anticipate shortages in the supply of personal respiratory devices (respirators) available for use by healthcare workers in mitigating further transmission of COVID–19.

To help prevent the spread of COVID–19, the Secretary of Health and Human Services shall take all appropriate and necessary steps with respect to general use respirators to facilitate their emergency use by healthcare personnel in healthcare facilities and elsewhere, including under the authorities granted by section 319F–3 of the Public Health Service Act (42 U.S.C. 247d–6d) and section 564 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb–3). Additionally, the Secretary of Labor shall consider all appropriate and necessary steps to increase the availability of respirators.

The Secretary of Health and Human Services is authorized and directed to publish this memorandum in the Federal Register.

DONALD J. TRUMP.

§ 360bbb–3a. Emergency use of medical products

(a) Definitions

In this section:

(1) Eligible product

The term ''eligible product'' means a product that—

(A) is approved or cleared under this subchapter, conditionally approved under section 360ccc of this title, or licensed under section 351 of the Public Health Service Act [42 U.S.C. 262];

(B)(i) is intended for use to prevent, diagnose, or treat a disease or condition involving a biological, chemical, radiological, or nuclear agent or agents; or

(ii) is intended for use to prevent, diagnose, or treat a serious or life-threatening disease or condition caused by a product described in clause (i); and

(C) is intended for use during the circumstances under which—

(i) a determination described in subparagraph (A), (B), or (C) of section 360bbb–3(b)(1) of this title has been made by the Secretary of Homeland Security, the Secretary of Defense, or the Secretary, respectively; or

(ii) the identification of a material threat described in subparagraph (D) of section 360bbb–3(b)(1) of this title has been made pursuant to section 319F–2 of the Public Health Service Act [42 U.S.C. 247d–6b].

(2) Product

The term ''product'' means a drug, device, or biological product.

(b) Expiration dating

(1) In general

The Secretary may extend the expiration date and authorize the introduction or delivery for introduction into interstate commerce of an eligible product after the expiration date provided by the manufacturer if—

(A) the expiration date extension is intended to support the United States ability to protect—

(i) the public health; or

(ii) military preparedness and effectiveness; and

(B) the expiration date extension is supported by an appropriate scientific evaluation that is conducted or accepted by the Secretary.

(2) Requirements and conditions

Any extension of an expiration date under paragraph (1) shall, as part of the extension, identify—

(A) each specific lot, batch, or other unit of the product for which extended expiration is authorized;

(B) the duration of the extension; and

(C) any other requirements or conditions as the Secretary may deem appropriate for the protection of the public health, which may include requirements for, or conditions on, product sampling, storage, packaging or repackaging, transport, labeling, notice to product recipients, recordkeeping, periodic testing or retesting, or product disposition.

(3) Effect

Notwithstanding any other provision of this chapter or the Public Health Service Act [42 U.S.C. 201 et seq.], an eligible product shall not be considered an unapproved product (as defined in section 360bbb–3(a)(2)(A) of this title) and shall not be deemed adulterated or misbranded under this chapter because, with respect to such product, the Secretary has, under paragraph (1), extended the expiration date and authorized the introduction or delivery for introduction into interstate commerce of such product after the expiration date provided by the manufacturer.

(4) Expiration date

For purposes of this subsection, the term ''expiration date'' means the date established through appropriate stability testing required by the regulations issued by the Secretary to ensure that the product meets applicable standards of identity, strength, quality, and purity at the time of use.

(c) Current good manufacturing practice

(1) In general

The Secretary may, when the circumstances of a domestic, military, or public health emergency or material threat described in subsection (a)(1)(C) so warrant, authorize, with respect to an eligible product, deviations from current good manufacturing practice requirements otherwise applicable to the manufacture, processing, packing, or holding of products subject to regulation under this chapter, including requirements under section 351 or 360j(f)(1) of this title or applicable conditions prescribed with respect to the eligible product by an order under section 360j(f)(2) of this title.

(2) Effect

Notwithstanding any other provision of this chapter or the Public Health Service Act [42 U.S.C. 201 et seq.], an eligible product shall not be considered an unapproved product (as defined in section 360bbb–3(a)(2)(A) of this title) and shall not be deemed adulterated or misbranded under this chapter because, with respect to such product, the Secretary has authorized deviations from current good manufacturing practices under paragraph (1).

(d) Emergency dispensing

The requirements of subsections (b) and (f) of section 353, section 354, and section 360j(e) of this title shall not apply to an eligible product, and the product shall not be considered an unapproved product (as defined in section 360bbb–3(a)(2)(A) of this title) and shall not be deemed adulterated or misbranded under this chapter because it is dispensed without an individual prescription, if—

(1) the product is dispensed during the circumstances described in subsection (a)(1)(C); and

(2) such dispensing without an individual prescription occurs—

(A) as permitted under the law of the State in which the product is dispensed; or

(B) in accordance with an order issued by the Secretary, for the purposes and duration of the circumstances described in subsection (a)(1)(C).

(e) Emergency use instructions

(1) In general

The Secretary, acting through an appropriate official within the Department of Health and Human Services, may create and issue emergency use instructions to inform health care providers or individuals to whom an eligible product is to be administered concerning such product's approved, licensed, or cleared conditions of use.

(2) Effect

Notwithstanding any other provisions of this chapter or the Public Health Service Act [42 U.S.C. 201 et seq.], a product shall not be considered an unapproved product and shall not be deemed adulterated or misbranded under this chapter because of the issuance of emergency use instructions under paragraph (1) with respect to such product or the introduction or delivery for introduction of such product into interstate commerce accompanied by such instructions—

(A) during an emergency response to an actual emergency that is the basis for a determination described in subsection (a)(1)(C); or

(B) by a government entity (including a Federal, State, local, or tribal government entity), or a person acting on behalf of such a government entity, in preparation for an emergency response.

(June 25, 1938, ch. 675, §564A, as added Pub. L. 113–5, title III, §302(b), Mar. 13, 2013, 127 Stat. 183; amended Pub. L. 114–255, div. A, title III, §3088(c), Dec. 13, 2016, 130 Stat. 1149; Pub. L. 116–22, title VII, §705(c), June 24, 2019, 133 Stat. 964.)

Editorial Notes

REFERENCES IN TEXT

The Public Health Service Act, referred to in subsecs. (b)(3), (c)(2), and (e)(2), is act July 1, 1944, ch. 373, 58 Stat. 682, which is classified generally to chapter 6A (§201 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 201 of Title 42 and Tables.

AMENDMENTS

2019—Subsec. (e)(2)(A). Pub. L. 116–22 substituted ''subsection (a)(1)(C)'' for ''subsection (a)(1)(C)(i)''.

2016—Subsec. (a)(1)(A). Pub. L. 114–255, §3088(c)(1), inserted '', conditionally approved under section 360ccc of this title,'' after ''subchapter''.

Subsec. (d). Pub. L. 114–255, §3088(c)(2), substituted ''subsections (b) and (f) of section 353, section 354, and section 360j(e) of this title'' for ''sections 353(b) and 360j(e) of this title'' in introductory provisions.

§ 360bbb–3b. Products held for emergency use

It is not a violation of any section of this chapter or of the Public Health Service Act [42 U.S.C. 201 et seq.] for a government entity (including a Federal, State, local, or tribal government entity), or a person acting on behalf of such a government entity, to introduce into interstate commerce a product (as defined in section 360bbb–3(a)(4) of this title) intended for emergency use, if that product—

(1) is intended to be held and not used; and

(2) is held and not used, unless and until that product—

(A) is approved, cleared, or licensed under section 355, 360(k), 360b, or 360e of this title or section 351 of the Public Health Service Act [42 U.S.C. 262] or conditionally approved under section 360ccc of this title;

(B) is authorized for investigational use under section 355, 360b, or 360j of this title or section 351 of the Public Health Service Act [42 U.S.C. 262]; or

(C) is authorized for use under section 360bbb–3 of this title or section 360bbb–3a of this title.

(June 25, 1938, ch. 675, §564B, as added Pub. L. 113–5, title III, §302(d), Mar. 13, 2013, 127 Stat. 185; amended Pub. L. 114–255, div. A, title III, §3088(d), Dec. 13, 2016, 130 Stat. 1149; Pub. L. 116–22, title VII, §705(d), June 24, 2019, 133 Stat. 964.)

Editorial Notes

REFERENCES IN TEXT

The Public Health Service Act, referred to in text, is act July 1, 1944, ch. 373, 58 Stat. 682, which is classified generally to chapter 6A (§ 201 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 201 of Title 42 and Tables.

AMENDMENTS

2019—Par. (2)(B). Pub. L. 116–22, § 705(d)(1), inserted comma after ''355''.

Par. (2)(C). Pub. L. 116–22, § 705(d)(2), inserted ''or section 360bbb–3a of this title'' before period at end.

2016—Par. (2)(A). Pub. L. 114–255, § 3088(d)(1), substituted ''360b, or 360e of this title'' for ''or 360e of this title'' and inserted ''or conditionally approved under section 360ccc of this title'' after ''Public Health Service Act''.

Par. (2)(B). Pub. L. 114–255, § 3088(d)(2), substituted ''360b, or 360j of this title'' for ''or 360j of this title''.

§ 360bbb–3c. Expedited development and review of medical products for emergency uses

(1) In general

The Secretary of Defense may request that the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs, take actions to expedite the development of a medical product, review of investigational new drug applications under section 355(i) of this title, review of investigational device exemptions under section 360j(g) of this title, and review of applications for approval and clearance of medical products under sections 355, 360(k), and 360e of this title and section 262 of title 42, including applications for licensing of vaccines or blood as biological products under such section 262 of title 42, or applications for review of regenerative medicine advanced therapy products under section 356(g) of this title, if there is a military emergency, or significant potential for a military emergency, involving a specific and imminently life-threatening risk to United States military forces of attack with an agent or agents, and the medical product that is the subject of such application, submission, or notification would be reasonably likely to diagnose, prevent, treat, or mitigate such life-threatening risk.

(2) Actions

Upon a request by the Secretary of Defense under paragraph (1), the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs, shall take action to expedite the development and review of an applicable application or notification with respect to a medical product described in paragraph (1), which may include, as appropriate—

(A) holding meetings with the sponsor and the review team throughout the development of the medical product;

(B) providing timely advice to, and interactive communication with, the sponsor regarding the development of the medical product to ensure that the development program to gather the nonclinical and clinical data necessary for approval or clearance is as efficient as practicable;

(C) involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review;

(D) assigning a cross-disciplinary project lead for the review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor;

(E) taking steps to ensure that the design of the clinical trials is as efficient as practicable, when scientifically appropriate, such as by minimizing the number of patients exposed to a potentially less efficacious treatment;

(F) applying any applicable Food and Drug Administration program intended to expedite the development and review of a medical product; and

(G) in appropriate circumstances, permitting expanded access to the medical product during the investigational phase, in accordance with applicable requirements of the Food and Drug Administration.

(3) Enhanced collaboration and communication

In order to facilitate enhanced collaboration and communication with respect to the most current priorities of the Department of Defense—

(A) the Food and Drug Administration shall meet with the Department of Defense and any other appropriate development partners, such as the Biomedical Advanced Research and Development Authority, on a semi-annual basis for the purposes of conducting a full review of the relevant products in the Department of Defense portfolio; and

(B) the Director of the Center for Biologics Evaluation and Research shall meet quarterly with the Department of Defense to discuss the development status of regenerative medicine advanced therapy, blood, and vaccine medical products and projects that are the highest priorities to the Department of Defense (which may include freeze dried plasma products and platelet alternatives),

unless the Secretary of Defense determines that any such meetings are not necessary.

(4) Medical product

In this subsection, the term ''medical product'' means a drug (as defined in section 321 of this title), a device (as defined in such section 321 of this title), or a biological product (as defined in section 262 of title 42).

(Pub. L. 115–92, § 1(b), Dec. 12, 2017, 131 Stat. 2023.)

Editorial Notes

CODIFICATION

Section was enacted as part of Pub. L. 115–92, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

§ 360bbb–4. Countermeasure development, review, and technical assistance

(a) Definitions

In this section—

(1) the term ''countermeasure'' means a qualified countermeasure, a security countermeasure, and a qualified pandemic or epidemic product;

(2) the term ''qualified countermeasure'' has the meaning given such term in section 247d–6a of title 42;

(3) the term ''security countermeasure'' has the meaning given such term in section 247d–6b of title 42; and

(4) the term ''qualified pandemic or epidemic product'' means a product that meets the definition given such term in section 247d–6d of title 42 and—

(A) that has been identified by the Department of Health and Human Services or the Department of Defense as receiving funding directly related to addressing chemical, biological, radiological, or nuclear threats, including pandemic influenza; or

(B) is included under this paragraph pursuant to a determination by the Secretary.

(b) General duties

In order to accelerate the development, stockpiling, approval, licensure, and clearance of qualified countermeasures, security countermeasures, and qualified pandemic or epidemic products, the Secretary, in consultation with the Assistant Secretary for Preparedness and Response, shall—

(1) ensure the appropriate involvement of Food and Drug Administration personnel in interagency activities related to countermeasure advanced research and development, consistent with sections 247d–6, 247d–6a, 247d–6b, 247d–6d, 247d–7e, and 300hh–10 of title 42;

(2) ensure the appropriate involvement and consultation of Food and Drug Administration personnel in any flexible manufacturing activities carried out under section 247d–7e of title 42, including with respect to meeting regulatory requirements set forth in this chapter;

(3) promote countermeasure expertise within the Food and Drug Administration by—

(A) ensuring that Food and Drug Administration personnel involved in reviewing countermeasures for approval, licensure, or clearance are informed by the Assistant Secretary for Preparedness and Response on the material threat assessment conducted under section 247d–6b of title 42 for the agent or agents for which the countermeasure under review is intended;

(B) training Food and Drug Administration personnel regarding review of countermeasures for approval, licensure, or clearance;

(C) holding public meetings at least twice annually to encourage the exchange of scientific ideas; and

(D) establishing protocols to ensure that countermeasure reviewers have sufficient training or experience with countermeasures;

(4) maintain teams, composed of Food and Drug Administration personnel with expertise on countermeasures, including specific countermeasures, populations with special clinical needs (including children and pregnant women that may use countermeasures, as applicable and appropriate), classes or groups of countermeasures, or other countermeasure-related technologies and capabilities, that shall—

(A) consult with countermeasure experts, including countermeasure sponsors and applicants, to identify and help resolve scientific issues related to the approval, licensure, or clearance of countermeasures, through workshops or public meetings; and

(B) improve and advance the science relating to the development of new tools, standards, and approaches to assessing and evaluating countermeasures—

(i) in order to inform the process for countermeasure approval, clearance, and licensure; and

(ii) with respect to the development of countermeasures for populations with special clinical needs, including children and pregnant women, in order to meet the needs of such populations, as necessary and appropriate; and

(5) establish within the Food and Drug Administration a team of experts on manufacturing and regulatory activities (including compliance with current Good Manufacturing Practice) to provide both off-site and on-site technical assistance to the manufacturers of qualified countermeasures (as defined in section 247d–6a of title 42), security countermeasures (as defined in section 247d–6b of title 42), or vaccines, at the request of such a manufacturer and at the discretion of the Secretary, if the Secretary determines that a shortage or potential shortage may occur in the United States in the supply of such vaccines or countermeasures and that the provision of such assistance would be beneficial in helping alleviate or avert such shortage.

(c) Final guidance on development of animal models

(1) In general

Not later than 1 year after March 13, 2013, the Secretary shall provide final guidance to industry regarding the development of animal models to support approval, clearance, or licensure of countermeasures referred to in subsection (a) when human efficacy studies are not ethical or feasible.

(2) Authority to extend deadline

The Secretary may extend the deadline for providing final guidance under paragraph (1) by not more than 6 months upon submission by the Secretary of a report on the status of such guidance to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate.

(d) Development and animal modeling procedures

(1) Availability of animal model meetings

To facilitate the timely development of animal models and support the development, stockpiling, licensure, approval, and clearance of countermeasures, the Secretary shall, not later than 180 days after March 13, 2013, establish a procedure by which a sponsor or applicant that is developing a countermeasure for which human efficacy studies are not ethical or practicable, and that has an approved investigational new drug application or investigational device exemption, may request and receive—

(A) a meeting to discuss proposed animal model development activities; and

(B) a meeting prior to initiating pivotal animal studies.

(2) Pediatric models

To facilitate the development and selection of animal models that could translate to pediatric studies, any meeting conducted under paragraph (1) shall include discussion of animal models for pediatric populations, as appropriate.

(e) Review and approval of countermeasures

(1) Material threat

When evaluating an application or submission for approval, licensure, or clearance of a countermeasure, the Secretary shall take into account the material threat posed by the chemical, biological, radiological, or nuclear agent or agents identified under section 247d–6b of title 42 for which the countermeasure under review is intended.

(2) Review expertise

When practicable and appropriate, teams of Food and Drug Administration personnel reviewing applications or submissions described under paragraph (1) shall include a reviewer with sufficient training or experience with countermeasures pursuant to the protocols established under subsection (b)(3)(D).

(f) Regulatory management plan

(1) Definition

In this subsection, the term ''eligible countermeasure'' means—

(A) a security countermeasure with respect to which the Secretary has entered into a procurement contract under section 247d–6b(c) of title 42; or

(B) a countermeasure with respect to which the Biomedical Advanced Research and Development Authority has provided funding under section 247d–7e of title 42 for advanced research and development.

(2) Regulatory management plan process

The Secretary, in consultation with the Assistant Secretary for Preparedness and Response and the Director of the Biomedical Advanced Research and Development Authority, shall establish a formal process for obtaining scientific feedback and interactions regarding the development and regulatory review of eligible countermeasures by facilitating the development of written regulatory management plans in accordance with this subsection.

(3) Publication

The Secretary shall make available on the internet website of the Food and Drug Administration information regarding regulatory management plans, including—

(A) the process by which an applicant may submit a request for a regulatory management plan;

(B) the timeframe by which the Secretary is required to respond to such request;

(C) the information required for the submission of such request;

(D) a description of the types of development milestones and performance targets that could be discussed and included in such plans; and

(E) contact information for beginning the regulatory management plan process.

(4) Submission of request and proposed plan by sponsor or applicant

(A) In general

A sponsor or applicant of an eligible countermeasure may initiate the process described under paragraph (2) upon submission of a written request to the Secretary. Such request shall include a proposed regulatory management plan.

(B) Timing of submission

A sponsor or applicant may submit a written request under subparagraph (A) after the eligible countermeasure has an investigational new drug or investigational device exemption in effect.

(C) Response by Secretary

The Secretary shall direct the Food and Drug Administration, upon submission of a written request by a sponsor or applicant under subparagraph (A), to work with the sponsor or applicant to agree on a regulatory management plan within a reasonable time not to exceed 90 days. If the Secretary determines that no plan can be agreed upon, the Secretary shall provide to the sponsor or applicant, in writing, the scientific or regulatory rationale why such agreement cannot be reached.

(5) Plan

The content of a regulatory management plan agreed to by the Secretary and a sponsor or applicant shall include—

(A) an agreement between the Secretary and the sponsor or applicant regarding developmental milestones that will trigger responses by the Secretary as described in subparagraph (B);

(B) performance targets and goals for timely and appropriate responses by the Secretary to the triggers described under subparagraph (A), including meetings between the Secretary and the sponsor or applicant, written feedback, decisions by the Secretary, and other activities carried out as part of the development and review process; and

(C) an agreement on how the plan shall be modified, if needed.

(6) Milestones and performance targets

The developmental milestones described in paragraph (5)(A) and the performance targets and goals described in paragraph (5)(B) shall include—

(A) feedback from the Secretary regarding the data required to support the approval, clearance, or licensure of the eligible countermeasure involved;

(B) feedback from the Secretary regarding the data necessary to inform any authorization under section 360bbb–3 of this title;

(C) feedback from the Secretary regarding the data necessary to support the positioning and delivery of the eligible countermeasure, including to the Strategic National Stockpile;

(D) feedback from the Secretary regarding the data necessary to support the submission of protocols for review under section 355(b)(5)(B) of this title;

(E) feedback from the Secretary regarding any gaps in scientific knowledge that will need resolution prior to approval, licensure, or clearance of the eligible countermeasure and plans for conducting the necessary scientific research;

(F) identification of the population for which the countermeasure sponsor or applicant seeks approval, licensure, or clearance and the population for which desired labeling would not be appropriate, if known; and

(G) as necessary and appropriate, and to the extent practicable, a plan for demonstrating safety and effectiveness in pediatric populations, and for developing pediatric dosing, formulation, and administration with respect to the eligible countermeasure, provided that such plan would not delay authorization under section 360bbb–3 of this title, approval, licensure, or clearance for adults.

(7) Prioritization

(A) Plans for security countermeasures

The Secretary shall establish regulatory management plans for all security countermeasures for which a request is submitted under paragraph (4)(A).

(B) Plans for other eligible countermeasures

The Secretary shall determine whether resources are available to establish regulatory management plans for eligible countermeasures that are not security countermeasures. If resources are available to establish regulatory management plans for eligible countermeasures that are not security countermeasures, and if resources are not available to establish regulatory management plans for all eligible countermeasures for which requests have been submitted, the Director of the Biomedical Advanced Research and Development Authority, in consultation with the Commissioner, shall prioritize which eligible countermeasures may receive regulatory management plans.

(g) Annual report

Not later than 180 days after March 13, 2013, and annually thereafter, the Secretary shall make publicly available on the Web site of the Food and Drug Administration a report that details the countermeasure development and review activities of the Food and Drug Administration, including—

(1) with respect to the development of new tools, standards, and approaches to assess and evaluate countermeasures—

(A) the identification of the priorities of the Food and Drug Administration and the progress made on such priorities; and

(B) the identification of scientific gaps that impede the development, approval, licensure, or clearance of countermeasures for populations with special clinical needs, including children and pregnant women, and the progress made on resolving these challenges;

(2) with respect to countermeasures for which a regulatory management plan has been agreed upon under subsection (f), the extent to which the performance targets and goals set forth in subsection (f)(4)(B) and the regulatory management plan have been met, including, for each such countermeasure—

(A) whether the regulatory management plan was completed within the required timeframe, and the length of time taken to complete such plan;

(B) whether the Secretary adhered to the timely and appropriate response times set forth in such plan; and

(C) explanations for any failure to meet such performance targets and goals;

(3) the number of regulatory teams established pursuant to subsection (b)(4), the number of products, classes of products, or technologies assigned to each such team, and the number of, type of, and any progress made as a result of consultations carried out under subsection (b)(4)(A);

(4) an estimate of resources obligated to countermeasure development and regulatory assessment, including—

(A) Center-specific objectives and accomplishments; and

(B) the number of full-time equivalent employees of the Food and Drug Administration who directly support the review of countermeasures;

(5) the number of countermeasure applications and submissions submitted, the number of countermeasures approved, licensed, or cleared, the status of remaining submitted applications and submissions, and the number of each type of authorization issued pursuant to section 360bbb–3 of this title;

(6) the number of written requests for a regulatory management plan submitted under subsection (f)(3)(A), the number of regulatory management plans developed, and the number of such plans developed for security countermeasures; and

(7) the number, type, and frequency of meetings between the Food and Drug Administration and—

(A) sponsors of a countermeasure as defined in subsection (a); or

(B) another agency engaged in development or management of portfolios for such countermeasures, including the Centers for Disease Control and Prevention, the Biomedical Advanced Research and Development Authority, the National Institutes of Health, and the appropriate agencies of the Department of Defense.

(h) Accelerating countermeasure development and review during an emergency

(1) Acceleration of countermeasure development and review

The Secretary may, at the request of the sponsor of a countermeasure, during a domestic, military, or public health emergency or material threat described in section 360bbb–3a(a)(1)(C) of this title, expedite the development and review of countermeasures that are intended to address such domestic, mili-

tary, or public health emergency or material threat for approval, licensure, clearance, or authorization under this title or section 262 of title 42.

(2) Actions

The actions to expedite the development and review of a countermeasure under paragraph (1) may include the following:

(A) Expedited review of submissions made by sponsors of countermeasures to the Food and Drug Administration, including rolling submissions of countermeasure applications and other submissions.

(B) Expedited and increased engagement with sponsors regarding countermeasure development and manufacturing, including—

(i) holding meetings with the sponsor and the review team and providing timely advice to, and interactive communication with, the sponsor regarding the development of the countermeasure to ensure that the development program to gather the nonclinical and clinical data necessary for approval, licensure, clearance, or authorization is as efficient as practicable;

(ii) involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review;

(iii) assigning a cross-disciplinary project lead for the review team to facilitate;

(iv) taking steps to ensure that the design of the clinical trials is as efficient as practicable, when scientifically appropriate, such as by minimizing the number of patients exposed to a potentially less efficacious treatment; and

(v) streamlining the review of approved, licensed, cleared, or authorized countermeasures to treat or prevent new or emerging threats, including the review of any changes to such countermeasures.

(C) Expedited issuance of guidance documents and publication of other regulatory information regarding countermeasure development and manufacturing.

(D) Other steps to expedite the development and review of a countermeasure application submitted for approval, licensure, clearance, or authorization, as the Secretary determines appropriate.

(3) Limitation of effect

Nothing in this subsection shall be construed to require the Secretary to grant, or take any other action related to, a request of a sponsor to expedite the development and review of a countermeasure for approval, licensure, clearance, or authorization under paragraph (1).

(i) Third party evaluation of tests used during an emergency

(1) In general

For purposes of conducting evaluations regarding whether an in vitro diagnostic product (as defined in section 809.3 of title 21, Code of Federal Regulations (or any successor regulations)) for which a request for emergency use authorization is submitted under section 360bbb–3 of this title meets the criteria for issuance of such authorization, the Secretary may, as appropriate, consult with persons with appropriate expertise with respect to such evaluations or enter into cooperative agreements or contracts with such persons under which such persons conduct such evaluations and make such recommendations, including, as appropriate, evaluations and recommendations regarding the scope of authorization and conditions of authorization.

(2) Requirements regarding evaluations and recommendations

(A) In general

In evaluating and making recommendations to the Secretary regarding the validity, accuracy, and reliability of in vitro diagnostic products, as described in paragraph (1), a person shall consider and document whether the relevant criteria under subsection (c)(2) of section 360bbb–3 of this title for issuance of authorization under such section are met with respect to the in vitro diagnostic product.

(B) Written recommendations

Recommendations made by a person under this subsection shall be submitted to the Secretary in writing, and shall include the reasons for such recommendation and other information that may be requested by the Secretary.

(3) Rule of construction

Nothing in this subsection shall be construed to require the Secretary to consult with, or enter into cooperative agreements or contracts with, persons as described in paragraph (1) for purposes of authorizing an in vitro diagnostic product or otherwise affecting the emergency use authorization authorities under this section or section 360bbb–3 of this title.

(June 25, 1938, ch. 675, § 565, as added Pub. L. 109–417, title IV, § 404, Dec. 19, 2006, 120 Stat. 2875; amended Pub. L. 113–5, title III, §§ 303–306, Mar. 13, 2013, 127 Stat. 185–190; Pub. L. 116–22, title V, § 503, June 24, 2019, 133 Stat. 951; Pub. L. 117–328, div. FF, title II, §§ 2501, 2502(a), Dec. 29, 2022, 136 Stat. 5796, 5797.)

Editorial Notes

AMENDMENTS

2022—Subsec. (h). Pub. L. 117–328, § 2501, added subsec. (h).

Subsec. (i). Pub. L. 117–328, § 2502(a), added subsec. (i).

2019—Subsec. (f)(3) to (5). Pub. L. 116–22, § 503(1), (2), added par. (3) and redesignated former pars. (3) and (4) as (4) and (5), respectively. Former par. (5) redesignated (6).

Subsec. (f)(6). Pub. L. 116–22, § 503(1), (3), redesignated par. (5) as (6) and, in introductory provisions, substituted ''paragraph (5)(A)'' for ''paragraph (4)(A)'' and ''paragraph (5)(B)'' for ''paragraph (4)(B)''. Former par. (6) redesignated (7).

Subsec. (f)(7). Pub. L. 116–22, § 503(1), redesignated par. (6) as (7).

Subsec. (f)(7)(A). Pub. L. 116–22, § 503(4), substituted ''paragraph (4)(A)'' for ''paragraph (3)(A)''.

2013—Pub. L. 113–5, § 304(1), substituted ''Countermeasure development, review, and technical assistance'' for ''Technical assistance'' in section catchline.

Pub. L. 113–5, § 303, designated existing provisions as subsec. (b) and inserted heading.

Subsec. (a). Pub. L. 113–5, § 303, added subsec. (a).

Subsec. (b). Pub. L. 113–5, § 304(2), reenacted heading without change, substituted ''In order to accelerate the development, stockpiling, approval, licensure, and clearance of qualified countermeasures, security countermeasures, and qualified pandemic or epidemic products, the Secretary, in consultation with the Assistant Secretary for Preparedness and Response, shall—'' for ''The Secretary, in consultation with the Commissioner of Food and Drugs, shall'', added pars. (1) to (4), and designated remainder of existing provisions as par. (5).

Subsecs. (c) to (e). Pub. L. 113–5, § 304(3), added subsecs. (c) to (e).

Subsec. (f). Pub. L. 113–5, § 305, added subsec. (f).

Subsec. (g). Pub. L. 113–5, § 306, added subsec. (g).

Statutory Notes and Related Subsidiaries

GUIDANCE

Pub. L. 117–328, div. FF, title II, § 2502(b), Dec. 29, 2022, 136 Stat. 5798, provided that: ''Not later than 1 year after the date of enactment of this Act [Dec. 29, 2022], the Secretary of Health and Human Services (referred to in this subsection as the 'Secretary') shall issue draft guidance on consultations with persons under subsection (i) of section 565 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb–4), as added by subsection (a), including considerations concerning conflicts of interest, compensation arrangements, and information sharing. Not later than 1 year after the public comment period on such draft guidance ends, the Secretary shall issue a revised draft guidance or final guidance.''

PREDICTABLE REVIEW TIMELINES OF VACCINES BY THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

Pub. L. 114–255, div. A, title III, § 3091, Dec. 13, 2016, 130 Stat. 1149, provided that:

''(a) CONSIDERATION OF NEW VACCINES.—Upon the licensure of any vaccine or any new indication for a vaccine, the Advisory Committee on Immunization Practices (in this section referred to as the 'Advisory Committee') shall, as appropriate, consider the use of the vaccine at its next regularly scheduled meeting.

''(b) ADDITIONAL INFORMATION.—If the Advisory Committee does not make a recommendation with respect to the use of a vaccine at the Advisory Committee's first regularly scheduled meeting after the licensure of the vaccine or any new indication for the vaccine, the Advisory Committee shall provide an update on the status of such committee's review.

''(c) CONSIDERATION FOR BREAKTHROUGH THERAPIES AND FOR POTENTIAL USE DURING PUBLIC HEALTH EMERGENCY.—The Advisory Committee shall make recommendations with respect to the use of certain vaccines in a timely manner, as appropriate, including vaccines that—

''(1) are designated as a breakthrough therapy under section 506 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356) and licensed under section 351 of the Public Health Service Act (42 U.S.C. 262); or

''(2) could be used in a public health emergency.

''(d) DEFINITION.—In this section, the terms 'Advisory Committee on Immunization Practices' and 'Advisory Committee' mean the Advisory Committee on Immunization Practices established by the Secretary pursuant to section 222 of the Public Health Service Act (42 U.S.C. 217a), acting through the Director of the Centers for Disease Control and Prevention.''

§ 360bbb–4a. Priority review to encourage treatments for agents that present national security threats

(a) Definitions

In this section:

(1) Human drug application

The term ''human drug application'' has the meaning given such term in section 379g(1) of this title.

(2) Priority review

The term ''priority review'', with respect to a human drug application, means review and action by the Secretary on such application not later than 6 months after receipt by the Secretary of such application, as described in the Manual of Policies and Procedures in the Food and Drug Administration and goals identified in the letters described in section 101(b) of the Food and Drug Administration Safety and Innovation Act.

(3) Priority review voucher

The term ''priority review voucher'' means a voucher issued by the Secretary to the sponsor of a material threat medical countermeasure application that entitles the holder of such voucher to priority review of a single human drug application submitted under section 355(b)(1) of this title or section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)] after the date of approval of the material threat medical countermeasure application.

(4) Material threat medical countermeasure application

The term ''material threat medical countermeasure application'' means an application that—

(A) is a human drug application for a drug intended for use—

(i) to prevent, or treat harm from a biological, chemical, radiological, or nuclear agent identified as a material threat under section 319F–2(c)(2)(A)(ii) of the Public Health Service Act [42 U.S.C. 247d–6b(c)(2)(A)(ii)]; or

(ii) to mitigate, prevent, or treat harm from a condition that may result in adverse health consequences or death and may be caused by administering a drug, or biological product against such agent; and

(B) the Secretary determines eligible for priority review;

(C) is approved after December 13, 2016; and

(D) is for—

(i) a human drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under section 355(b)(1) of this title; or

(ii) a biological product, no active ingredient of which has been approved in any other application under section 351 of the Public Health Service Act [42 U.S.C. 262].

(b) Priority review voucher

(1) In general

The Secretary shall award a priority review voucher to the sponsor of a material threat medical countermeasure application upon approval by the Secretary of such material threat medical countermeasure application.

(2) Transferability

The sponsor of a material threat medical countermeasure application that receives a

priority review voucher under this section may transfer (including by sale) the entitlement to such voucher to a sponsor of a human drug for which an application under section 355(b)(1) of this title or section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)] will be submitted after the date of the approval of the material threat medical countermeasure application. There is no limit on the number of times a priority review voucher may be transferred before such voucher is used.

(3) Notification

(A) In general

The sponsor of a human drug application shall notify the Secretary not later than 90 calendar days prior to submission of the human drug application that is the subject of a priority review voucher of an intent to submit the human drug application, including the date on which the sponsor intends to submit the application. Such notification shall be a legally binding commitment to pay for the user fee to be assessed in accordance with this section.

(B) Transfer after notice

The sponsor of a human drug application that provides notification of the intent of such sponsor to use the voucher for the human drug application under subparagraph (A) may transfer the voucher after such notification is provided, if such sponsor has not yet submitted the human drug application described in the notification.

(c) Priority review user fee

(1) In general

The Secretary shall establish a user fee program under which a sponsor of a human drug application that is the subject of a priority review voucher shall pay to the Secretary a fee determined under paragraph (2). Such fee shall be in addition to any fee required to be submitted by the sponsor under subchapter VII.

(2) Fee amount

The amount of the priority review user fee shall be determined each fiscal year by the Secretary and based on the average cost incurred by the agency in the review of a human drug application subject to priority review in the previous fiscal year.

(3) Annual fee setting

The Secretary shall establish, before the beginning of each fiscal year beginning after September 30, 2016, for that fiscal year, the amount of the priority review user fee.

(4) Payment

(A) In general

The priority review user fee required by this subsection shall be due upon the submission of a human drug application under section 355(b)(1) of this title or section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)] for which the priority review voucher is used.

(B) Complete application

An application described under subparagraph (A) for which the sponsor requests the use of a priority review voucher shall be considered incomplete if the fee required by this subsection and all other applicable user fees are not paid in accordance with the Secretary's procedures for paying such fees.

(C) No waivers, exemptions, reductions, or refunds

The Secretary may not grant a waiver, exemption, reduction, or refund of any fees due and payable under this section.

(5) Offsetting collections

Fees collected pursuant to this subsection for any fiscal year—

(A)[1] shall be deposited and credited as offsetting collections to the account providing appropriations to the Food and Drug Administration; and

(6)[2] shall not be collected for any fiscal year except to the extent provided in advance in appropriation Acts.

(d) Notice of issuance of voucher and approval of products under voucher

The Secretary shall publish a notice in the Federal Register and on the Internet website of the Food and Drug Administration not later than 30 calendar days after the occurrence of each of the following:

(1) The Secretary issues a priority review voucher under this section.

(2) The Secretary approves a drug pursuant to an application submitted under section 355(b) of this title or section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)] for which the sponsor of the application used a priority review voucher issued under this section.

(e) Eligibility for other programs

Nothing in this section precludes a sponsor who seeks a priority review voucher under this section from participating in any other incentive program, including under this chapter, except that no sponsor of a material threat medical countermeasure application may receive more than one priority review voucher issued under any section of this chapter with respect to such drug.

(f) Relation to other provisions

The provisions of this section shall supplement, not supplant, any other provisions of this chapter or the Public Health Service Act [42 U.S.C. 201 et seq.] that encourage the development of medical countermeasures.

(g) Sunset

The Secretary may not award any priority review vouchers under subsection (b) after October 1, 2023.

(June 25, 1938, ch. 675, § 565A, as added Pub. L. 114–255, div. A, title III, § 3086, Dec. 13, 2016, 130 Stat. 1144; Pub. L. 117–9, § 1(a)(5), Apr. 23, 2021, 135 Stat. 258.)

Editorial Notes

REFERENCES IN TEXT

Section 101(b) of the Food and Drug Administration Safety and Innovation Act, referred to in subsec. (a)(2),

[1] So in original. No subpar. (B) has been enacted.

[2] So in original. Probably should be designated as subpar. (B).

is section 101(b) of Pub. L. 112–144, which is set out as a note under section 379g of this title.

The Public Health Service Act, referred to in subsec. (f), is act July 1, 1944, ch. 373, 58 Stat. 682, which is classified generally to chapter 6A (§ 201 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 201 of Title 42 and Tables.

AMENDMENTS

2021—Subsec. (a)(4)(D). Pub. L. 117–9 amended subpar. (D) generally. Prior to amendment, subpar. (D) read as follows: ''is for a human drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under section 355(b)(1) of this title or section 351(a) of the Public Health Service Act.''

§ 360bbb–4b. Medical countermeasure master files

(a) Applicability of reference

(1) In general

A person may submit data and information in a master file to the Secretary with the intent to reference, or to authorize, in writing, another person to reference, such data or information to support a medical countermeasure submission (including a supplement or amendment to any such submission), without requiring the master file holder to disclose the data and information to any such persons authorized to reference the master file. Such data and information shall be available for reference by the master file holder or by a person authorized by the master file holder, in accordance with applicable privacy and confidentiality protocols and regulations.

(2) Reference of certain master files

In the case that data or information within a medical countermeasure master file is used only to support the conditional approval of an application filed under section 360ccc of this title, such master file may be relied upon to support the effectiveness of a product that is the subject of a subsequent medical countermeasure submission only if such application is supplemented by additional data or information to support review and approval in a manner consistent with the standards applicable to such review and approval for such countermeasure, qualified countermeasure, or qualified pandemic or epidemic product.

(b) Medical countermeasure master file content

(1) In general

A master file under this section may include data or information to support—

(A) the development of medical countermeasure submissions to support the approval, licensure, classification, clearance, conditional approval, or authorization of one or more security countermeasures, qualified countermeasures, or qualified pandemic or epidemic products; and

(B) the manufacture of security countermeasures, qualified countermeasures, or qualified pandemic or epidemic products.

(2) Required updates

The Secretary may require, as appropriate, that the master file holder ensure that the contents of such master file are updated during the time such master file is referenced for a medical countermeasure submission.

(c) Sponsor reference

(1) In general

Each incorporation of data or information within a medical countermeasure master file shall describe the incorporated material in a manner in which the Secretary determines appropriate and that permits the review of such information within such master file without necessitating resubmission of such data or information. Master files shall be submitted in an electronic format in accordance with sections 360b(b)(4), 360ccc(a)(4), and 379k–1 of this title, as applicable, and as specified in applicable guidance.

(2) Reference by a master file holder

A master file holder that is the sponsor of a medical countermeasure submission shall notify the Secretary in writing of the intent to reference the medical countermeasure master file as a part of the submission.

(3) Reference by an authorized person

A person submitting an application for review may, where the Secretary determines appropriate, incorporate by reference all or part of the contents of a medical countermeasure master file, if the master file holder authorizes the incorporation in writing.

(d) Acknowledgment of and reliance upon a master file by the Secretary

(1) In general

The Secretary shall provide the master file holder with a written notification indicating that the Secretary has reviewed and relied upon specified data or information within a master file and the purposes for which such data or information was incorporated by reference if the Secretary has reviewed and relied upon such specified data or information to support the approval, classification, conditional approval, clearance, licensure, or authorization of a security countermeasure, qualified countermeasure, or qualified pandemic or epidemic product. The Secretary may rely upon the data and information within the medical countermeasure master file for which such written notification was provided in additional applications, as applicable and appropriate and upon the request of the master file holder so notified in writing or by an authorized person of such holder.

(2) Certain applications

If the Secretary has reviewed and relied upon specified data or information within a medical countermeasure master file to support the conditional approval of an application under section 360ccc of this title to subsequently support the approval, clearance, licensure, or authorization of a security countermeasure, qualified countermeasure, or qualified pandemic or epidemic product, the Secretary shall provide a brief written description to the master file holder regarding the elements of the application fulfilled by the data or information within the master file and how

such data or information contained in such application meets the standards of evidence under subsection (c) or (d) of section 355 of this title, subsection (d) of section 360b of this title, or section 351 of the Public Health Service Act [42 U.S.C. 262] (as applicable), which shall not include any trade secret or confidential commercial information.

(e) Rules of construction

Nothing in this section shall be construed to—

(1) limit the authority of the Secretary to approve, license, clear, conditionally approve, or authorize drugs, biological products, or devices pursuant to, as applicable, this Act [this chapter] or section 351 of the Public Health Service Act [42 U.S.C. 262] (as such applicable Act is in effect on the day before June 24, 2019), including the standards of evidence, and applicable conditions, for approval under the applicable Act;

(2) alter the standards of evidence with respect to approval, licensure, or clearance, as applicable, of drugs, biological products, or devices under this Act [this chapter] or section 351 of the Public Health Service Act [42 U.S.C. 262], including, as applicable, the substantial evidence standards under sections 355(d) and 360b(d) of this title and section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)]; or

(3) alter the authority of the Secretary under this Act [this chapter] or the Public Health Service Act [42 U.S.C. 201 et seq.] to determine the types of data or information previously submitted by a sponsor or any other person that may be incorporated by reference in an application, request, or notification for a drug, biological product, or device submitted under sections 355(i), 355(b), 355(j), 360b(b)(1), 360b(b)(2), 360b(j), 360bbb–3, 360ccc, 360j(g), 360e(c), 360c(f)(2), or 360(k) of this title, or subsection (a) or (k) of section 351 of the Public Health Service Act [42 U.S.C. 262], including a supplement or amendment to any such submission, and the requirements associated with such reference.

(f) Definitions

In this section:

(1) The term ''master file holder'' means a person who submits data and information to the Secretary with the intent to reference or authorize another person to reference such data or information to support a medical countermeasure submission, as described in subsection (a).

(2) The term ''medical countermeasure submission'' means an investigational new drug application under section 355(i) of this title, a new drug application under section 355(b) of this title, or an abbreviated new drug application under section 355(j) of this title, a biological product license application under section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)] or a biosimilar biological product license application under section 351(k) of the Public Health Service Act [42 U.S.C. 262(k)], a new animal drug application under section 360b(b)(1) of this title or abbreviated new animal drug application under section 360b(b)(2) of this title, an application for conditional approval of a new animal drug under section 360ccc of this title, an investigational device application under section 360j(g) of this title, an application with respect to a device under section 360e(c) of this title, a request for classification of a device under section 360c(f)(2) of this title, a notification with respect to a device under section 360(k) of this title, or a request for an emergency use authorization under section 360bbb–3 of this title to support—

(A) the approval, licensure, classification, clearance, conditional approval, or authorization of a security countermeasure, qualified countermeasure, or qualified pandemic or epidemic product; or

(B) a new indication to an approved security countermeasure, qualified countermeasure, or qualified pandemic or epidemic product.

(3) The terms ''qualified countermeasure'', ''security countermeasure'', and ''qualified pandemic or epidemic product'' have the meanings given such terms in sections 319F–1, 319F–2, and 319F–3, respectively, of the Public Health Service Act [42 U.S.C. 247d–6a, 247d–6b, 247d–6d].

(June 25, 1938, ch. 675, § 565B, as added Pub. L. 116–22, title VI, § 603(b), June 24, 2019, 133 Stat. 953.)

Editorial Notes

REFERENCES IN TEXT

This Act, referred to in subsec. (e), is the Federal Food, Drug, and Cosmetic Act, act June 25, 1938, ch. 675, 52 Stat. 1040, which is classified generally to this chapter (§ 301 et seq.). For complete classification of this Act to the Code, see section 301 of this title and Tables.

The Public Health Service Act, referred to in subsec. (e)(3), is act July 1, 1944, ch. 373, 58 Stat. 682, which is classified generally to chapter 6A (§ 201 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 201 of Title 42 and Tables.

Statutory Notes and Related Subsidiaries

MEDICAL COUNTERMEASURE MASTER FILES

Pub. L. 116–22, title VI, § 603, June 24, 2019, 133 Stat. 953, provided that:

''(a) IN GENERAL.—The purpose of this section (including section 565B of the Federal Food, Drug, and Cosmetic Act [this section], as added by subsection (b)) is to support and advance the development or manufacture of security countermeasures, qualified countermeasures, and qualified pandemic or epidemic products by facilitating and encouraging submission of data and information to support the development of such products, and through clarifying the authority to cross-reference to data and information previously submitted to the Secretary of Health and Human Services (referred to in this section as the 'Secretary'), including data and information submitted to medical countermeasure master files or other master files.

''(b) MEDICAL COUNTERMEASURE MASTER FILES.—[Enacted this section.]

''(c) STAKEHOLDER INPUT.—Not later than 18 months after the date of enactment of this Act [June 24, 2019], the Secretary, acting through the Commissioner of Food and Drugs and in consultation with the Assistant Secretary for Preparedness and Response, shall solicit input from stakeholders, including stakeholders developing security countermeasures, qualified countermeasures, or qualified pandemic or epidemic products,

and stakeholders developing technologies to assist in the development of such countermeasures with respect to how the Food and Drug Administration can advance the use of tools and technologies to support and advance the development or manufacture of security countermeasures, qualified countermeasures, and qualified pandemic or epidemic products, including through reliance on cross-referenced data and information contained within master files and submissions previously submitted to the Secretary as set forth in section 565B of the Federal Food, Drug, and Cosmetic Act, as added by subsection (b).

''(d) GUIDANCE.—Not later than 2 years after the date of enactment of this Act, the Secretary, acting through the Commissioner of Food and Drugs, shall publish draft guidance about how reliance on cross-referenced data and information contained within master files under section 565B of the Federal Food, Drug, and Cosmetic Act, as added by subsection (b) or submissions otherwise submitted to the Secretary may be used for specific tools or technologies (including platform technologies) that have the potential to support and advance the development or manufacture of security countermeasures, qualified countermeasures, and qualified pandemic or epidemic products. The Secretary, acting through the Commissioner of Food and Drugs, shall publish the final guidance not later than 3 years after the enactment of this Act.''

§ 360bbb–5. Critical Path Public-Private Partnerships

(a) Establishment

The Secretary, acting through the Commissioner of Food and Drugs, may enter into collaborative agreements, to be known as Critical Path Public-Private Partnerships, with one or more eligible entities to implement the Critical Path Initiative of the Food and Drug Administration by developing innovative, collaborative projects in research, education, and outreach for the purpose of fostering medical product innovation, enabling the acceleration of medical product development, manufacturing, and translational therapeutics, and enhancing medical product safety.

(b) Eligible entity

In this section, the term ''eligible entity'' means an entity that meets each of the following:

(1) The entity is—

(A) an institution of higher education (as such term is defined in section 1001 of title 20) or a consortium of such institutions; or

(B) an organization described in section 501(c)(3) of title 26 and exempt from tax under section 501(a) of such title.

(2) The entity has experienced personnel and clinical and other technical expertise in the biomedical sciences, which may include graduate training programs in areas relevant to priorities of the Critical Path Initiative.

(3) The entity demonstrates to the Secretary's satisfaction that the entity is capable of—

(A) developing and critically evaluating tools, methods, and processes—

(i) to increase efficiency, predictability, and productivity of medical product development; and

(ii) to more accurately identify the benefits and risks of new and existing medical products;

(B) establishing partnerships, consortia, and collaborations with health care practitioners and other providers of health care goods or services; pharmacists; pharmacy benefit managers and purchasers; health maintenance organizations and other managed health care organizations; health care insurers; government agencies; patients and consumers; manufacturers of prescription drugs, biological products, diagnostic technologies, and devices; and academic scientists; and

(C) securing funding for the projects of a Critical Path Public-Private Partnership from Federal and nonfederal governmental sources, foundations, and private individuals.

(c) Funding

The Secretary may not enter into a collaborative agreement under subsection (a) unless the eligible entity involved provides an assurance that the entity will not accept funding for a Critical Path Public-Private Partnership project from any organization that manufactures or distributes products regulated by the Food and Drug Administration unless the entity provides assurances in its agreement with the Food and Drug Administration that the results of the Critical Path Public-Private Partnership project will not be influenced by any source of funding.

(d) Annual report

Not later than 18 months after September 27, 2007, and annually thereafter, the Secretary, in collaboration with the parties to each Critical Path Public-Private Partnership, shall submit a report to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives—

(1) reviewing the operations and activities of the Partnerships in the previous year; and

(2) addressing such other issues relating to this section as the Secretary determines to be appropriate.

(e) Definition

In this section, the term ''medical product'' includes a drug, a biological product as defined in section 262 of title 42, a device, and any combination of such products.

(f) Authorization of appropriations

To carry out this section, there is authorized to be appropriated $1,380,822 for the period beginning on October 1, 2022 and ending on December 23, 2022.[1]

(June 25, 1938, ch. 675, § 566, as added Pub. L. 110–85, title VI, § 603, Sept. 27, 2007, 121 Stat. 898; amended Pub. L. 112–144, title XI, § 1102, July 9, 2012, 126 Stat. 1108; Pub. L. 115–52, title VI, § 602, Aug. 18, 2017, 131 Stat. 1048; Pub. L. 117–180, div. F, title V, § 5005, Sept. 30, 2022, 136 Stat. 2167; Pub. L. 117–229, div. C, title III, § 301, Dec. 16, 2022, 136 Stat. 2311; Pub. L. 117–328, div. FF, title III, § 3101, Dec. 29, 2022, 136 Stat. 5807.)

[1] See 2022 Amendment notes below.

Editorial Notes

AMENDMENTS

2022—Subsec. (f). Pub. L. 117–328, which directed the substitution of ''$6,000,000 for each of fiscal years 2023 through 2027'' for ''$1,265,753 for the period beginning on October 1, 2022 and ending on December 23, 2022'', could not be executed because ''$1,265,753'' did not appear after the intervening amendment by section 301 of Pub. L. 117–229. See below.

Pub. L. 117–229 substituted ''$1,380,822 for the period beginning on October 1, 2022 and ending on December 23, 2022'' for ''$1,265,753 for the period beginning on October 1, 2022 and ending on December 16, 2022''.

Pub. L. 117–180 substituted ''$1,265,753 for the period beginning on October 1, 2022 and ending on December 16, 2022'' for ''$6,000,000 for each of fiscal years 2018 through 2022''.

2017—Subsec. (f). Pub. L. 115–52 substituted ''2018 through 2022'' for ''2013 through 2017''.

2012—Subsec. (f). Pub. L. 112–144 amended subsec. (f) generally. Prior to amendment, text read as follows: ''To carry out this section, there are authorized to be appropriated $5,000,000 for fiscal year 2008 and such sums as may be necessary for each of fiscal years 2009 through 2012.''

§ 360bbb–5a. Emerging technology program

(a) Program establishment

(1) In general

The Secretary shall establish a program to support the adoption of, and improve the development of, innovative approaches to drug design and manufacturing.

(2) Actions

In carrying out the program under paragraph (1), the Secretary may—

(A) facilitate and increase communication between public and private entities, consortia, and individuals with respect to innovative drug product design and manufacturing;

(B) solicit information regarding, and conduct or support research on, innovative approaches to drug product design and manufacturing;

(C) convene meetings with representatives of industry, academia, other Federal agencies, international agencies, and other interested persons, as appropriate;

(D) convene working groups to support drug product design and manufacturing research and development;

(E) support education and training for regulatory staff and scientists related to innovative approaches to drug product design and manufacturing;

(F) advance regulatory science related to the development and review of innovative approaches to drug product design and manufacturing;

(G) convene or participate in working groups to support the harmonization of international regulatory requirements related to innovative approaches to drug product design and manufacturing; and

(H) award grants or contracts to carry out or support the program under paragraph (1).

(3) Grants and contracts

To seek a grant or contract under this section, an entity shall submit an application—

(A) in such form and manner as the Secretary may require; and

(B) containing such information as the Secretary may require, including a description of—

(i) how the entity will conduct the activities to be supported through the grant or contract; and

(ii) how such activities will further research and development related to, or adoption of, innovative approaches to drug product design and manufacturing.

(b) Guidance

The Secretary shall—

(1) issue or update guidance to help facilitate the adoption of, and advance the development of, innovative approaches to drug product design and manufacturing; and

(2) include in such guidance descriptions of—

(A) any regulatory requirements related to the development or review of technologies related to innovative approaches to drug product design and manufacturing, including updates and improvements to such technologies after product approval; and

(B) data that can be used to demonstrate the identity, safety, purity, and potency of drugs manufactured using such technologies.

(c) Report to Congress

Not later than 4 years after December 29, 2022, the Secretary shall submit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate a report containing—

(1) an annual accounting of the allocation of funds made available to carry out this section;

(2) a description of how Food and Drug Administration staff were utilized to carry out this section and, as applicable, any challenges or limitations related to staffing;

(3) the number of public meetings held or participated in by the Food and Drug Administration pursuant to this section, including meetings convened as part of a working group described in subparagraph (D) or (G) of subsection (a)(2), and the topics of each such meeting; and

(4) the number of drug products approved or licensed, after December 29, 2022, using an innovative approach to drug product design and manufacturing.

(June 25, 1938, ch. 675, § 566A, as added Pub. L. 117–328, div. FF, title III, § 3203, Dec. 29, 2022, 136 Stat. 5814.)

§ 360bbb–6. Risk communication

(a) Advisory Committee on Risk Communication

(1) In general

The Secretary shall establish an advisory committee to be known as the ''Advisory Committee on Risk Communication'' (referred to in this section as the ''Committee'').

(2) Duties of Committee

The Committee shall advise the Commissioner on methods to effectively communicate risks associated with the products regulated by the Food and Drug Administration.

(3) Members

The Secretary shall ensure that the Committee is composed of experts on risk communication, experts on the risks described in subsection (b), and representatives of patient, consumer, and health professional organizations.

(4) Permanence of Committee

Section 1013 of title 5 shall not apply to the Committee established under this subsection.

(b) Partnerships for risk communication

(1) In general

The Secretary shall partner with professional medical societies, medical schools, academic medical centers, and other stakeholders to develop robust and multi-faceted systems for communication to health care providers about emerging postmarket drug risks.

(2) Partnerships

The systems developed under paragraph (1) shall—

(A) account for the diversity among physicians in terms of practice, willingness to adopt technology, and medical specialty; and

(B) include the use of existing communication channels, including electronic communications, in place at the Food and Drug Administration.

(June 25, 1938, ch. 675, §567, as added Pub. L. 110–85, title IX, §917, Sept. 27, 2007, 121 Stat. 960; amended Pub. L. 117–286, §4(a)(157), Dec. 27, 2022, 136 Stat. 4323.)

Editorial Notes

AMENDMENTS

2022—Subsec. (a)(4). Pub. L. 117–286 substituted ''Section 1013 of title 5'' for ''Section 14 of the Federal Advisory Committee Act''.

§ 360bbb–7. Notification

(a) Notification to Secretary

With respect to a drug, the Secretary may require notification to the Secretary by a regulated person if the regulated person knows—

(1) that the use of such drug in the United States may result in serious injury or death;

(2) of a significant loss or known theft of such drug intended for use in the United States; or

(3) that—

(A) such drug has been or is being counterfeited; and

(B)(i) the counterfeit product is in commerce in the United States or could be reasonably expected to be introduced into commerce in the United States; or

(ii) such drug has been or is being imported into the United States or may reasonably be expected to be offered for import into the United States.

(b) Manner of notification

Notification under this section shall be made in such manner and by such means as the Secretary may specify by regulation or guidance.

(c) Savings clause

Nothing in this section shall be construed as limiting any other authority of the Secretary to require notifications related to a drug under any other provision of this chapter or the Public Health Service Act [42 U.S.C. 201 et seq.].

(d) Definition

In this section, the term ''regulated person'' means—

(1) a person who is required to register under section 360 or 381(s) of this title;

(2) a wholesale distributor of a drug product; or

(3) any other person that distributes drugs except a person that distributes drugs exclusively for retail sale.

(June 25, 1938, ch. 675, §568, as added Pub. L. 112–144, title VII, §715(b), July 9, 2012, 126 Stat. 1075.)

Editorial Notes

REFERENCES IN TEXT

The Public Health Service Act, referred to in subsec. (c), is act July 1, 1944, ch. 373, 58 Stat. 682, which is classified generally to chapter 6A (§201 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 201 of Title 42 and Tables.

§ 360bbb–8. Consultation with external experts on rare diseases, targeted therapies, and genetic targeting of treatments

(a) In general

For the purpose of promoting the efficiency of and informing the review by the Food and Drug Administration of new drugs and biological products for rare diseases and drugs and biological products that are genetically targeted, the following shall apply:

(1) Consultation with stakeholders

Consistent with sections X.C and IX.E.4 of the PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 through 2017, as referenced in the letters described in section 101(b) of the Prescription Drug User Fee Amendments of 2012, the Secretary shall ensure that opportunities exist, at a time the Secretary determines appropriate, for consultations with stakeholders on the topics described in subsection (b).

(2) Consultation with external experts

(A) In general

The Secretary shall develop and maintain a list of external experts who, because of their special expertise, are qualified to provide advice on rare disease issues, including topics described in subsection (b). The Secretary may, when appropriate to address a specific regulatory question, consult such external experts on issues related to the review of new drugs and biological products for rare diseases and drugs and biological products that are genetically targeted, including the topics described in subsection (b), when such consultation is necessary because the Secretary lacks the specific scientific, medical, or technical expertise necessary for the performance of the Secretary's regulatory responsibilities and the necessary expertise can be provided by the external experts.

(B) External experts

For purposes of subparagraph (A), external experts are individuals who possess scientific or medical training that the Secretary lacks with respect to one or more rare diseases.

(b) Topics for consultation

Topics for consultation pursuant to this section may include—

(1) rare diseases;

(2) the severity of rare diseases;

(3) the unmet medical need associated with rare diseases;

(4) the willingness and ability of individuals with a rare disease to participate in clinical trials;

(5) an assessment of the benefits and risks of therapies to treat rare diseases;

(6) the general design of clinical trials for rare disease populations and subpopulations;

(7) the demographics and the clinical description of patient populations; and

(8) the science of small population studies.

(c) Classification as special government employees

The external experts who are consulted under this section may be considered special government employees, as defined under section 202 of title 18.

(d) Protection of confidential information and trade secrets

(1) Rule of construction

Nothing in this section shall be construed to alter the protections offered by laws, regulations, and policies governing disclosure of confidential commercial or trade secret information, and any other information exempt from disclosure pursuant to section 552(b) of title 5 as such provisions would be applied to consultation with individuals and organizations prior to July 9, 2012.

(2) Consent required for disclosure

The Secretary shall not disclose confidential commercial or trade secret information to an expert consulted under this section without the written consent of the sponsor unless the expert is a special government employee (as defined under section 202 of title 18) or the disclosure is otherwise authorized by law.

(e) Other consultation

Nothing in this section shall be construed to limit the ability of the Secretary to consult with individuals and organizations as authorized prior to July 9, 2012.

(f) No right or obligation

(1) No right to consultation

Nothing in this section shall be construed to create a legal right for a consultation on any matter or require the Secretary to meet with any particular expert or stakeholder.

(2) No altering of goals

Nothing in this section shall be construed to alter agreed upon goals and procedures identified in the letters described in section 101(b) of the Prescription Drug User Fee Amendments of 2012.

(3) No change to number of review cycles

Nothing in this section is intended to increase the number of review cycles as in effect before July 9, 2012.

(g) No delay in product review

(1) In general

Prior to a consultation with an external expert, as described in this section, relating to an investigational new drug application under section 355(i) of this title, a new drug application under section 355(b) of this title, or a biologics license application under section 262 of title 42, the Director of the Center for Drug Evaluation and Research or the Director of the Center for Biologics Evaluation and Research (or appropriate Division Director), as appropriate, shall determine that—

(A) such consultation will—

(i) facilitate the Secretary's ability to complete the Secretary's review; and

(ii) address outstanding deficiencies in the application; or

(B) the sponsor authorized such consultation.

(2) Limitation

The requirements of this subsection shall apply only in instances where the consultation is undertaken solely under the authority of this section. The requirements of this subsection shall not apply to any consultation initiated under any other authority.

(June 25, 1938, ch. 675, § 569, as added Pub. L. 112–144, title IX, § 903, July 9, 2012, 126 Stat. 1088; amended Pub. L. 114–255, div. A, title III, § 3101(a)(2)(O), Dec. 13, 2016, 130 Stat. 1154; Pub. L. 117–328, div. FF, title III, § 3202(e), Dec. 29, 2022, 136 Stat. 5812.)

Editorial Notes

REFERENCES IN TEXT

Section 101(b) of the Prescription Drug User Fee Amendments of 2012, referred to in subsecs. (a)(1) and (f)(2), is section 101(b) of Pub. L. 112–144, which is set out as a note under section 379g of this title.

AMENDMENTS

2022—Subsec. (b)(8). Pub. L. 117–328 added par. (8).

2016—Subsec. (a)(2)(A). Pub. L. 114–255 substituted ''subsection (b)'' for ''subsection (c)'' before period in first sentence.

§ 360bbb–8a. Optimizing global clinical trials

(a) In general

The Secretary shall—

(1) work with other regulatory authorities of similar standing, medical research companies, and international organizations to foster and encourage uniform, scientifically driven clinical trial standards with respect to medical products around the world; and

(2) enhance the commitment to provide consistent parallel scientific advice to manufacturers seeking simultaneous global development of new medical products in order to—

(A) enhance medical product development;

(B) facilitate the use of foreign data; and

(C) minimize the need to conduct duplicative clinical studies, preclinical studies, or nonclinical studies.

(b) Medical product

In this section, the term ''medical product'' means a drug, as defined in subsection (g) of section 321 of this title, a device, as defined in subsection (h) of such section, or a biological product, as defined in section 351(i) of the Public Health Service Act [42 U.S.C. 262(i)].

(c) Savings clause

Nothing in this section shall alter the criteria for evaluating the safety or effectiveness of a medical product under this chapter or under the Public Health Service Act [42 U.S.C. 201 et seq.].

(June 25, 1938, ch. 675, § 569A, as added Pub. L. 112–144, title XI, § 1123, July 9, 2012, 126 Stat. 1113; amended Pub. L. 114–255, div. A, title III, § 3101(a)(2)(P), Dec. 13, 2016, 130 Stat. 1154.)

Editorial Notes

REFERENCES IN TEXT

The Public Health Service Act, referred to in subsec. (c), is act July 1, 1944, ch. 373, 58 Stat. 682, which is classified generally to chapter 6A (§ 201 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 201 of Title 42 and Tables.

AMENDMENTS

2016—Subsec. (c). Pub. L. 114–255 inserted ''or under the Public Health Service Act'' before period at end.

§ 360bbb–8b. Use of clinical investigation data from outside the United States

(a) In general

In determining whether to approve, license, or clear a drug, biological product, or device pursuant to an application submitted under this subchapter, the Secretary shall accept data from clinical investigations conducted outside of the United States, including the European Union, if the applicant demonstrates that such data are adequate under applicable standards to support approval, licensure, or clearance of the drug, biological product, or device in the United States.

(b) Notice to sponsor

If the Secretary finds under subsection (a) that the data from clinical investigations conducted outside the United States, including in the European Union, are inadequate for the purpose of making a determination on approval, clearance, or licensure of a drug, biological product, or device pursuant to an application submitted under this subchapter, the Secretary shall provide written notice to the sponsor of the application of such finding and include the rationale for such finding.

(June 25, 1938, ch. 675, § 569B, as added Pub. L. 112–144, title XI, § 1123, July 9, 2012, 126 Stat. 1113; amended Pub. L. 114–255, div. A, title III, § 3101(a)(2)(Q), Dec. 13, 2016, 130 Stat. 1155.)

Editorial Notes

AMENDMENTS

2016—Pub. L. 114–255 substituted ''drug, biological product, or device'' for ''drug or device'' wherever appearing.

§ 360bbb–8c. Patient participation in medical product discussion

(a) Patient engagement in drugs and devices

(1) In general

The Secretary shall develop and implement strategies to solicit the views of patients during the medical product development process and consider the perspectives of patients during regulatory discussions, including by—

(A) fostering participation of a patient representative who may serve as a special government employee in appropriate agency meetings with medical product sponsors and investigators; and

(B) exploring means to provide for identification of patient representatives who do not have any, or have minimal, financial interests in the medical products industry.

(2) Protection of proprietary information

Nothing in this section shall be construed to alter the protections offered by laws, regulations, or policies governing disclosure of confidential commercial or trade secret information and any other information exempt from disclosure pursuant to section 552(b) of title 5 as such laws, regulations, or policies would apply to consultation with individuals and organizations prior to July 9, 2012.

(3) Other consultation

Nothing in this section shall be construed to limit the ability of the Secretary to consult with individuals and organizations as authorized prior to July 9, 2012.

(4) No right or obligation

Nothing in this section shall be construed to create a legal right for a consultation on any matter or require the Secretary to meet with any particular expert or stakeholder. Nothing in this section shall be construed to alter agreed upon goals and procedures identified in the letters described in section 101(b) of the Prescription Drug User Fee Amendments of 2012. Nothing in this section is intended to increase the number of review cycles as in effect before July 9, 2012.

(5) Financial interest

In this section, the term ''financial interest'' means a financial interest under section 208(a) of title 18.

(b) Statement of patient experience

(1) In general

Following the approval of an application that was submitted under section 355(b) of this title or section 262(a) of title 42 at least 180 days after December 13, 2016, the Secretary shall make public a brief statement regarding the patient experience data and related information, if any, submitted and reviewed as part of such application.

(2) Data and information

The data and information referred to in paragraph (1) are—

(A) patient experience data;

(B) information on patient-focused drug development tools; and

(C) other relevant information, as determined by the Secretary.

(c) Patient experience data

For purposes of this section, the term ''patient experience data'' includes data that—

(1) are collected by any persons (including patients, family members and caregivers of patients, patient advocacy organizations, disease research foundations, researchers, and drug manufacturers); and

(2) are intended to provide information about patients' experiences with a disease or condition, including—

(A) the impact (including physical and psychosocial impacts) of such disease or condition, or a related therapy or clinical investigation on patients' lives; and

(B) patient preferences with respect to treatment of such disease or condition.

(June 25, 1938, ch. 675, § 569C, as added Pub. L. 112–144, title XI, § 1137, July 9, 2012, 126 Stat. 1124; amended Pub. L. 114–255, div. A, title III, § 3001, Dec. 13, 2016, 130 Stat. 1083; Pub. L. 115–52, title VI, § 605, Aug. 18, 2017, 131 Stat. 1048.)

Editorial Notes

REFERENCES IN TEXT

Section 101(b) of the Prescription Drug User Fee Amendments of 2012, referred to in subsec. (a)(4), is section 101(b) of Pub. L. 112–144, which is set out as a note under section 379g of this title.

AMENDMENTS

2017—Subsec. (c)(2)(A). Pub. L. 115–52 substituted ''impact (including physical and psychosocial impacts) of such disease or condition, or a related therapy or clinical investigation'' for ''impact of such disease or condition, or a related therapy,''.

2016—Subsec. (a). Pub. L. 114–255, § 3001(1), (2), substituted ''Patient engagement in drugs and devices'' for ''In general'' in subsec. heading, designated existing provisions as par. (1) and inserted par. heading, redesignated former pars. (1) and (2) as subpars. (A) and (B), respectively, of par. (1), redesignated subsecs. (b) to (e) as as pars. (2) to (5), respectively, and realigned margins.

Subsecs. (b), (c). Pub. L. 114–255, § 3001(3), added subsecs. (b) and (c). Former subsecs. (b) and (c) redesignated pars. (2) and (3), respectively, of subsec. (a).

Subsecs. (d), (e). Pub. L. 114–255, § 3001(2), redesignated subsecs. (d) and (e) as pars. (4) and (5), respectively, of subsec. (a).

Statutory Notes and Related Subsidiaries

PATIENT-FOCUSED DRUG DEVELOPMENT GUIDANCE

Pub. L. 114–255, div. A, title III, § 3002, Dec. 13, 2016, 130 Stat. 1084, provided that:

''(a) PUBLICATION OF GUIDANCE DOCUMENTS.—Not later than 180 days after the date of enactment of this Act [Dec. 13, 2016], the Secretary of Health and Human Services (referred to in this section as the 'Secretary'), acting through the Commissioner of Food and Drugs, shall develop a plan to issue draft and final versions of one or more guidance documents, over a period of 5 years, regarding the collection of patient experience data, and the use of such data and related information in drug development. Not later than 18 months after the date of enactment of this Act, the Secretary shall issue a draft version of at least one such guidance document. Not later than 18 months after the public comment period on the draft guidance ends, the Secretary shall issue a revised draft guidance or final guidance.

''(b) PATIENT EXPERIENCE DATA.—For purposes of this section, the term 'patient experience data' has the meaning given such term in section 569C of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360bbb–8c] (as added by section 3001).

''(c) CONTENTS.—The guidance documents described in subsection (a) shall address—

''(1) methodological approaches that a person seeking to collect patient experience data for submission to, and proposed use by, the Secretary in regulatory decisionmaking may use, that are relevant and objective and ensure that such data are accurate and representative of the intended population, including methods to collect meaningful patient input throughout the drug development process and methodological considerations for data collection, reporting, management, and analysis;

''(2) methodological approaches that may be used to develop and identify what is most important to patients with respect to burden of disease, burden of treatment, and the benefits and risks in the management of the patient's disease;

''(3) approaches to identifying and developing methods to measure impacts to patients that will help facilitate collection of patient experience data in clinical trials;

''(4) methodologies, standards, and technologies to collect and analyze clinical outcome assessments for purposes of regulatory decisionmaking;

''(5) how a person seeking to develop and submit proposed draft guidance relating to patient experience data for consideration by the Secretary may submit such proposed draft guidance to the Secretary;

''(6) the format and content required for submissions under this section to the Secretary, including with respect to the information described in paragraph (1);

''(7) how the Secretary intends to respond to submissions of information described in paragraph (1), if applicable, including any timeframe for response when such submission is not part of a regulatory application or other submission that has an associated timeframe for response; and

''(8) how the Secretary, if appropriate, anticipates using relevant patient experience data and related information, including with respect to the structured risk-benefit assessment framework described in section 505(d) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(d)), to inform regulatory decisionmaking.''

STREAMLINING PATIENT INPUT

Pub. L. 114–255, div. A, title III, § 3003, Dec. 13, 2016, 130 Stat. 1085, provided that: ''Chapter 35 of title 44, United States Code, shall not apply to the collection of information to which a response is voluntary, that is initiated by the Secretary under section 569C of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb–8c) (as amended by section 3001) or section 3002 [set out as a note above].''

§ 360bbb–8d. Notification, nondistribution, and recall of controlled substances

(a) Order to cease distribution and recall

(1) In general

If the Secretary determines there is a reasonable probability that a controlled substance would cause serious adverse health consequences or death, the Secretary may, after providing the appropriate person with an opportunity to consult with the agency, issue an order requiring manufacturers, importers, distributors, or pharmacists, who distribute such controlled substance to immediately cease distribution of such controlled substance.

(2) Hearing

An order under paragraph (1) shall provide the person subject to the order with an oppor-

tunity for an informal hearing, to be held not later than 10 days after the date of issuance of the order, on whether adequate evidence exists to justify an amendment to the order, and what actions are required by such amended order pursuant to subparagraph (3).

(3) Order resolution

After an order is issued according to the process under paragraphs (1) and (2), the Secretary shall, except as provided in paragraph (4)—

(A) vacate the order, if the Secretary determines that inadequate grounds exist to support the actions required by the order;

(B) continue the order ceasing distribution of the controlled substance until a date specified in such order; or

(C) amend the order to require a recall of the controlled substance, including any requirements to notify appropriate persons, a timetable for the recall to occur, and a schedule for updates to be provided to the Secretary regarding such recall.

(4) Risk assessment

If the Secretary determines that the risk of recalling a controlled substance presents a greater health risk than the health risk of not recalling such controlled substance from use, an amended order under subparagraph (B) or (C) of paragraph (3) shall not include either a recall order for, or an order to cease distribution of, such controlled substance, as applicable.

(5) Action following order

Any person who is subject to an order pursuant to subparagraph (B) or (C) of paragraph (3) shall immediately cease distribution of or recall, as applicable, the controlled substance and provide notification as required by such order.

(b) Notice to persons affected

If the Secretary determines necessary, the Secretary may require the person subject to an order pursuant to paragraph (1) or an amended order pursuant to subparagraph (B) or (C) of paragraph (3) to provide either a notice of a recall order for, or an order to cease distribution of, such controlled substance, as applicable, under this section to appropriate persons, including persons who manufacture, distribute, import, or offer for sale such product that is the subject of an order and to the public. In providing such notice, the Secretary may use the assistance of health professionals who prescribed or dispensed such controlled substances.

(c) Nondelegation

An order described in subsection (a)(3) shall be ordered by the Secretary or an official designated by the Secretary. An official may not be so designated under this section unless the official is the Director of the Center for Drug Evaluation and Research or an official senior to such Director.

(d) Savings clause

Nothing contained in this section shall be construed as limiting—

(1) the authority of the Secretary to issue an order to cease distribution of, or to recall, any drug under any other provision of this chapter or the Public Health Service Act [42 U.S.C. 201 et seq.]; or

(2) the ability of the Secretary to request any person to perform a voluntary activity related to any drug subject to this chapter or the Public Health Service Act.

(June 25, 1938, ch. 675, § 569D, as added Pub. L. 115–271, title III, § 3012(b), Oct. 24, 2018, 132 Stat. 3935.)

Editorial Notes

REFERENCES IN TEXT

The Public Health Service Act, referred to in subsec. (d), is act July 1, 1944, ch. 373, 58 Stat. 682, which is classified generally to chapter 6A (§ 201 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 201 of Title 42 and Tables.

PART F—NEW ANIMAL DRUGS FOR MINOR USE AND MINOR SPECIES

§ 360ccc. Conditional approval of new animal drugs for minor use and minor species and certain new animal drugs

(a) Application requirements

(1)(A) Except as provided in paragraph (3), any person may file with the Secretary an application for conditional approval of—

(i) a new animal drug intended for a minor use or a minor species; or

(ii) a new animal drug not intended for a minor use or minor species—

(I) that is intended to treat a serious or life-threatening disease or condition or addresses an unmet animal or human health need; and

(II) for which the Secretary determines that a demonstration of effectiveness would require a complex or particularly difficult study or studies.

(B) The Secretary shall, not later than September 30, 2019, issue guidance or regulations further clarifying the criteria specified in subparagraph (A)(ii).

(C) An application under this paragraph shall comply in all respects with the provisions of section 360b of this title except for subsections (a)(4), (b)(2), (c)(1), (c)(2), (c)(3), (d)(1), (e), (h), and (n) of such section unless otherwise stated in this section, and any additional provisions of this section.

(D) New animal drugs for which conditional approval is sought under this section are subject to the same safety standards that would be applied to new animal drugs under section 360b(d) of this title (including, for antimicrobial new animal drugs, with respect to antimicrobial resistance).

(2) The applicant shall submit to the Secretary as part of an application for the conditional approval of a new animal drug—

(A) all information necessary to meet the requirements of section 360b(b)(1) of this title except section 360b(b)(1)(A) of this title;

(B) full reports of investigations which have been made to show whether or not such drug is safe under section 360b(d) of this title (in-

cluding, for an antimicrobial new animal drug, with respect to antimicrobial resistance) and there is a reasonable expectation of effectiveness for use;

(C) data for establishing a conditional dose;

(D) projections of expected need and the justification for that expectation based on the best information available;

(E) information regarding the quantity of drug expected to be distributed on an annual basis to meet the expected need; and

(F) a commitment that the applicant will conduct additional investigations to meet the requirements for the full demonstration of effectiveness under section 360b(d)(1)(E) of this title within 5 years.

(3)(A) A person may not file an application under paragraph (1) if—

(i) the application seeks conditional approval of a new animal drug that is contained in, or is a product of, a transgenic animal.[1]

(ii) the person has previously filed an application for conditional approval under paragraph (1) for the same drug in the same dosage form for the same intended use whether or not subsequently conditionally approved by the Secretary under subsection (b); or

(iii) the person obtained the application, or data or other information contained therein, directly or indirectly from the person who filed for conditional approval under paragraph (1) for the same drug in the same dosage form for the same intended use whether or not subsequently conditionally approved by the Secretary under subsection (b).

(B) A person may not file an application under paragraph (1)(A)(ii) if the application seeks conditional approval of a new animal drug that contains an antimicrobial active ingredient.

(4) Beginning on October 1, 2018, all applications or submissions pursuant to this subsection shall be submitted by electronic means in such format as the Secretary may require.

(b) Order of approval or hearing

Within 180 days after the filing of an application pursuant to subsection (a), or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either—

(1) issue an order, effective for one year, conditionally approving the application if the Secretary finds that none of the grounds for denying conditional approval, specified in subsection (c) of this section applies and publish a Federal Register notice of the conditional approval, or

(2) give the applicant notice of an opportunity for an informal hearing on the question whether such application can be conditionally approved.

(c) Order of approval or refusal after hearing

If the Secretary finds, after giving the applicant notice and an opportunity for an informal hearing, that—

(1) any of the provisions of section 360b(d)(1)(A) through (D) or (F) through (I) of this title are applicable;

(2) the information submitted to the Secretary as part of the application and any other information before the Secretary with respect to such drug, is insufficient to show that there is a reasonable expectation that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or

(3) another person has received approval under section 360b of this title for the same drug in the same dosage form for the same intended use, and that person is able to assure the availability of sufficient quantities of the drug to meet the needs for which the drug is intended;

the Secretary shall issue an order refusing to conditionally approve the application. If, after such notice and opportunity for an informal hearing, the Secretary finds that paragraphs (1) through (3) do not apply, the Secretary shall issue an order conditionally approving the application effective for one year and publish a Federal Register notice of the conditional approval. Any order issued under this subsection refusing to conditionally approve an application shall state the findings upon which it is based.

(d) Effective period; renewal; refusal of renewal

A conditional approval under this section is effective for a 1-year period and is thereafter renewable by the Secretary annually for up to 4 additional 1-year terms. A conditional approval shall be in effect for no more than 5 years from the date of approval under subsection (b)(1) or (c) of this section unless extended as provided for in subsection (h) of this section. The following shall also apply:

(1) No later than 90 days from the end of the 1-year period for which the original or renewed conditional approval is effective, the applicant may submit a request to renew a conditional approval for an additional 1-year term.

(2) A conditional approval shall be deemed renewed at the end of the 1-year period, or at the end of a 90-day extension that the Secretary may, at the Secretary's discretion, grant by letter in order to complete review of the renewal request, unless the Secretary determines before the expiration of the 1-year period or the 90-day extension that—

(A) the applicant failed to submit a timely renewal request;

(B) the request fails to contain sufficient information to show that—

(i) the applicant is making sufficient progress toward meeting approval requirements under section 360b(d)(1)(E) of this title, and is likely to be able to fulfill those requirements and obtain an approval under section 360b of this title before the expiration of the 5-year maximum term of the conditional approval;

(ii) the quantity of the drug that has been distributed is consistent with the conditionally approved intended use and conditions of use, unless there is adequate explanation that ensures that the drug is only used for its intended purpose; or

(iii) the same drug in the same dosage form for the same intended use has not re-

[1] So in original. The period probably should be a semicolon.

ceived approval under section 360b of this title, or if such a drug has been approved, that the holder of the approved application is unable to assure the availability of sufficient quantities of the drug to meet the needs for which the drug is intended; or

(C) any of the provisions of section 360b(e)(1)(A) through (B) or (D) through (F) of this title are applicable.

(3) If the Secretary determines before the end of the 1-year period or the 90-day extension, if granted, that a conditional approval should not be renewed, the Secretary shall issue an order refusing to renew the conditional approval, and such conditional approval shall be deemed withdrawn and no longer in effect. The Secretary shall thereafter provide an opportunity for an informal hearing to the applicant on the issue whether the conditional approval shall be reinstated.

(4)(A) In the case of an application under subsection (a) with respect to a drug for which the Secretary provides notice to the sponsor that the Secretary intends to issue a scientific and medical evaluation and recommend controls under the Controlled Substances Act [21 U.S.C. 801 et seq.], conditional approval of such application shall not take effect until the interim final rule controlling the drug is issued in accordance with section 201(j) of the Controlled Substances Act [21 U.S.C. 811(j)].

(B) For purposes of this section, with respect to an application described in subparagraph (A), the term ''date of approval'' shall mean the later of—

(i) the date an application under subsection (a) is conditionally approved under subsection (b); or

(ii) the date of issuance of the interim final rule controlling the drug.

(e) Withdrawal of conditional approval

(1) The Secretary shall issue an order withdrawing conditional approval of an application filed pursuant to subsection (a) if the Secretary finds that another person has received approval under section 360b of this title for the same drug in the same dosage form for the same intended use and that person is able to assure the availability of sufficient quantities of the drug to meet the needs for which the drug is intended.

(2) The Secretary shall, after due notice and opportunity for an informal hearing to the applicant, issue an order withdrawing conditional approval of an application filed pursuant to subsection (a) if the Secretary finds that—

(A) any of the provisions of section 360b(e)(1)(A) through (B) or (D) through (F) of this title are applicable; or

(B) on the basis of new information before the Secretary with respect to such drug, evaluated together with the evidence available to the Secretary when the application was conditionally approved, that there is not a reasonable expectation that such drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof.

(3) The Secretary may also, after due notice and opportunity for an informal hearing to the applicant, issue an order withdrawing conditional approval of an application filed pursuant to subsection (a) if the Secretary finds that any of the provisions of section 360b(e)(2) of this title are applicable.

(f) Labeling

(1) The label and labeling of a new animal drug with a conditional approval under this section shall for the conditionally approved use—

(A) bear the statement, ''conditionally approved by FDA pending a full demonstration of effectiveness under application number''; and

(B) contain such other information as prescribed by the Secretary.

(2) The Secretary shall, through regulation or guidance, determine under what conditions an intended use that is the subject of a conditional approval under this section may be included in the same product label with any intended use approved under section 360b of this title.

(g) Amendment of application

A conditionally approved new animal drug application may not be amended or supplemented to add indications for use.

(h) Order of approval after conditional approval period termination

180 days prior to the termination date established under subsection (d) of this section, an applicant shall have submitted all the information necessary to support a complete new animal drug application in accordance with section 360b(b)(1) of this title or the conditional approval issued under this section is no longer in effect. Following review of this information, the Secretary shall either—

(1) issue an order approving the application under section 360b(c) of this title if the Secretary finds that none of the grounds for denying approval specified in section 360b(d)(1) of this title applies, or

(2) give the applicant an opportunity for a hearing before the Secretary under section 360b(d) of this title on the question whether such application can be approved.

Upon issuance of an order approving the application, product labeling and administrative records of approval shall be modified accordingly. If the Secretary has not issued an order under section 360b(c) of this title approving such application prior to the termination date established under subsection (d) of this section, the conditional approval issued under this section is no longer in effect unless the Secretary grants an extension of an additional 180-day period so that the Secretary can complete review of the application. The decision to grant an extension is committed to the discretion of the Secretary and not subject to judicial review.

(i) Judicial review

The decision of the Secretary under subsection (c), (d), or (e) of this section refusing or withdrawing conditional approval of an application shall constitute final agency action subject to judicial review.

(j) Definition

In this section and section 360ccc–1 of this title, the term ''transgenic animal'' means an

animal whose genome contains a nucleotide sequence that has been intentionally modified in vitro, and the progeny of such an animal; Provided that the term ''transgenic animal'' does not include an animal of which the nucleotide sequence of the genome has been modified solely by selective breeding.

(k) Sunset

(1) The Secretary's authority to grant conditional approval of new animal drugs not intended for a minor use or minor species pursuant to subsection (a)(1)(A)(ii) terminates on October 1, 2028.

(2) The Secretary—

(A) may not accept any new applications for such conditional approval pursuant to subsection (a)(1)(A)(ii) on or after such date; and

(B) may continue all activities under this section with respect to drugs that were conditionally approved pursuant to[2] (a)(1)(A)(ii) prior to such date.

(3) The Secretary may, until October 1, 2032, accept applications for approval under[3] 360b of this title of drugs conditionally approved pursuant to[2] (a)(1)(A)(ii).

(June 25, 1938, ch. 675, § 571, as added Pub. L. 108–282, title I, § 102(b)(4), Aug. 2, 2004, 118 Stat. 892; amended Pub. L. 114–89, § 2(a)(3)(B), Nov. 25, 2015, 129 Stat. 699; Pub. L. 115–234, title III, §§ 301(b), 304(a), Aug. 14, 2018, 132 Stat. 2436.)

Editorial Notes

REFERENCES IN TEXT

The Controlled Substances Act, referred to in subsec. (d)(4)(A), is title II of Pub. L. 91–513, Oct. 27, 1970, 84 Stat. 1242, which is classified principally to subchapter I (§ 801 et seq.) of chapter 13 of this title. For complete classification of this Act to the Code, see Short Title note set out under section 801 of this title and Tables.

AMENDMENTS

2018—Pub. L. 115–234, § 304(a)(1), substituted ''species and certain new animal drugs'' for ''species'' in section catchline.

Subsec. (a)(1). Pub. L. 115–234, § 304(a)(2)(A), amended par. (1) generally. Prior to amendment, par. (1) read as follows: ''Except as provided in paragraph (3) of this section, any person may file with the Secretary an application for conditional approval of a new animal drug intended for a minor use or a minor species. Such an application may not be a supplement to an application approved under section 360b of this title. Such application must comply in all respects with the provisions of section 360b of this title except sections 360b(a)(4), 360b(b)(2), 360b(c)(1), 360b(c)(2), 360b(c)(3), 360b(d)(1), 360b(e), 360b(h), and 360b(n) of this title unless otherwise stated in this section, and any additional provisions of this section. New animal drugs are subject to application of the same safety standards that would be applied to such drugs under section 360b(d) of this title (including, for antimicrobial new animal drugs, with respect to antimicrobial resistance).''

Subsec. (a)(3). Pub. L. 115–234, § 304(a)(2)(B), designated existing provisions as subpar. (A), redesignated former subpars. (A) to (C) as cls. (i) to (iii), respectively, of subpar. (A), and added subpar. (B).

Subsec. (a)(4). Pub. L. 115–234, § 301(b), added par. (4).

Subsec. (f)(1). Pub. L. 115–234, § 304(a)(3)(A), inserted ''for the conditionally approved use'' after ''shall'' in introductory provisions.

Subsec. (f)(2). Pub. L. 115–234, § 304(a)(3)(B), substituted ''The Secretary shall, through regulation or guidance, determine under what conditions an intended use'' for ''An intended use'' and ''may be included'' for ''shall not be included''.

Subsec. (k). Pub. L. 115–234, § 304(a)(4), added subsec. (k).

2015—Subsec. (d)(4). Pub. L. 114–89 added par. (4).

Statutory Notes and Related Subsidiaries

FINDINGS

Pub. L. 108–282, title I, § 102(a), Aug. 2, 2004, 118 Stat. 891, provided that: ''Congress makes the following findings:

''(1) There is a severe shortage of approved new animal drugs for use in minor species.

''(2) There is a severe shortage of approved new animal drugs for treating animal diseases and conditions that occur infrequently or in limited geographic areas.

''(3) Because of the small market shares, low-profit margins involved, and capital investment required, it is generally not economically feasible for new animal drug applicants to pursue approvals for these species, diseases, and conditions.

''(4) Because the populations for which such new animal drugs are intended may be small and conditions of animal management may vary widely, it is often difficult to design and conduct studies to establish drug safety and effectiveness under traditional new animal drug approval processes.

''(5) It is in the public interest and in the interest of animal welfare to provide for special procedures to allow the lawful use and marketing of certain new animal drugs for minor species and minor uses that take into account these special circumstances and that ensure that such drugs do not endanger animal or public health.

''(6) Exclusive marketing rights for clinical testing expenses have helped encourage the development of 'orphan' drugs for human use, and comparable incentives should encourage the development of new animal drugs for minor species and minor uses.''

REGULATIONS

Pub. L. 108–282, title I, § 102(b)(6), Aug. 2, 2004, 118 Stat. 905, provided that: ''On the date of enactment of this Act [Aug. 2, 2004], the Secretary of Health and Human Services shall implement sections 571 and 573 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360ccc, 360ccc–2] and subsequently publish implementing regulations. Not later than 12 months after the date of enactment of this Act, the Secretary shall issue proposed regulations to implement section 573 of the Federal Food, Drug, and Cosmetic Act (as added by this Act), and not later than 24 months after the date of enactment of this Act, the Secretary shall issue final regulations implementing section 573 of the Federal Food, Drug, and Cosmetic Act. Not later than 18 months after the date of enactment of this Act, the Secretary shall issue proposed regulations to implement section 572 of the Federal Food, Drug, and Cosmetic Act (as added by this Act) [21 U.S.C. 360ccc–1], and not later than 36 months after the date of enactment of this Act, the Secretary shall issue final regulations implementing section 572 of the Federal Food, Drug, and Cosmetic Act. Not later than 30 months after the date of enactment of this Act, the Secretary shall issue proposed regulations to implement section 571 of the Federal Food, Drug, and Cosmetic Act (as added by this Act), and not later than 42 months after the date of enactment of this Act, the Secretary shall issue final regulations implementing section 571 of the Federal Food, Drug, and Cosmetic Act. These timeframes shall be extended by 12 months for each fiscal year, in which the funds authorized to be appropriated under subsection (i) [no subsection (i) of section 102 has been enacted] are not in fact appropriated.''

[2] So in original. The word ''subsection'' probably should appear.

[3] So in original. The word ''section'' probably should appear.

§ 360ccc–1. Index of legally marketed unapproved new animal drugs for minor species

(a) Establishment and content

(1) The Secretary shall establish an index limited to—

(A) new animal drugs intended for use in a minor species for which there is a reasonable certainty that the animal or edible products from the animal will not be consumed by humans or food-producing animals; and

(B) new animal drugs intended for use only in a hatchery, tank, pond, or other similar contained man-made structure in an early, non-food life stage of a food-producing minor species, where safety for humans is demonstrated in accordance with the standard of section 360b(d) of this title (including, for an antimicrobial new animal drug, with respect to antimicrobial resistance).

(2) The index shall not include a new animal drug that is contained in or a product of a transgenic animal.

(b) Conferences

Any person intending to file a request under this section shall be entitled to one or more conferences to discuss the requirements for indexing a new animal drug.

(c) Request for determination of eligibility for inclusion in index

(1) Any person may submit a request to the Secretary for a determination whether a new animal drug may be eligible for inclusion in the index. Such a request shall include—

(A) information regarding the need for the new animal drug, the species for which the new animal drug is intended, the proposed intended use and conditions of use, and anticipated annual distribution;

(B) information to support the conclusion that the proposed use meets the conditions of subparagraph (A) or (B) of subsection (a)(1) of this section;

(C) information regarding the components and composition of the new animal drug;

(D) a description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such new animal drug;

(E) an environmental assessment that meets the requirements of the National Environmental Policy Act of 1969 [42 U.S.C. 4321 et seq.], as amended, and as defined in 21 CFR Part 25, as it appears on August 2, 2004, and amended thereafter or information to support a categorical exclusion from the requirement to prepare an environmental assessment;

(F) information sufficient to support the conclusion that the proposed use of the new animal drug is safe under section 360b(d) of this title with respect to individuals exposed to the new animal drug through its manufacture or use; and

(G) such other information as the Secretary may deem necessary to make this eligibility determination.

(2) Within 90 days after the submission of a request for a determination of eligibility for indexing based on subsection (a)(1)(A) of this section, or 180 days for a request submitted based on subsection (a)(1)(B) of this section, the Secretary shall grant or deny the request, and notify the person who requested such determination of the Secretary's decision. The Secretary shall grant the request if the Secretary finds that—

(A) the same drug in the same dosage form for the same intended use is not approved or conditionally approved;

(B) the proposed use of the drug meets the conditions of subparagraph (A) or (B) of subsection (a)(1), as appropriate;

(C) the person requesting the determination has established appropriate specifications for the manufacture and control of the new animal drug and has demonstrated an understanding of the requirements of current good manufacturing practices;

(D) the new animal drug will not significantly affect the human environment; and

(E) the new animal drug is safe with respect to individuals exposed to the new animal drug through its manufacture or use.

If the Secretary denies the request, the Secretary shall thereafter provide due notice and an opportunity for an informal conference. A decision of the Secretary to deny an eligibility request following an informal conference shall constitute final agency action subject to judicial review.

(d) Request for addition to index

(1) With respect to a new animal drug for which the Secretary has made a determination of eligibility under subsection (c), the person who made such a request may ask that the Secretary add the new animal drug to the index established under subsection (a). The request for addition to the index shall include—

(A) a copy of the Secretary's determination of eligibility issued under subsection (c);

(B) a written report that meets the requirements in subsection (d)(2) of this section;

(C) a proposed index entry;

(D) facsimile labeling;

(E) anticipated annual distribution of the new animal drug;

(F) a written commitment to manufacture the new animal drug and animal feeds bearing or containing such new animal drug according to current good manufacturing practices;

(G) a written commitment to label, distribute, and promote the new animal drug only in accordance with the index entry;

(H) upon specific request of the Secretary, information submitted to the expert panel described in paragraph (3); and

(I) any additional requirements that the Secretary may prescribe by general regulation or specific order.

(2) The report required in paragraph (1) shall—

(A) be authored by a qualified expert panel;

(B) include an evaluation of all available target animal safety and effectiveness information, including anecdotal information;

(C) state the expert panel's opinion regarding whether the benefits of using the new animal drug for the proposed use in a minor species outweigh its risks to the target animal,

taking into account the harm being caused by the absence of an approved or conditionally approved new animal drug for the minor species in question;

(D) include information from which labeling can be written; and

(E) include a recommendation regarding whether the new animal drug should be limited to use under the professional supervision of a licensed veterinarian.

(3) A qualified expert panel, as used in this section, is a panel that—

(A) is composed of experts qualified by scientific training and experience to evaluate the target animal safety and effectiveness of the new animal drug under consideration;

(B) operates external to FDA; and

(C) is not subject to chapter 10 of title 5.

The Secretary shall define the criteria for selection of a qualified expert panel and the procedures for the operation of the panel by regulation.

(4) Within 180 days after the receipt of a request for listing a new animal drug in the index, the Secretary shall grant or deny the request. The Secretary shall grant the request if the request for indexing continues to meet the eligibility criteria in subsection (a) and the Secretary finds, on the basis of the report of the qualified expert panel and other information available to the Secretary, that the benefits of using the new animal drug for the proposed use in a minor species outweigh its risks to the target animal, taking into account the harm caused by the absence of an approved or conditionally-approved new animal drug for the minor species in question. If the Secretary denies the request, the Secretary shall thereafter provide due notice and the opportunity for an informal conference. The decision of the Secretary following an informal conference shall constitute final agency action subject to judicial review.

(e) Index contents; publication

(1) The index established under subsection (a) shall include the following information for each listed drug—

(A) the name and address of the person who holds the index listing;

(B) the name of the drug and the intended use and conditions of use for which it is being indexed;

(C) product labeling; and

(D) conditions and any limitations that the Secretary deems necessary regarding use of the drug.

(2) The Secretary shall publish the index, and revise it periodically.

(3) The Secretary may establish by regulation a process for reporting changes in the conditions of manufacturing or labeling of indexed products.

(f) Removal from index; suspended listing

(1) If the Secretary finds, after due notice to the person who requested the index listing and an opportunity for an informal conference, that—

(A) the expert panel failed to meet the requirements as set forth by the Secretary by regulation;

(B) on the basis of new information before the Secretary, evaluated together with the evidence available to the Secretary when the new animal drug was listed in the index, the benefits of using the new animal drug for the indexed use do not outweigh its risks to the target animal;

(C) the conditions of subsection (c)(2) of this section are no longer satisfied;

(D) the manufacture of the new animal drug is not in accordance with current good manufacturing practices;

(E) the labeling, distribution, or promotion of the new animal drug is not in accordance with the index entry;

(F) the conditions and limitations of use associated with the index listing have not been followed; or

(G) the request for indexing contains any untrue statement of material fact,

the Secretary shall remove the new animal drug from the index. The decision of the Secretary following an informal conference shall constitute final agency action subject to judicial review.

(2) If the Secretary finds that there is a reasonable probability that the use of the drug would present a risk to the health of humans or other animals, the Secretary may—

(A) suspend the listing of such drug immediately;

(B) give the person listed in the index prompt notice of the Secretary's action; and

(C) afford that person the opportunity for an informal conference.

The decision of the Secretary following an informal conference shall constitute final agency action subject to judicial review.

(g) Regulations concerning exemptions for investigational use

For purposes of indexing new animal drugs under this section, to the extent consistent with the public health, the Secretary shall promulgate regulations for exempting from the operation of section 360b of this title minor species new animal drugs and animal feeds bearing or containing new animal drugs intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of minor species animal drugs. Such regulations may, at the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such article, of data (including but not limited to analytical reports by investigators) obtained as a result of such investigational use of such article, as the Secretary finds will enable the Secretary to evaluate the safety and effectiveness of such article in the event of the filing of a request for an index listing pursuant to this section.

(h) Labeling contents

The labeling of a new animal drug that is the subject of an index listing shall state, prominently and conspicuously—

(1) ''LEGAL STATUS—In order to be legally marketed, a new animal drug intended for a minor species must be Approved, Conditionally Approved, or Indexed by the Food and Drug Administration. THIS PRODUCT IS INDEXED—MIF #'' (followed by the applicable minor species index file number and a period) ''Extra-label use is prohibited.'';

(2) except in the case of new animal drugs indexed for use in an early life stage of a food-producing animal, ''This product is not to be used in animals intended for use as food for humans or food-producing animals.''; and

(3) such other information as may be prescribed by the Secretary in the index listing.

(i) Records and reports

(1) In the case of any new animal drug for which an index listing pursuant to subsection (a) is in effect, the person who has an index listing shall establish and maintain such records, and make such reports to the Secretary, of data relating to experience, and other data or information, received or otherwise obtained by such person with respect to such drug, or with respect to animal feeds bearing or containing such drug, as the Secretary may by general regulation, or by order with respect to such listing, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (f). Such regulation or order shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulation or order is applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this subsection to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

(j) Public disclosure of safety and effectiveness data

(1) Safety and effectiveness data and information which has been submitted in support of a request for a new animal drug to be indexed under this section and which has not been previously disclosed to the public shall be made available to the public, upon request, unless extraordinary circumstances are shown—

(A) if no work is being or will be undertaken to have the drug indexed in accordance with the request,

(B) if the Secretary has determined that such drug cannot be indexed and all legal appeals have been exhausted,

(C) if the indexing of such drug is terminated and all legal appeals have been exhausted, or

(D) if the Secretary has determined that such drug is not a new animal drug.

(2) Any request for data and information pursuant to paragraph (1) shall include a verified statement by the person making the request that any data or information received under such paragraph shall not be disclosed by such person to any other person—

(A) for the purpose of, or as part of a plan, scheme, or device for, obtaining the right to make, use, or market, or making, using, or marketing, outside the United States, the drug identified in the request for indexing; and

(B) without obtaining from any person to whom the data and information are disclosed an identical verified statement, a copy of which is to be provided by such person to the Secretary, which meets the requirements of this paragraph.

(k) Date of determination in the case of recommended controls under the CSA

In the case of a request under subsection (d) to add a drug to the index under subsection (a) with respect to a drug for which the Secretary provides notice to the person filing the request that the Secretary intends to issue a scientific and medical evaluation and recommend controls under the Controlled Substances Act [21 U.S.C. 801 et seq.], a determination to grant the request to add such drug to the index shall not take effect until the interim final rule controlling the drug is issued in accordance with section 201(j) of the Controlled Substances Act [21 U.S.C. 811(j)].

(June 25, 1938, ch. 675, §572, as added Pub. L. 108–282, title I, §102(b)(4), Aug. 2, 2004, 118 Stat. 896; amended Pub. L. 114–89, §2(a)(3)(C), Nov. 25, 2015, 129 Stat. 699; Pub. L. 115–234, title III, §302, Aug. 14, 2018, 132 Stat. 2436; Pub. L. 117–286, §4(a)(158), Dec. 27, 2022, 136 Stat. 4323.)

Editorial Notes

REFERENCES IN TEXT

The National Environmental Policy Act of 1969, referred to in subsec. (c)(1)(E), is Pub. L. 91–190, Jan. 1, 1970, 83 Stat. 852, which is classified generally to chapter 55 (§4321 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 4321 of Title 42 and Tables.

The Controlled Substances Act, referred to in subsec. (k), is title II of Pub. L. 91–513, Oct. 27, 1970, 84 Stat. 1242, which is classified principally to subchapter I (§801 et seq.) of chapter 13 of this title. For complete classification of this Act to the Code, see Short Title note set out under section 801 of this title and Tables.

AMENDMENTS

2022—Subsec. (d)(3)(C). Pub. L. 117–286 substituted ''chapter 10 of title 5.'' for ''the Federal Advisory Committee Act.''

2018—Subsec. (h)(1). Pub. L. 115–234, §302(1), amended par. (1) generally. Prior to amendment, par. (1) read as follows: '' 'NOT APPROVED BY FDA.—Legally marketed as an FDA indexed product. Extra-label use is prohibited.';''.

Subsec. (h)(2). Pub. L. 115–234, §302(2), substituted ''or food-producing animals'' for ''or other animals''.

2015—Subsec. (k). Pub. L. 114–89 added subsec. (k).

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE OF 2018 AMENDMENT

Pub. L. 115–234, title III, §302, Aug. 14, 2018, 132 Stat. 2436, provided that the amendment made by section 302 is effective Oct. 1, 2018.

§ 360ccc–2. Designated new animal drugs for minor use or minor species

(a) Designation

(1) The manufacturer or the sponsor of a new animal drug for a minor use or use in a minor

species may request that the Secretary declare that drug a ''designated new animal drug''. A request for designation of a new animal drug shall be made before the submission of an application under section 360b(b) of this title or section 360ccc of this title for the new animal drug.

(2) The Secretary may declare a new animal drug a ''designated new animal drug'' if—

(A) it is intended for a minor use or use in a minor species; and

(B) the same drug in the same dosage form for the same intended use is not approved under section 360b or 360ccc of this title or designated under this section at the time the request is made.

(3) Regarding the termination of a designation—

(A) the sponsor of a new animal drug shall notify the Secretary of any decision to discontinue active pursuit of approval under section 360b or 360ccc of this title of an application for a designated new animal drug. The Secretary shall terminate the designation upon such notification;

(B) the Secretary may also terminate designation if the Secretary independently determines that the sponsor is not actively pursuing approval under section 360b or 360ccc of this title with due diligence;

(C) the sponsor of an approved designated new animal drug shall notify the Secretary of any discontinuance of the manufacture of such new animal drug at least one year before discontinuance. The Secretary shall terminate the designation upon such notification; and

(D) the designation shall terminate upon the expiration of any applicable exclusivity period under subsection (c).

(4) Notice respecting the designation or termination of designation of a new animal drug shall be made available to the public.

(b) Grants and contracts for development of designated new animal drugs

(1) The Secretary may make grants to and enter into contracts with public and private entities and individuals to assist in defraying the costs of qualified safety and effectiveness testing expenses and manufacturing expenses incurred in connection with the development of designated new animal drugs.

(2) For purposes of paragraph (1) of this section—

(A) The term ''qualified safety and effectiveness testing'' means testing—

(i) which occurs after the date such new animal drug is designated under this section and before the date on which an application with respect to such drug is submitted under section 360b of this title; and

(ii) which is carried out under an investigational exemption under section 360b(j) of this title.

(B) The term ''manufacturing expenses'' means expenses incurred in developing processes and procedures associated with manufacture of the designated new animal drug which occur after the new animal drug is designated under this section and before the date on which an application with respect to such new animal drug is submitted under section 360b or 360ccc of this title.

(c) Exclusivity for designated new animal drugs

(1) Except as provided in subsection (c)(2), if the Secretary approves or conditionally approves an application for a designated new animal drug, the Secretary may not approve or conditionally approve another application submitted for such new animal drug with the same intended use as the designated new animal drug for another applicant before the expiration of seven years from the date of approval or conditional approval of the application.

(2) If an application filed pursuant to section 360b of this title or section 360ccc of this title is approved for a designated new animal drug, the Secretary may, during the 7-year exclusivity period beginning on the date of the application approval or conditional approval, approve or conditionally approve another application under section 360b of this title or section 360ccc of this title for such drug for such minor use or minor species for another applicant if—

(A) the Secretary finds, after providing the holder of such an approved application notice and opportunity for the submission of views, that in the granted exclusivity period the holder of the approved application cannot assure the availability of sufficient quantities of the drug to meet the needs for which the drug was designated; or

(B) such holder provides written consent to the Secretary for the approval or conditional approval of other applications before the expiration of such exclusivity period.

(3) For purposes of determining the 7-year period of exclusivity under paragraph (1) for a drug for which the Secretary intends to issue a scientific and medical evaluation and recommend controls under the Controlled Substances Act [21 U.S.C. 801 et seq.], the drug shall not be considered approved or conditionally approved until the date that the interim final rule controlling the drug is issued in accordance with section 201(j) of the Controlled Substances Act [21 U.S.C. 811(j)].

(June 25, 1938, ch. 675, §573, as added Pub. L. 108–282, title I, §102(b)(4), Aug. 2, 2004, 118 Stat. 900; amended Pub. L. 114–89, §2(a)(4), Nov. 25, 2015, 129 Stat. 700.)

Editorial Notes

REFERENCES IN TEXT

The Controlled Substances Act, referred to in subsec. (c)(3), is title II of Pub. L. 91–513, Oct. 27, 1970, 84 Stat. 1242, which is classified principally to subchapter I (§801 et seq.) of chapter 13 of this title. For complete classification of this Act to the Code, see Short Title note set out under section 801 of this title and Tables.

AMENDMENTS

2015—Subsec. (c)(3). Pub. L. 114–89 added par. (3).

PART G—MEDICAL GASES

§ 360ddd. Definitions

In this part:

(1) The term ''designated medical gas'' means any of the following:

(A) Oxygen that meets the standards set forth in an official compendium.

(B) Nitrogen that meets the standards set forth in an official compendium.

(C) Nitrous oxide that meets the standards set forth in an official compendium.

(D) Carbon dioxide that meets the standards set forth in an official compendium.

(E) Helium that meets the standards set forth in an official compendium.

(F) Carbon monoxide that meets the standards set forth in an official compendium.

(G) Medical air that meets the standards set forth in an official compendium.

(H) Any other medical gas deemed appropriate by the Secretary, after taking into account any investigational new drug application or investigational new animal drug application for the same medical gas submitted in accordance with regulations applicable to such applications in title 21 of the Code of Federal Regulations, unless any period of exclusivity for a new drug under section 355(c)(3)(E)(ii) of this title or section 355(j)(5)(F)(ii) of this title, or the extension of any such period under section 355a of this title, or any period of exclusivity for a new animal drug under section 360b(c)(2)(F) of this title, applicable to such medical gas has not expired.

(2) The term ''medical gas'' means a drug that—

(A) is manufactured or stored in a liquefied, nonliquefied, or cryogenic state; and

(B) is administered as a gas.

(June 25, 1938, ch. 675, §575, as added Pub. L. 112–144, title XI, §1111, July 9, 2012, 126 Stat. 1108; amended Pub. L. 114–255, div. A, title III, §3101(a)(2)(R), Dec. 13, 2016, 130 Stat. 1155.)

Editorial Notes

AMENDMENTS

2016—Par. (1)(H). Pub. L. 114–255 inserted ''for a new drug'' after ''any period of exclusivity'' and ''or any period of exclusivity for a new animal drug under section 360b(c)(2)(F) of this title,'' after ''section 355a of this title,''.

Statutory Notes and Related Subsidiaries

CHANGES TO REGULATIONS

Pub. L. 112–144, title XI, §1112, July 9, 2012, 126 Stat. 1111, provided that:

''(a) REPORT.—Not later than 18 months after the date of the enactment of this Act [July 9, 2012], the Secretary, after obtaining input from medical gas manufacturers and any other interested members of the public, shall—

''(1) determine whether any changes to the Federal drug regulations are necessary for medical gases; and

''(2) submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives a report regarding any such changes.

''(b) REGULATIONS.—If the Secretary determines under subsection (a) that changes to the Federal drug regulations are necessary for medical gases, the Secretary shall issue final regulations revising the Federal drug regulations with respect to medical gases not later than 48 months after the date of the enactment of this Act [July 9, 2012].

''(c) DEFINITIONS.—In this section:

''(1) The term 'Federal drug regulations' means regulations in title 21 of the Code of Federal Regulations pertaining to drugs.

''(2) The term 'medical gas' has the meaning given to such term in section 575 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360ddd], as added by section 1111 of this Act.

''(3) The term 'Secretary' means the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs.''

RULES OF CONSTRUCTION

Pub. L. 112–144, title XI, §1113, July 9, 2012, 126 Stat. 1112, provided that: ''Nothing in this subtitle [subtitle B (§§1111–1113) of title XI of Pub. L. 112–144, enacting this section and sections 360ddd–1 and 360ddd–2 of this title and provisions set out as notes under this section] and the amendments made by this subtitle applies with respect to—

''(1) a drug that is approved prior to May 1, 2012, pursuant to an application submitted under section 505 or 512 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355, 360b);

''(2) any gas listed in subparagraphs (A) through (G) of section 575(1) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360ddd(1)], as added by section 1111 of this Act, or any combination of any such gases, for an indication that—

''(A) is not included in, or is different from, those specified in subclauses (I) through (VII) of section 576(a)(3)(A)(i) of such Act [21 U.S.C. 360ddd–1(a)(3)(A)(i)]; and

''(B) is approved on or after May 1, 2012, pursuant to an application submitted under section 505 or 512 [21 U.S.C. 355, 360b]; or

''(3) any designated medical gas added pursuant to subparagraph (H) of section 575(1) of such Act [21 U.S.C. 360ddd(1)] for an indication that—

''(A) is not included in, or is different from, those originally added pursuant to subparagraph (H) of section 575(1) [21 U.S.C. 360ddd(1)(H)] and section 576(a)(3)(A)(i)(VIII) [21 U.S.C. 360ddd–1(a)(3)(A)(i)(VIII)]; and

''(B) is approved on or after May 1, 2012, pursuant to an application submitted under section 505 or 512 of such Act [21 U.S.C. 355, 360b].''

§ 360ddd–1. Regulation of medical gases

(a) Certification of designated medical gases

(1) Submission

Beginning 180 days after July 9, 2012, any person who seeks to initially introduce or deliver for introduction a designated medical gas into interstate commerce may file with the Secretary a request for certification of a medical gas as a designated medical gas. Any such request shall contain the following information:

(A) A description of the medical gas.

(B) The name and address of the sponsor.

(C) The name and address of the facility or facilities where the medical gas is or will be manufactured.

(D) Any other information deemed appropriate by the Secretary to determine whether the medical gas is a designated medical gas.

(2) Grant of certification

The certification requested under paragraph (1) is deemed to be granted unless, within 60 days of the filing of such request, the Secretary finds that—

(A) the medical gas subject to the certification is not a designated medical gas;

(B) the request does not contain the information required under paragraph (1) or otherwise lacks sufficient information to permit the Secretary to determine that the medical gas is a designated medical gas; or

(C) denying the request is necessary to protect the public health.

(3) Effect of certification

(A) In general

(i) Approved uses

A designated medical gas for which a certification is granted under paragraph (2) is deemed, alone or in combination, as medically appropriate, with another designated medical gas or gases for which a certification or certifications have been granted, to have in effect an approved application under section 355 or 360b of this title, subject to all applicable postapproval requirements, for the following indications for use:

(I) In the case of oxygen, the treatment or prevention of hypoxemia or hypoxia.

(II) In the case of nitrogen, use in hypoxic challenge testing.

(III) In the case of nitrous oxide, analgesia.

(IV) In the case of carbon dioxide, use in extracorporeal membrane oxygenation therapy or respiratory stimulation.

(V) In the case of helium, the treatment of upper airway obstruction or increased airway resistance.

(VI) In the case of medical air, to reduce the risk of hyperoxia.

(VII) In the case of carbon monoxide, use in lung diffusion testing.

(VIII) Any other indication for use for a designated medical gas or combination of designated medical gases deemed appropriate by the Secretary, unless any period of exclusivity for a new drug under clause (iii) or (iv) of section 355(c)(3)(E) of this title, clause (iii) or (iv) of section 355(j)(5)(F) of this title, or section 360cc of this title, or the extension of any such period under section 355a of this title, applicable to such indication for use for such gas or combination of gases has not expired.

(ii) Labeling

The requirements of sections 353(b)(4) and 352(f) of this title are deemed to have been met for a designated medical gas if the labeling on the final use container for such medical gas bears—

(I) the information required by section 353(b)(4) of this title;

(II) a warning statement concerning the use of the medical gas as determined by the Secretary by regulation; and

(III) appropriate directions and warnings concerning storage and handling.

(B) Inapplicability of exclusivity provisions

(i) No exclusivity for a certified medical gas

No designated medical gas deemed under subparagraph (A)(i) to have in effect an approved application is eligible for any period of exclusivity for a new drug under section 355(c), 355(j), or 360cc of this title, or the extension of any such period under section 355a of this title, on the basis of such deemed approval.

(ii) Effect on certification

No period of exclusivity under section 355(c), 355(j), or section 360cc of this title, or the extension of any such period under section 355a of this title, with respect to an application for a drug product, shall prohibit, limit, or otherwise affect the submission, grant, or effect of a certification under this section, except as provided in subsection (a)(3)(A)(i)(VIII) and section 360ddd(1)(H) of this title.

(4) Withdrawal, suspension, or revocation of approval

(A) Withdrawal, suspension of approval

Nothing in this part limits the Secretary's authority to withdraw or suspend approval of a drug product, including a designated medical gas deemed under this section to have in effect an approved application under section 355 of this title or section 360b of this title.

(B) Revocation of certification

The Secretary may revoke the grant of a certification under paragraph (2) if the Secretary determines that the request for certification contains any material omission or falsification.

(b) Prescription requirement

(1) In general

A designated medical gas shall be subject to the requirements of section 353(b)(1) of this title unless the Secretary exercises the authority provided in section 353(b)(3) of this title to remove such medical gas from the requirements of section 353(b)(1) of this title, the gas is approved for use without a prescription pursuant to an application under section 355 or 360b of this title, or the use in question is authorized pursuant to another provision of this chapter relating to use of medical products in emergencies.

(2) Oxygen

(A) No prescription required for certain uses

Notwithstanding paragraph (1), oxygen may be provided without a prescription for the following uses:

(i) For use in the event of depressurization or other environmental oxygen deficiency.

(ii) For oxygen deficiency or for use in emergency resuscitation, when administered by properly trained personnel.

(B) Labeling

For oxygen provided pursuant to subparagraph (A), the requirements of section 353(b)(4) of this title shall be deemed to have been met if its labeling bears a warning that the oxygen can be used for emergency use only and for all other medical applications a prescription is required.

(June 25, 1938, ch. 675, § 576, as added Pub. L. 112–144, title XI, § 1111, July 9, 2012, 126 Stat. 1109; amended Pub. L. 114–255, div. A, title III, § 3101(a)(2)(S), Dec. 13, 2016, 130 Stat. 1155.)

Editorial Notes

AMENDMENTS

2016—Subsec. (a)(1). Pub. L. 114–255, § 3101(a)(2)(S)(i), inserted ''who seeks to initially introduce or deliver for introduction a designated medical gas into interstate commerce'' after ''any person'' in introductory provisions.

Subsec. (a)(3)(A)(i)(VIII). Pub. L. 114–255, § 3101(a)(2)(S)(ii)(I)(aa), inserted ''for a new drug'' after ''any period of exclusivity''.

Subsec. (a)(3)(A)(ii). Pub. L. 114–255, § 3101(a)(2)(S)(ii)(I)(bb), inserted ''the'' before ''final use'' in introductory provisions.

Subsec. (a)(3)(B)(i). Pub. L. 114–255, § 3101(a)(2)(S)(ii)(II)(aa), inserted ''for a new drug'' after ''any period of exclusivity''.

Subsec. (a)(3)(B)(ii). Pub. L. 114–255, § 3101(a)(2)(S)(ii)(II)(bb), inserted comma after ''drug product''.

§ 360ddd–2. Inapplicability of drug fees to designated medical gases

A designated medical gas, alone or in combination with another designated gas or gases (as medically appropriate) deemed under section 360ddd–1 of this title to have in effect an approved application shall not be assessed fees under section 379h(a) or 379j–12(a) of this title on the basis of such deemed approval.

(June 25, 1938, ch. 675, § 577, as added Pub. L. 112–144, title XI, § 1111, July 9, 2012, 126 Stat. 1111; amended Pub. L. 114–255, div. A, title III, § 3101(a)(2)(T), Dec. 13, 2016, 130 Stat. 1155.)

Editorial Notes

AMENDMENTS

2016—Pub. L. 114–255 inserted ''or 379j–12(a)'' after ''section 379h(a)''.

PART H—PHARMACEUTICAL DISTRIBUTION SUPPLY CHAIN

§ 360eee. Definitions

In this part:

(1) Affiliate

The term ''affiliate'' means a business entity that has a relationship with a second business entity if, directly or indirectly—

(A) one business entity controls, or has the power to control, the other business entity; or

(B) a third party controls, or has the power to control, both of the business entities.

(2) Authorized

The term ''authorized'' means—

(A) in the case of a manufacturer or repackager, having a valid registration in accordance with section 360 of this title;

(B) in the case of a wholesale distributor, having a valid license under State law or section 360eee–2 of this title, in accordance with section 360eee–1(a)(6) of this title, and complying with the licensure reporting requirements under section 353(e) of this title;

(C) in the case of a third-party logistics provider, having a valid license under State law or section 360eee–3(a)(1) of this title, in accordance with section 360eee–1(a)(7) of this title, and complying with the licensure reporting requirements under section 360eee–3(b) of this title; and

(D) in the case of a dispenser, having a valid license under State law.

(3) Dispenser

The term ''dispenser''—

(A) means a retail pharmacy, hospital pharmacy, a group of chain pharmacies under common ownership and control that do not act as a wholesale distributor, or any other person authorized by law to dispense or administer prescription drugs, and the affiliated warehouses or distribution centers of such entities under common ownership and control that do not act as a wholesale distributor; and

(B) does not include a person who dispenses only products to be used in animals in accordance with section 360b(a)(5) of this title.

(4) Disposition

The term ''disposition'', with respect to a product within the possession or control of an entity, means the removal of such product from the pharmaceutical distribution supply chain, which may include disposal or return of the product for disposal or other appropriate handling and other actions, such as retaining a sample of the product for further additional physical examination or laboratory analysis of the product by a manufacturer or regulatory or law enforcement agency.

(5) Distribute or distribution

The term ''distribute'' or ''distribution'' means the sale, purchase, trade, delivery, handling, storage, or receipt of a product, and does not include the dispensing of a product pursuant to a prescription executed in accordance with section 353(b)(1) of this title or the dispensing of a product approved under section 360b(b) of this title.

(6) Exclusive distributor

The term ''exclusive distributor'' means the wholesale distributor that directly purchased the product from the manufacturer and is the sole distributor of that manufacturer's product to a subsequent repackager, wholesale distributor, or dispenser.

(7) Homogeneous case

The term ''homogeneous case'' means a sealed case containing only product that has a single National Drug Code number belonging to a single lot.

(8) Illegitimate product

The term ''illegitimate product'' means a product for which credible evidence shows that the product—

(A) is counterfeit, diverted, or stolen;

(B) is intentionally adulterated such that the product would result in serious adverse health consequences or death to humans;

(C) is the subject of a fraudulent transaction; or

(D) appears otherwise unfit for distribution such that the product would be reasonably likely to result in serious adverse health consequences or death to humans.

(9) Licensed

The term ''licensed'' means—

(A) in the case of a wholesale distributor, having a valid license in accordance with section 353(e) of this title or section 360eee–1(a)(6) of this title, as applicable;

(B) in the case of a third-party logistics provider, having a valid license in accordance with section 360eee–3(a) of this title or section 360eee–1(a)(7) of this title, as applicable; and

(C) in the case of a dispenser, having a valid license under State law.

(10) Manufacturer

The term ''manufacturer'' means, with respect to a product—

(A) a person that holds an application approved under section 355 of this title or a license issued under section 262 of title 42 for such product, or if such product is not the subject of an approved application or license, the person who manufactured the product;

(B) a co-licensed partner of the person described in subparagraph (A) that obtains the product directly from a person described in this subparagraph or subparagraph (A) or (C); or

(C) an affiliate of a person described in subparagraph (A) or (B) that receives the product directly from a person described in this subparagraph or subparagraph (A) or (B).

(11) Package

(A) In general

The term ''package'' means the smallest individual saleable unit of product for distribution by a manufacturer or repackager that is intended by the manufacturer for ultimate sale to the dispenser of such product.

(B) Individual saleable unit

For purposes of this paragraph, an ''individual saleable unit'' is the smallest container of product introduced into commerce by the manufacturer or repackager that is intended by the manufacturer or repackager for individual sale to a dispenser.

(12) Prescription drug

The term ''prescription drug'' means a drug for human use subject to section 353(b)(1) of this title.

(13) Product

The term ''product'' means a prescription drug in a finished dosage form for administration to a patient without substantial further manufacturing (such as capsules, tablets, and lyophilized products before reconstitution), but for purposes of section 360eee–1 of this title, does not include blood or blood components intended for transfusion, radioactive drugs or radioactive biological products (as defined in section 600.3(ee) of title 21, Code of Federal Regulations) that are regulated by the Nuclear Regulatory Commission or by a State pursuant to an agreement with such Commission under section 2021 of title 42, imaging drugs, an intravenous product described in clause (xiv), (xv), or (xvi) of paragraph (24)(B), any medical gas (as defined in section 360ddd of this title), homeopathic drugs marketed in accordance with applicable guidance under this chapter, or a drug compounded in compliance with section 353a or 353b of this title.

(14) Product identifier

The term ''product identifier'' means a standardized graphic that includes, in both human-readable form and on a machine-readable data carrier that conforms to the standards developed by a widely recognized international standards development organization, the standardized numerical identifier, lot number, and expiration date of the product.

(15) Quarantine

The term ''quarantine'' means the storage or identification of a product, to prevent distribution or transfer of the product, in a physically separate area clearly identified for such use or through other procedures.

(16) Repackager

The term ''repackager'' means a person who owns or operates an establishment that repacks and relabels a product or package for—

(A) further sale; or

(B) distribution without a further transaction.

(17) Return

The term ''return'' means providing product to the authorized immediate trading partner from which such product was purchased or received, or to a returns processor or reverse logistics provider for handling of such product.

(18) Returns processor or reverse logistics provider

The term ''returns processor'' or ''reverse logistics provider'' means a person who owns or operates an establishment that dispositions or otherwise processes saleable or nonsaleable product received from an authorized trading partner such that the product may be processed for credit to the purchaser, manufacturer, or seller or disposed of for no further distribution.

(19) Specific patient need

The term ''specific patient need'' refers to the transfer of a product from one pharmacy to another to fill a prescription for an identified patient. Such term does not include the transfer of a product from one pharmacy to another for the purpose of increasing or replenishing stock in anticipation of a potential need.

(20) Standardized numerical identifier

The term ''standardized numerical identifier'' means a set of numbers or characters used to uniquely identify each package or homogenous case that is composed of the National Drug Code that corresponds to the specific product (including the particular package configuration) combined with a unique alphanumeric serial number of up to 20 characters.

(21) Suspect product

The term ''suspect product'' means a product for which there is reason to believe that such product—

(A) is potentially counterfeit, diverted, or stolen;

(B) is potentially intentionally adulterated such that the product would result in serious adverse health consequences or death to humans;

(C) is potentially the subject of a fraudulent transaction; or

(D) appears otherwise unfit for distribution such that the product would result in serious adverse health consequences or death to humans.

(22) Third-party logistics provider

The term ''third-party logistics provider'' means an entity that provides or coordinates warehousing, or other logistics services of a product in interstate commerce on behalf of a manufacturer, wholesale distributor, or dispenser of a product, but does not take ownership of the product, nor have responsibility to direct the sale or disposition of the product.

(23) Trading partner

The term ''trading partner'' means—

(A) a manufacturer, repackager, wholesale distributor, or dispenser from whom a manufacturer, repackager, wholesale distributor, or dispenser accepts direct ownership of a product or to whom a manufacturer, repackager, wholesale distributor, or dispenser transfers direct ownership of a product; or

(B) a third-party logistics provider from whom a manufacturer, repackager, wholesale distributor, or dispenser accepts direct possession of a product or to whom a manufacturer, repackager, wholesale distributor, or dispenser transfers direct possession of a product.

(24) Transaction

(A) In general

The term ''transaction'' means the transfer of product between persons in which a change of ownership occurs.

(B) Exemptions

The term ''transaction'' does not include—

(i) intracompany distribution of any product between members of an affiliate or within a manufacturer;

(ii) the distribution of a product among hospitals or other health care entities that are under common control;

(iii) the distribution of a product for emergency medical reasons including a public health emergency declaration pursuant to section 247d of title 42, except that a drug shortage not caused by a public health emergency shall not constitute an emergency medical reason;

(iv) the dispensing of a product pursuant to a prescription executed in accordance with section 353(b)(1) of this title;

(v) the distribution of product samples by a manufacturer or a licensed wholesale distributor in accordance with section 353(d) of this title;

(vi) the distribution of blood or blood components intended for transfusion;

(vii) the distribution of minimal quantities of product by a licensed retail pharmacy to a licensed practitioner for office use;

(viii) the sale, purchase, or trade of a drug or an offer to sell, purchase, or trade a drug by a charitable organization described in section 501(c)(3) of title 26 to a nonprofit affiliate of the organization to the extent otherwise permitted by law;

(ix) the distribution of a product pursuant to the sale or merger of a pharmacy or pharmacies or a wholesale distributor or wholesale distributors, except that any records required to be maintained for the product shall be transferred to the new owner of the pharmacy or pharmacies or wholesale distributor or wholesale distributors;

(x) the dispensing of a product approved under section 360b(c) of this title;

(xi) products transferred to or from any facility that is licensed by the Nuclear Regulatory Commission or by a State pursuant to an agreement with such Commission under section 2021 of title 42;

(xii) a combination product that is not subject to approval under section 355 of this title or licensure under section 262 of title 42, and that is—

(I) a product comprised of a device and 1 or more other regulated components (such as a drug/device, biologic/device, or drug/device/biologic) that are physically, chemically, or otherwise combined or mixed and produced as a single entity;

(II) 2 or more separate products packaged together in a single package or as a unit and comprised of a drug and device or device and biological product; or

(III) 2 or more finished medical devices plus one or more drug or biological products that are packaged together in what is referred to as a ''medical convenience kit'' as described in clause (xiii);

(xiii) the distribution of a collection of finished medical devices, which may include a product or biological product, assembled in kit form strictly for the convenience of the purchaser or user (referred to in this clause as a ''medical convenience kit'') if—

(I) the medical convenience kit is assembled in an establishment that is registered with the Food and Drug Administration as a device manufacturer in accordance with section 360(b)(2) of this title;

(II) the medical convenience kit does not contain a controlled substance that appears in a schedule contained in the Comprehensive Drug Abuse Prevention and Control Act of 1970 [21 U.S.C. 801 et seq.];

(III) in the case of a medical convenience kit that includes a product, the person that manufacturers the kit—

(aa) purchased such product directly from the pharmaceutical manufacturer

or from a wholesale distributor that purchased the product directly from the pharmaceutical manufacturer; and

(bb) does not alter the primary container or label of the product as purchased from the manufacturer or wholesale distributor; and

(IV) in the case of a medical convenience kit that includes a product, the product is—

(aa) an intravenous solution intended for the replenishment of fluids and electrolytes;

(bb) a product intended to maintain the equilibrium of water and minerals in the body;

(cc) a product intended for irrigation or reconstitution;

(dd) an anesthetic;

(ee) an anticoagulant;

(ff) a vasopressor; or

(gg) a sympathomimetic;

(xiv) the distribution of an intravenous product that, by its formulation, is intended for the replenishment of fluids and electrolytes (such as sodium, chloride, and potassium) or calories (such as dextrose and amino acids);

(xv) the distribution of an intravenous product used to maintain the equilibrium of water and minerals in the body, such as dialysis solutions;

(xvi) the distribution of a product that is intended for irrigation, or sterile water, whether intended for such purposes or for injection;

(xvii) the distribution of a medical gas (as defined in section 360ddd of this title); or

(xviii) the distribution or sale of any licensed product under section 262 of title 42 that meets the definition of a device under section 321(h) of this title.

(25) Transaction history

The term ''transaction history'' means a statement in paper or electronic form, including the transaction information for each prior transaction going back to the manufacturer of the product.

(26) Transaction information

The term ''transaction information'' means—

(A) the proprietary or established name or names of the product;

(B) the strength and dosage form of the product;

(C) the National Drug Code number of the product;

(D) the container size;

(E) the number of containers;

(F) the lot number of the product;

(G) the date of the transaction;

(H) the date of the shipment, if more than 24 hours after the date of the transaction;

(I) the business name and address of the person from whom ownership is being transferred; and

(J) the business name and address of the person to whom ownership is being transferred.

(27) Transaction statement

The ''transaction statement'' is a statement, in paper or electronic form, that the entity transferring ownership in a transaction—

(A) is authorized as required under the Drug Supply Chain Security Act;

(B) received the product from a person that is authorized as required under the Drug Supply Chain Security Act;

(C) received transaction information and a transaction statement from the prior owner of the product, as required under section 360eee–1 of this title;

(D) did not knowingly ship a suspect or illegitimate product;

(E) had systems and processes in place to comply with verification requirements under section 360eee–1 of this title;

(F) did not knowingly provide false transaction information; and

(G) did not knowingly alter the transaction history.

(28) Verification or verify

The term ''verification'' or ''verify'' means determining whether the product identifier affixed to, or imprinted upon, a package or homogeneous case corresponds to the standardized numerical identifier or lot number and expiration date assigned to the product by the manufacturer or the repackager, as applicable in accordance with section 360eee–1 of this title.

(29) Wholesale distributor

The term ''wholesale distributor'' means a person (other than a manufacturer, a manufacturer's co-licensed partner, a third-party logistics provider, or repackager) engaged in wholesale distribution (as defined in section 353(e)(4) of this title).

(June 25, 1938, ch. 675, § 581, as added Pub. L. 113–54, title II, § 202, Nov. 27, 2013, 127 Stat. 599.)

Editorial Notes

REFERENCES IN TEXT

The Comprehensive Drug Abuse Prevention and Control Act of 1970, referred to in par. (24)(B)(xiii)(II), is Pub. L. 91–513, Oct. 27, 1970, 84 Stat. 1236, which is classified principally to chapter 13 (§ 801 et seq.) of this title. For complete classification of this Act to the Code, see Short Title note set out under section 801 of this title and Tables.

The Drug Supply Chain Security Act, referred to in par. (27)(A), (B), is Pub. L. 113–54, title II, Nov. 27, 2013, 127 Stat. 599. For complete classification of this Act to the Code, see Short Title note set out under section 301 of this title and Tables.

§ 360eee–1. Requirements

(a) In general

(1) Other activities

Each manufacturer, repackager, wholesale distributor, and dispenser shall comply with the requirements set forth in this section with respect to the role of such manufacturer, repackager, wholesale distributor, or dispenser in a transaction involving product. If an entity meets the definition of more than one of the entities listed in the preceding sentence,

such entity shall comply with all applicable requirements in this section, but shall not be required to duplicate requirements.

(2) Initial standards

(A) In general

The Secretary shall, in consultation with other appropriate Federal officials, manufacturers, repackagers, wholesale distributors, dispensers, and other pharmaceutical distribution supply chain stakeholders, issue a draft guidance document that establishes standards for the interoperable exchange of transaction information, transaction history, and transaction statements, in paper or electronic format, for compliance with this subsection and subsections (b), (c), (d), and (e). In establishing such standards, the Secretary shall consider the feasibility of establishing standardized documentation to be used by members of the pharmaceutical distribution supply chain to convey the transaction information, transaction history, and transaction statement to the subsequent purchaser of a product and to facilitate the exchange of lot level data. The standards established under this paragraph shall take into consideration the standards established under section 355e of this title and shall comply with a form and format developed by a widely recognized international standards development organization.

(B) Public input

Prior to issuing the draft guidance under subparagraph (A), the Secretary shall gather comments and information from stakeholders and maintain such comments and information in a public docket for at least 60 days prior to issuing such guidance.

(C) Publication

The Secretary shall publish the standards established under subparagraph (A) not later than 1 year after November 27, 2013.

(3) Waivers, exceptions, and exemptions

(A) In general

Not later than 2 years after November 27, 2013, the Secretary shall, by guidance—

(i) establish a process by which an authorized manufacturer, repackager, wholesale distributor, or dispenser may request a waiver from any of the requirements set forth in this section, which the Secretary may grant if the Secretary determines that such requirements would result in an undue economic hardship or for emergency medical reasons, including a public health emergency declaration pursuant to section 247d of title 42;

(ii) establish a process by which the Secretary determines exceptions, and a process through which a manufacturer or repackager may request such an exception, to the requirements relating to product identifiers if a product is packaged in a container too small or otherwise unable to accommodate a label with sufficient space to bear the information required for compliance with this section; and

(iii) establish a process by which the Secretary may determine other products or transactions that shall be exempt from the requirements of this section.

(B) Content

The guidance issued under subparagraph (A) shall include a process for the biennial review and renewal of such waivers, exceptions, and exemptions, as applicable.

(C) Process

In issuing the guidance under this paragraph, the Secretary shall provide an effective date that is not later than 180 days prior to the date on which manufacturers are required to affix or imprint a product identifier to each package and homogenous case of product intended to be introduced in a transaction into commerce consistent with this section.

(4) Self-executing requirements

Except where otherwise specified, the requirements of this section may be enforced without further regulations or guidance from the Secretary.

(5) Grandfathering product

(A) Product identifier

Not later than 2 years after November 27, 2013, the Secretary shall finalize guidance specifying whether and under what circumstances product that is not labeled with a product identifier and that is in the pharmaceutical distribution supply chain at the time of the effective date of the requirements of this section shall be exempted from the requirements of this section.

(B) Tracing

For a product that entered the pharmaceutical distribution supply chain prior to January 1, 2015—

(i) authorized trading partners shall be exempt from providing transaction information as required under subsections (b)(1)(A)(i), (c)(1)(A)(ii), (d)(1)(A)(ii), and (e)(1)(A)(ii);

(ii) transaction history required under this section shall begin with the owner of such product on such date; and

(iii) the owners of such product on such date shall be exempt from asserting receipt of transaction information and transaction statement from the prior owner as required under this section.

(6) Wholesale distributor licenses

Notwithstanding section 360eee(9)(A) of this title, until the effective date of the wholesale distributor licensing regulations under section 360eee–2 of this title, the term ''licensed'' or ''authorized'', as it relates to a wholesale distributor with respect to prescription drugs, shall mean a wholesale distributor with a valid license under State law.

(7) Third-party logistics provider licenses

Until the effective date of the third-party logistics provider licensing regulations under section 360eee–3 of this title, a third-party logistics provider shall be considered ''licensed'' under section 360eee(9)(B) of this title unless the Secretary has made a finding that the

third-party logistics provider does not utilize good handling and distribution practices and publishes notice thereof.

(8) Label changes

Changes made to package labels solely to incorporate the product identifier may be submitted to the Secretary in the annual report of an establishment, in accordance with section 314.70(d) of chapter[1] 21, Code of Federal Regulations (or any successor regulation).

(9) Product identifiers

With respect to any requirement relating to product identifiers under this part—

(A) unless the Secretary allows, through guidance, the use of other technologies for data instead of or in addition to the technologies described in clauses (i) and (ii), the applicable data—

(i) shall be included in a 2-dimensional data matrix barcode when affixed to, or imprinted upon, a package; and

(ii) shall be included in a linear or 2-dimensional data matrix barcode when affixed to, or imprinted upon, a homogeneous case; and

(B) verification of the product identifier may occur by using human-readable or machine-readable methods.

(b) Manufacturer requirements

(1) Product tracing

(A) In general

Beginning not later than January 1, 2015, a manufacturer shall—

(i) prior to, or at the time of, each transaction in which such manufacturer transfers ownership of a product, provide the subsequent owner with transaction history, transaction information, and a transaction statement, in a single document in an[2] paper or electronic format; and

(ii) capture the transaction information (including lot level information), transaction history, and transaction statement for each transaction and maintain such information, history, and statement for not less than 6 years after the date of the transaction.

(B) Requests for information

Upon a request by the Secretary or other appropriate Federal or State official, in the event of a recall or for the purpose of investigating a suspect product or an illegitimate product, a manufacturer shall, not later than 1 business day, and not to exceed 48 hours, after receiving the request, or in other such reasonable time as determined by the Secretary, based on the circumstances of the request, provide the applicable transaction information, transaction history, and transaction statement for the product.

(C) Electronic format

(i) In general

Beginning not later than 4 years after November 27, 2013, except as provided under clause (ii), a manufacturer shall provide the transaction information, transaction history, and transaction statement required under subparagraph (A)(i) in electronic format.

(ii) Exception

A manufacturer may continue to provide the transaction information, transaction history, and transaction statement required under subparagraph (A)(i) in a paper format to a licensed health care practitioner authorized to prescribe medication under State law or other licensed individual under the supervision or direction of such a practitioner who dispenses product in the usual course of professional practice.

(2) Product identifier

(A) In general

Beginning not later than 4 years after November 27, 2013, a manufacturer shall affix or imprint a product identifier to each package and homogenous case of a product intended to be introduced in a transaction into commerce. Such manufacturer shall maintain the product identifier information for such product for not less than 6 years after the date of the transaction.

(B) Exception

A package that is required to have a standardized numerical identifier is not required to have a unique device identifier.

(3) Authorized trading partners

Beginning not later than January 1, 2015, the trading partners of a manufacturer may be only authorized trading partners.

(4) Verification

Beginning not later than January 1, 2015, a manufacturer shall have systems in place to enable the manufacturer to comply with the following requirements:

(A) Suspect product

(i) In general

Upon making a determination that a product in the possession or control of the manufacturer is a suspect product, or upon receiving a request for verification from the Secretary that has made a determination that a product within the possession or control of a manufacturer is a suspect product, a manufacturer shall—

(I) quarantine such product within the possession or control of the manufacturer from product intended for distribution until such product is cleared or dispositioned; and

(II) promptly conduct an investigation in coordination with trading partners, as applicable, to determine whether the product is an illegitimate product, which shall include validating any applicable transaction history and transaction information in the possession of the manufacturer and otherwise investigating to determine whether the product is an illegitimate product, and, beginning 4 years

[1] So in original. Probably should be ''title''.

[2] So in original. Probably should be ''a''.

after November 27, 2013, verifying the product at the package level, including the standardized numerical identifier.

(ii) Cleared product

If the manufacturer makes the determination that a suspect product is not an illegitimate product, the manufacturer shall promptly notify the Secretary, if applicable, of such determination and such product may be further distributed.

(iii) Records

A manufacturer shall keep records of the investigation of a suspect product for not less than 6 years after the conclusion of the investigation.

(B) Illegitimate product

(i) In general

Upon determining that a product in the possession or control of a manufacturer is an illegitimate product, the manufacturer shall, in a manner consistent with the systems and processes of such manufacturer—

(I) quarantine such product within the possession or control of the manufacturer from product intended for distribution until such product is dispositioned;

(II) disposition the illegitimate product within the possession or control of the manufacturer;

(III) take reasonable and appropriate steps to assist a trading partner to disposition an illegitimate product not in the possession or control of the manufacturer; and

(IV) retain a sample of the product for further physical examination or laboratory analysis of the product by the manufacturer or Secretary (or other appropriate Federal or State official) upon request by the Secretary (or other appropriate Federal or State official), as necessary and appropriate.

(ii) Making a notification

(I) Illegitimate product

Upon determining that a product in the possession or control of the manufacturer is an illegitimate product, the manufacturer shall notify the Secretary and all immediate trading partners that the manufacturer has reason to believe may have received such illegitimate product of such determination not later than 24 hours after making such determination.

(II) High risk of illegitimacy

A manufacturer shall notify the Secretary and immediate trading partners that the manufacturer has reason to believe may have in the trading partner's possession a product manufactured by, or purported to be a product manufactured by, the manufacturer not later than 24 hours after determining or being notified by the Secretary or a trading partner that there is a high risk that such product is an illegitimate product. For purposes of this subclause, a ''high risk'' may include a specific high risk that could increase the likelihood that illegitimate product will enter the pharmaceutical distribution supply chain and other high risks as determined by the Secretary in guidance pursuant to subsection (h).

(iii) Responding to a notification

Upon the receipt of a notification from the Secretary or a trading partner that a determination has been made that a product is an illegitimate product, a manufacturer shall identify all illegitimate product subject to such notification that is in the possession or control of the manufacturer, including any product that is subsequently received, and shall perform the activities described in subparagraph (A).

(iv) Terminating a notification

Upon making a determination, in consultation with the Secretary, that a notification is no longer necessary, a manufacturer shall promptly notify immediate trading partners that the manufacturer notified pursuant to clause (ii) that such notification has been terminated.

(v) Records

A manufacturer shall keep records of the disposition of an illegitimate product for not less than 6 years after the conclusion of the disposition.

(C) Requests for verification

Beginning 4 years after November 27, 2013, upon receiving a request for verification from an authorized repackager, wholesale distributor, or dispenser that is in possession or control of a product such person believes to be manufactured by such manufacturer, a manufacturer shall, not later than 24 hours after receiving the request for verification or in other such reasonable time as determined by the Secretary, based on the circumstances of the request, notify the person making the request whether the product identifier, including the standardized numerical identifier, that is the subject of the request corresponds to the product identifier affixed or imprinted by the manufacturer. If a manufacturer responding to a request for verification identifies a product identifier that does not correspond to that affixed or imprinted by the manufacturer, the manufacturer shall treat such product as suspect product and conduct an investigation as described in subparagraph (A). If the manufacturer has reason to believe the product is an illegitimate product, the manufacturer shall advise the person making the request of such belief at the time such manufacturer responds to the request for verification.

(D) Electronic database

A manufacturer may satisfy the requirements of this paragraph by developing a secure electronic database or utilizing a secure electronic database developed or operated by another entity. The owner of such database shall establish the requirements and processes to respond to requests and may provide

for data access to other members of the pharmaceutical distribution supply chain, as appropriate. The development and operation of such a database shall not relieve a manufacturer of the requirement under this paragraph to respond to a request for verification submitted by means other than a secure electronic database.

(E) Saleable returned product

Beginning 4 years after November 27, 2013 (except as provided pursuant to subsection (a)(5)), upon receipt of a returned product that the manufacturer intends to further distribute, before further distributing such product, the manufacturer shall verify the product identifier, including the standardized numerical identifier, for each sealed homogeneous case of such product or, if such product is not in a sealed homogeneous case, verify the product identifier, including the standardized numerical identifier, on each package.

(F) Nonsaleable returned product

A manufacturer may return a nonsaleable product to the manufacturer or repackager, to the wholesale distributor from whom such product was purchased, or to a person acting on behalf of such a person, including a returns processor, without providing the information described in paragraph (1)(A)(i).

(c) Wholesale distributor requirements

(1) Product tracing

(A) In general

Beginning not later than January 1, 2015, the following requirements shall apply to wholesale distributors:

(i) A wholesale distributor shall not accept ownership of a product unless the previous owner prior to, or at the time of, the transaction provides the transaction history, transaction information, and a transaction statement for the product, as applicable under this subparagraph.

(ii)(I)(aa) If the wholesale distributor purchased a product directly from the manufacturer, the exclusive distributor of the manufacturer, or a repackager that purchased directly from the manufacturer, then prior to, or at the time of, each transaction in which the wholesale distributor transfers ownership of a product, the wholesale distributor shall provide to the subsequent purchaser—

(AA) a transaction statement, which shall state that such wholesale distributor, or a member of the affiliate of such wholesale distributor, purchased the product directly from the manufacturer, exclusive distributor of the manufacturer, or repackager that purchased the product directly from the manufacturer; and

(BB) subject to subclause (II), the transaction history and transaction information.

(bb) The wholesale distributor shall provide the transaction history, transaction information, and transaction statement under item (aa)—

(AA) if provided to a dispenser, on a single document in a paper or electronic format; and

(BB) if provided to a wholesale distributor, through any combination of self-generated paper, electronic data, or manufacturer-provided information on the product package.

(II) For purposes of transactions described in subclause (I), transaction history and transaction information shall not be required to include the lot number of the product, the initial transaction date, or the initial shipment date from the manufacturer (as defined in subparagraphs (F), (G), and (H) of section 360eee(26) of this title).

(iii) If the wholesale distributor did not purchase a product directly from the manufacturer, the exclusive distributor of the manufacturer, or a repackager that purchased directly from the manufacturer, as described in clause (ii), then prior to, or at the time of, each transaction or subsequent transaction, the wholesale distributor shall provide to the subsequent purchaser a transaction statement, transaction history, and transaction information, in a paper or electronic format that complies with the guidance document issued under subsection (a)(2).

(iv) For the purposes of clause (iii), the transaction history supplied shall begin only with the wholesale distributor described in clause (ii)(I), but the wholesale distributor described in clause (iii) shall inform the subsequent purchaser that such wholesale distributor received a direct purchase statement from a wholesale distributor described in clause (ii)(I).

(v) A wholesale distributor shall—

(I) capture the transaction information (including lot level information) consistent with the requirements of this section, transaction history, and transaction statement for each transaction described in clauses (i), (ii), and (iii) and maintain such information, history, and statement for not less than 6 years after the date of the transaction; and

(II) maintain the confidentiality of the transaction information (including any lot level information consistent with the requirements of this section), transaction history, and transaction statement for a product in a manner that prohibits disclosure to any person other than the Secretary or other appropriate Federal or State official, except to comply with clauses (ii) and (iii), and, as applicable, pursuant to an agreement under subparagraph (D).

(B) Returns

(i) Saleable returns

Notwithstanding subparagraph (A)(i), the following shall apply:

(I) Requirements

Until the date that is 6 years after November 27, 2013 (except as provided pur-

suant to subsection (a)(5)), a wholesale distributor may accept returned product from a dispenser or repackager pursuant to the terms and conditions of any agreement between the parties, and, notwithstanding subparagraph (A)(ii), may distribute such returned product without providing the transaction history. For transactions subsequent to the return, the transaction history of such product shall begin with the wholesale distributor that accepted the returned product, consistent with the requirements of this subsection.

(II) Enhanced requirements

Beginning 6 years after November 27, 2013 (except as provided pursuant to subsection (a)(5)), a wholesale distributor may accept returned product from a dispenser or repackager only if the wholesale distributor can associate returned product with the transaction information and transaction statement associated with that product. For all transactions after such date, the transaction history, as applicable, of such product shall begin with the wholesale distributor that accepted and verified the returned product. For purposes of this subparagraph, the transaction information and transaction history, as applicable, need not include transaction dates if it is not reasonably practicable to obtain such dates.

(ii) Nonsaleable returns

A wholesale distributor may return a nonsaleable product to the manufacturer or repackager, to the wholesale distributor from whom such product was purchased, or to a person acting on behalf of such a person, including a returns processor, without providing the information required under subparagraph (A)(i).

(C) Requests for information

Upon a request by the Secretary or other appropriate Federal or State official, in the event of a recall or for the purpose of investigating a suspect product or an illegitimate product, a wholesale distributor shall, not later than 1 business day, and not to exceed 48 hours, after receiving the request or in other such reasonable time as determined by the Secretary, based on the circumstances of the request, provide the applicable transaction information, transaction history, and transaction statement for the product.

(D) Trading partner agreements

Beginning 6 years after November 27, 2013, a wholesale distributor may disclose the transaction information, including lot level information, transaction history, or transaction statement of a product to the subsequent purchaser of the product, pursuant to a written agreement between such wholesale distributor and such subsequent purchaser. Nothing in this subparagraph shall be construed to limit the applicability of subparagraphs (A) through (C).

(2) Product identifier

Beginning 6 years after November 27, 2013, a wholesale distributor may engage in transactions involving a product only if such product is encoded with a product identifier (except as provided pursuant to subsection (a)(5)).

(3) Authorized trading partners

Beginning not later than January 1, 2015, the trading partners of a wholesale distributor may be only authorized trading partners.

(4) Verification

Beginning not later than January 1, 2015, a wholesale distributor shall have systems in place to enable the wholesale distributor to comply with the following requirements:

(A) Suspect product

(i) In general

Upon making a determination that a product in the possession or control of a wholesale distributor is a suspect product, or upon receiving a request for verification from the Secretary that has made a determination that a product within the possession or control of a wholesale distributor is a suspect product, a wholesale distributor shall—

(I) quarantine such product within the possession or control of the wholesale distributor from product intended for distribution until such product is cleared or dispositioned; and

(II) promptly conduct an investigation in coordination with trading partners, as applicable, to determine whether the product is an illegitimate product, which shall include validating any applicable transaction history and transaction information in the possession of the wholesale distributor and otherwise investigating to determine whether the product is an illegitimate product, and, beginning 6 years after November 27, 2013 (except as provided pursuant to subsection (a)(5)), verifying the product at the package level, including the standardized numerical identifier.

(ii) Cleared product

If the wholesale distributor determines that a suspect product is not an illegitimate product, the wholesale distributor shall promptly notify the Secretary, if applicable, of such determination and such product may be further distributed.

(iii) Records

A wholesale distributor shall keep records of the investigation of a suspect product for not less than 6 years after the conclusion of the investigation.

(B) Illegitimate product

(i) In general

Upon determining, in coordination with the manufacturer, that a product in the possession or control of a wholesale distributor is an illegitimate product, the wholesale distributor shall, in a manner that is consistent with the systems and processes of such wholesale distributor—

(I) quarantine such product within the possession or control of the wholesale distributor from product intended for distribution until such product is dispositioned;

(II) disposition the illegitimate product within the possession or control of the wholesale distributor;

(III) take reasonable and appropriate steps to assist a trading partner to disposition an illegitimate product not in the possession or control of the wholesale distributor; and

(IV) retain a sample of the product for further physical examination or laboratory analysis of the product by the manufacturer or Secretary (or other appropriate Federal or State official) upon request by the manufacturer or Secretary (or other appropriate Federal or State official), as necessary and appropriate.

(ii) Making a notification

Upon determining that a product in the possession or control of the wholesale distributor is an illegitimate product, the wholesale distributor shall notify the Secretary and all immediate trading partners that the wholesale distributor has reason to believe may have received such illegitimate product of such determination not later than 24 hours after making such determination.

(iii) Responding to a notification

Upon the receipt of a notification from the Secretary or a trading partner that a determination has been made that a product is an illegitimate product, a wholesale distributor shall identify all illegitimate product subject to such notification that is in the possession or control of the wholesale distributor, including any product that is subsequently received, and shall perform the activities described in subparagraph (A).

(iv) Terminating a notification

Upon making a determination, in consultation with the Secretary, that a notification is no longer necessary, a wholesale distributor shall promptly notify immediate trading partners that the wholesale distributor notified pursuant to clause (ii) that such notification has been terminated.

(v) Records

A wholesale distributor shall keep records of the disposition of an illegitimate product for not less than 6 years after the conclusion of the disposition.

(C) Electronic database

A wholesale distributor may satisfy the requirements of this paragraph by developing a secure electronic database or utilizing a secure electronic database developed or operated by another entity. The owner of such database shall establish the requirements and processes to respond to requests and may provide for data access to other members of the pharmaceutical distribution supply chain, as appropriate. The development and operation of such a database shall not relieve a wholesale distributor of the requirement under this paragraph to respond to a verification request submitted by means other than a secure electronic database.

(D) Verification of saleable returned product

Beginning 6 years after November 27, 2013, upon receipt of a returned product that the wholesale distributor intends to further distribute, before further distributing such product, the wholesale distributor shall verify the product identifier, including the standardized numerical identifier, for each sealed homogeneous case of such product or, if such product is not in a sealed homogeneous case, verify the product identifier, including the standardized numerical identifier, on each package.

(d) Dispenser requirements

(1) Product tracing

(A) In general

Beginning July 1, 2015, a dispenser—

(i) shall not accept ownership of a product, unless the previous owner prior to, or at the time of, the transaction, provides transaction history, transaction information, and a transaction statement;

(ii) prior to, or at the time of, each transaction in which the dispenser transfers ownership of a product (but not including dispensing to a patient or returns) shall provide the subsequent owner with transaction history, transaction information, and a transaction statement for the product, except that the requirements of this clause shall not apply to sales by a dispenser to another dispenser to fulfill a specific patient need; and

(iii) shall capture transaction information (including lot level information, if provided), transaction history, and transaction statements, as necessary to investigate a suspect product, and maintain such information, history, and statements for not less than 6 years after the transaction.

(B) Agreements with third parties

A dispenser may enter into a written agreement with a third party, including an authorized wholesale distributor, under which the third party confidentially maintains the transaction information, transaction history, and transaction statements required to be maintained under this subsection on behalf of the dispenser. If a dispenser enters into such an agreement, the dispenser shall maintain a copy of the written agreement and shall not be relieved of the obligations of the dispenser under this subsection.

(C) Returns

(i) Saleable returns

A dispenser may return product to the trading partner from which the dispenser obtained the product without providing the information required under subparagraph (A).

(ii) Nonsaleable returns

A dispenser may return a nonsaleable product to the manufacturer or repackager, to the wholesale distributor from whom such product was purchased, to a returns processor, or to a person acting on behalf of such a person without providing the information required under subparagraph (A).

(D) Requests for information

Upon a request by the Secretary or other appropriate Federal or State official, in the event of a recall or for the purpose of investigating a suspect or an illegitimate product, a dispenser shall, not later than 2 business days after receiving the request or in another such reasonable time as determined by the Secretary, based on the circumstances of the request, provide the applicable transaction information, transaction statement, and transaction history which the dispenser received from the previous owner, which shall not include the lot number of the product, the initial transaction date, or the initial shipment date from the manufacturer unless such information was included in the transaction information, transaction statement, and transaction history provided by the manufacturer or wholesale distributor to the dispenser. The dispenser may respond to the request by providing the applicable information in either paper or electronic format. Until the date that is 4 years after November 27, 2013, the Secretary or other appropriate Federal or State official shall grant a dispenser additional time, as necessary, only with respect to a request to provide lot level information described in subparagraph (F) of section 360eee(26) of this title that was provided to the dispenser in paper format, limit the request time period to the 6 months preceding the request or other relevant date, and, in the event of a recall, the Secretary, or other appropriate Federal or State official may request information only if such recall involves a serious adverse health consequence or death to humans.

(2) Product identifier

Beginning not later than 7 years after November 27, 2013, a dispenser may engage in transactions involving a product only if such product is encoded with a product identifier (except as provided pursuant to subsection (a)(5)).

(3) Authorized trading partners

Beginning not later than January 1, 2015, the trading partners of a dispenser may be only authorized trading partners.

(4) Verification

Beginning not later than January 1, 2015, a dispenser shall have systems in place to enable the dispenser to comply with the following requirements:

(A) Suspect product

(i) In general

Upon making a determination that a product in the possession or control of the dispenser is a suspect product, or upon receiving a request for verification from the Secretary that has made a determination that a product within the possession or control of a dispenser is a suspect product, a dispenser shall—

(I) quarantine such product within the possession or control of the dispenser from product intended for distribution until such product is cleared or dispositioned; and

(II) promptly conduct an investigation in coordination with trading partners, as applicable, to determine whether the product is an illegitimate product.

(ii) Investigation

An investigation conducted under clause (i)(II) shall include—

(I) beginning 7 years after November 27, 2013, verifying whether the lot number of a suspect product corresponds with the lot number for such product;

(II) beginning 7 years after November 27, 2013, verifying that the product identifier, including the standardized numerical identifier, of at least 3 packages or 10 percent of such suspect product, whichever is greater, or all packages, if there are fewer than 3, corresponds with the product identifier for such product;

(III) validating any applicable transaction history and transaction information in the possession of the dispenser; and

(IV) otherwise investigating to determine whether the product is an illegitimate product.

(iii) Cleared product

If the dispenser makes the determination that a suspect product is not an illegitimate product, the dispenser shall promptly notify the Secretary, if applicable, of such determination and such product may be further distributed or dispensed.

(iv) Records

A dispenser shall keep records of the investigation of a suspect product for not less than 6 years after the conclusion of the investigation.

(B) Illegitimate product

(i) In general

Upon determining, in coordination with the manufacturer, that a product in the possession or control of a dispenser is an illegitimate product, the dispenser shall—

(I) disposition the illegitimate product within the possession or control of the dispenser;

(II) take reasonable and appropriate steps to assist a trading partner to disposition an illegitimate product not in the possession or control of the dispenser; and

(III) retain a sample of the product for further physical examination or laboratory analysis of the product by the manufacturer or Secretary (or other appro-

priate Federal or State official) upon request by the manufacturer or Secretary (or other appropriate Federal or State official), as necessary and appropriate.

(ii) Making a notification

Upon determining that a product in the possession or control of the dispenser is an illegitimate product, the dispenser shall notify the Secretary and all immediate trading partners that the dispenser has reason to believe may have received such illegitimate product of such determination not later than 24 hours after making such determination.

(iii) Responding to a notification

Upon the receipt of a notification from the Secretary or a trading partner that a determination has been made that a product is an illegitimate product, a dispenser shall identify all illegitimate product subject to such notification that is in the possession or control of the dispenser, including any product that is subsequently received, and shall perform the activities described in subparagraph (A).

(iv) Terminating a notification

Upon making a determination, in consultation with the Secretary, that a notification is no longer necessary, a dispenser shall promptly notify immediate trading partners that the dispenser notified pursuant to clause (ii) that such notification has been terminated.

(v) Records

A dispenser shall keep records of the disposition of an illegitimate product for not less than 6 years after the conclusion of the disposition.

(C) Electronic database

A dispenser may satisfy the requirements of this paragraph by developing a secure electronic database or utilizing a secure electronic database developed or operated by another entity.

(5) Exception

Notwithstanding any other provision of law, the requirements under paragraphs (1) and (4) shall not apply to licensed health care practitioners authorized to prescribe or administer medication under State law or other licensed individuals under the supervision or direction of such practitioners who dispense or administer product in the usual course of professional practice.

(e) Repackager requirements

(1) Product tracing

(A) In general

Beginning not later than January 1, 2015, a repackager described in section 360eee(16)(A) of this title shall—

(i) not accept ownership of a product unless the previous owner, prior to, or at the time of, the transaction, provides transaction history, transaction information, and a transaction statement for the product;

(ii) prior to, or at the time of, each transaction in which the repackager transfers ownership of a product, provide the subsequent owner with transaction history, transaction information, and a transaction statement for the product; and

(iii) capture the transaction information (including lot level information), transaction history, and transaction statement for each transaction described in clauses (i) and (ii) and maintain such information, history, and statement for not less than 6 years after the transaction.

(B) Returns

(i) Nonsaleable product

A repackager described in section 360eee(16)(A) of this title may return a nonsaleable product to the manufacturer or repackager, or to the wholesale distributor from whom such product was purchased, or to a person acting on behalf of such a person, including a returns processor, without providing the information required under subparagraph (A)(ii).

(ii) Saleable or nonsaleable product

A repackager described in section 360eee(16)(B) of this title may return a saleable or nonsaleable product to the manufacturer, repackager, or to the wholesale distributor from whom such product was received without providing the information required under subparagraph (A)(ii) on behalf of the hospital or other health care entity that took ownership of such product pursuant to the terms and conditions of any agreement between such repackager and the entity that owns the product.

(C) Requests for information

Upon a request by the Secretary or other appropriate Federal or State official, in the event of a recall or for the purpose of investigating a suspect product or an illegitimate product, a repackager described in section 360eee(16)(A) of this title shall, not later than 1 business day, and not to exceed 48 hours, after receiving the request or in other such reasonable time as determined by the Secretary, provide the applicable transaction information, transaction history, and transaction statement for the product.

(2) Product identifier

(A) In general

Beginning not later than 5 years after November 27, 2013, a repackager described in section 360eee(16)(A) of this title—

(i) shall affix or imprint a product identifier to each package and homogenous case of product intended to be introduced in a transaction in commerce;

(ii) shall maintain the product identifier information for such product for not less than 6 years after the date of the transaction;

(iii) may engage in transactions involving a product only if such product is encoded with a product identifier (except as provided pursuant to subsection (a)(5)); and

(iv) shall maintain records for not less than 6 years to allow the repackager to associate the product identifier the repackager affixes or imprints with the product identifier assigned by the original manufacturer of the product.

(B) Exception

A package that is required to have a standardized numerical identifier is not required to have a unique device identifier.

(3) Authorized trading partners

Beginning January 1, 2015, the trading partners of a repackager described in section 360eee(16) of this title may be only authorized trading partners.

(4) Verification

Beginning not later than January 1, 2015, a repackager described in section 360eee(16)(A) of this title shall have systems in place to enable the repackager to comply with the following requirements:

(A) Suspect product

(i) In general

Upon making a determination that a product in the possession or control of the repackager is a suspect product, or upon receiving a request for verification from the Secretary that has made a determination that a product within the possession or control of a repackager is a suspect product, a repackager shall—

(I) quarantine such product within the possession or control of the repackager from product intended for distribution until such product is cleared or dispositioned; and

(II) promptly conduct an investigation in coordination with trading partners, as applicable, to determine whether the product is an illegitimate product, which shall include validating any applicable transaction history and transaction information in the possession of the repackager and otherwise investigating to determine whether the product is an illegitimate product, and, beginning 5 years after November 27, 2013 (except as provided pursuant to subsection (a)(5)), verifying the product at the package level, including the standardized numerical identifier.

(ii) Cleared product

If the repackager makes the determination that a suspect product is not an illegitimate product, the repackager shall promptly notify the Secretary, if applicable, of such determination and such product may be further distributed.

(iii) Records

A repackager shall keep records of the investigation of a suspect product for not less than 6 years after the conclusion of the investigation.

(B) Illegitimate product

(i) In general

Upon determining, in coordination with the manufacturer, that a product in the possession or control of a repackager is an illegitimate product, the repackager shall, in a manner that is consistent with the systems and processes of such repackager—

(I) quarantine such product within the possession or control of the repackager from product intended for distribution until such product is dispositioned;

(II) disposition the illegitimate product within the possession or control of the repackager;

(III) take reasonable and appropriate steps to assist a trading partner to disposition an illegitimate product not in the possession or control of the repackager; and

(IV) retain a sample of the product for further physical examination or laboratory analysis of the product by the manufacturer or Secretary (or other appropriate Federal or State official) upon request by the manufacturer or Secretary (or other appropriate Federal or State official), as necessary and appropriate.

(ii) Making a notification

Upon determining that a product in the possession or control of the repackager is an illegitimate product, the repackager shall notify the Secretary and all immediate trading partners that the repackager has reason to believe may have received the illegitimate product of such determination not later than 24 hours after making such determination.

(iii) Responding to a notification

Upon the receipt of a notification from the Secretary or a trading partner, a repackager shall identify all illegitimate product subject to such notification that is in the possession or control of the repackager, including any product that is subsequently received, and shall perform the activities described in subparagraph (A).

(iv) Terminating a notification

Upon making a determination, in consultation with the Secretary, that a notification is no longer necessary, a repackager shall promptly notify immediate trading partners that the repackager notified pursuant to clause (ii) that such notification has been terminated.

(v) Records

A repackager shall keep records of the disposition of an illegitimate product for not less than 6 years after the conclusion of the disposition.

(C) Requests for verification

Beginning 5 years after November 27, 2013, upon receiving a request for verification from an authorized manufacturer, wholesale distributor, or dispenser that is in possession or control of a product they believe to be repackaged by such repackager, a repackager shall, not later than 24 hours after receiving the verification request or in other such reasonable time as determined by the Secretary, based on the circumstances of the re-

quest, notify the person making the request whether the product identifier, including the standardized numerical identifier, that is the subject of the request corresponds to the product identifier affixed or imprinted by the repackager. If a repackager responding to a verification request identifies a product identifier that does not correspond to that affixed or imprinted by the repackager, the repackager shall treat such product as suspect product and conduct an investigation as described in subparagraph (A). If the repackager has reason to believe the product is an illegitimate product, the repackager shall advise the person making the request of such belief at the time such repackager responds to the verification request.

(D) Electronic database

A repackager may satisfy the requirements of paragraph (4) by developing a secure electronic database or utilizing a secure electronic database developed or operated by another entity. The owner of such database shall establish the requirements and processes to respond to requests and may provide for data access to other members of the pharmaceutical distribution supply chain, as appropriate. The development and operation of such a database shall not relieve a repackager of the requirement under subparagraph (C) to respond to a verification request submitted by means other than a secure electronic database.

(E) Verification of saleable returned product

Beginning 5 years after November 27, 2013, upon receipt of a returned product that the repackager intends to further distribute, before further distributing such product, the repackager shall verify the product identifier for each sealed homogeneous case of such product or, if such product is not in a sealed homogeneous case, verify the product identifier on each package.

(f) Drop shipments

(1) In general

A wholesale distributor that does not physically handle or store product shall be exempt from the provisions of this section, except the notification requirements under clauses (ii), (iii), and (iv) of subsection (c)(4)(B), provided that the manufacturer, repackager, or other wholesale distributor that distributes the product to the dispenser by means of a drop shipment for such wholesale distributor includes on the transaction information and transaction history to the dispenser the contact information of such wholesale distributor and provides the transaction information, transaction history, and transaction statement directly to the dispenser.

(2) Clarification

For purposes of this subsection, providing administrative services, including processing of orders and payments, shall not by itself, be construed as being involved in the handling, distribution, or storage of a product.

(g) Enhanced drug distribution security

(1) In general

On the date that is 10 years after November 27, 2013, the following interoperable, electronic tracing of product at the package level requirements shall go into effect:

(A) The transaction information and the transaction statements as required under this section shall be exchanged in a secure, interoperable, electronic manner in accordance with the standards established under the guidance issued pursuant to paragraphs (3) and (4) of subsection (h), including any revision of such guidance issued in accordance with paragraph (5) of such subsection.

(B) The transaction information required under this section shall include the product identifier at the package level for each package included in the transaction.

(C) Systems and processes for verification of product at the package level, including the standardized numerical identifier, shall be required in accordance with the standards established under the guidance issued pursuant to subsection (a)(2) and the guidances issued pursuant to paragraphs (2), (3), and (4) of subsection (h), including any revision of such guidances issued in accordance with paragraph (5) of such subsection, which may include the use of aggregation and inference as necessary.

(D) The systems and processes necessary to promptly respond with the transaction information and transaction statement for a product upon a request by the Secretary (or other appropriate Federal or State official) in the event of a recall or for the purposes of investigating a suspect product or an illegitimate product shall be required.

(E) The systems and processes necessary to promptly facilitate gathering the information necessary to produce the transaction information for each transaction going back to the manufacturer, as applicable, shall be required—

(i) in the event of a request by the Secretary (or other appropriate Federal or State official), on account of a recall or for the purposes of investigating a suspect product or an illegitimate product; or

(ii) in the event of a request by an authorized trading partner, in a secure manner that ensures the protection of confidential commercial information and trade secrets, for purposes of investigating a suspect product or assisting the Secretary (or other appropriate Federal or State official) with a request described in clause (i).

(F) Each person accepting a saleable return shall have systems and processes in place to allow acceptance of such product and may accept saleable returns only if such person can associate the saleable return product with the transaction information and transaction statement associated with that product.

(2) Compliance

(A) Information maintenance agreement

A dispenser may enter into a written agreement with a third party, including an

authorized wholesale distributor, under which the third party shall confidentially maintain any information and statements required to be maintained under this section. If a dispenser enters into such an agreement, the dispenser shall maintain a copy of the written agreement and shall not be relieved of the obligations of the dispenser under this subsection.

(B) Alternative methods

The Secretary, taking into consideration the assessment conducted under paragraph (3), shall provide for alternative methods of compliance with any of the requirements set forth in paragraph (1), including—

(i) establishing timelines for compliance by small businesses (including small business dispensers with 25 or fewer full-time employees) with such requirements, in order to ensure that such requirements do not impose undue economic hardship for small businesses, including small business dispensers for whom the criteria set forth in the assessment under paragraph (3) is not met, if the Secretary determines that such requirements under paragraph (1) would result in undue economic hardship; and

(ii) establishing a process by which a dispenser may request a waiver from any of the requirements set forth in paragraph (1) if the Secretary determines that such requirements would result in an undue economic hardship, which shall include a process for the biennial review and renewal of any such waiver.

(3) Assessment

(A) In general

Not later than the date that is 18 months after the Secretary issues the final guidance required under subsection (h), the Secretary shall enter into a contract with a private, independent consulting firm with expertise to conduct a technology and software assessment that looks at the feasibility of dispensers with 25 or fewer full-time employees conducting interoperable, electronic tracing of products at the package level. Such assessment shall be completed not later than 8½ years after November 27, 2013.

(B) Condition

As a condition of the award of the contract under subparagraph (A), the private, independent consulting firm shall agree to consult with dispensers with 25 or fewer full-time employees when conducting the assessment under such subparagraph.

(C) Content

The assessment under subparagraph (A) shall assess whether—

(i) the necessary software and hardware is readily accessible to such dispensers;

(ii) the necessary software and hardware is prohibitively expensive to obtain, install, and maintain for such dispensers; and

(iii) the necessary hardware and software can be integrated into business practices, such as interoperability with wholesale distributors, for such dispensers.

(D) Publication

The Secretary shall—

(i) publish the statement of work for the assessment under subparagraph (A) for public comment prior to beginning the assessment;

(ii) publish the final assessment for public comment not later than 30 calendar days after receiving such assessment; and

(iii) hold a public meeting not later than 180 calendar days after receiving the final assessment at which public stakeholders may present their views on the assessment.

(4) Procedure

Notwithstanding section 553 of title 5, the Secretary, in promulgating any regulation pursuant to this section, shall—

(A) provide appropriate flexibility by—

(i) not requiring the adoption of specific business systems for the maintenance and transmission of data;

(ii) prescribing alternative methods of compliance for any of the requirements set forth in paragraph (1) or set forth in regulations implementing such requirements, including—

(I) timelines for small businesses to comply with the requirements set forth in the regulations in order to ensure that such requirements do not impose undue economic hardship for small businesses (including small business dispensers for whom the criteria set forth in the assessment under paragraph (3) is not met), if the Secretary determines that such requirements would result in undue economic hardship; and

(II) the establishment of a process by which a dispenser may request a waiver from any of the requirements set forth in such regulations if the Secretary determines that such requirements would result in an undue economic hardship; and

(iii) taking into consideration—

(I) the results of pilot projects, including pilot projects pursuant to this section and private sector pilot projects, including those involving the use of aggregation and inference;

(II) the public meetings held and related guidance documents issued under this section;

(III) the public health benefits of any additional regulations in comparison to the cost of compliance with such requirements, including on entities of varying sizes and capabilities;

(IV) the diversity of the pharmaceutical distribution supply chain by providing appropriate flexibility for each sector, including both large and small businesses; and

(V) the assessment pursuant to paragraph (3) with respect to small business dispensers, including related public comment and the public meeting, and requirements under this section;

(B) issue a notice of proposed rulemaking that includes a copy of the proposed regulation;

(C) provide a period of not less than 60 days for comments on the proposed regulation; and

(D) publish in the Federal Register the final regulation not less than 2 years prior to the effective date of the regulation.

(h) Guidance documents

(1) In general

For the purposes of facilitating the successful and efficient adoption of secure, interoperable product tracing at the package level in order to enhance drug distribution security and further protect the public health, the Secretary shall issue the guidance documents as provided for in this subsection.

(2) Suspect and illegitimate product

(A) In general

Not later than 180 days after November 27, 2013, the Secretary shall issue a guidance document to aid trading partners in the identification of a suspect product and notification termination. Such guidance document shall—

(i) identify specific scenarios that could significantly increase the risk of a suspect product entering the pharmaceutical distribution supply chain;

(ii) provide recommendation on how trading partners may identify such product and make a determination on whether the product is a suspect product as soon as practicable; and

(iii) set forth the process by which manufacturers, repackagers, wholesale distributors, and dispensers shall terminate notifications in consultation with the Secretary regarding illegitimate product pursuant to subsections (b)(4)(B), (c)(4)(B), (d)(4)(B), and (e)(4)(B).

(B) Revised guidance

If the Secretary revises the guidance issued under subparagraph (A), the Secretary shall follow the procedure set forth in paragraph (5).

(3) Unit level tracing

(A) In general

In order to enhance drug distribution security at the package level, not later than 18 months after conducting a public meeting on the system attributes necessary to enable secure tracing of product at the package level, including allowing for the use of verification, inference, and aggregation, as necessary, the Secretary shall issue a final guidance document that outlines and makes recommendations with respect to the system attributes necessary to enable secure tracing at the package level as required under the requirements established under subsection (g). Such guidance document shall—

(i) define the circumstances under which the sectors within the pharmaceutical distribution supply chain may, in the most efficient manner practicable, infer the contents of a case, pallet, tote, or other aggregate of individual packages or containers of product, from a product identifier associated with the case, pallet, tote, or other aggregate, without opening each case, pallet, tote, or other aggregate or otherwise individually scanning each package;

(ii) identify methods and processes to enhance secure tracing of product at the package level, such as secure processes to facilitate the use of inference, enhanced verification activities, the use of aggregation and inference, processes that utilize the product identifiers to enhance tracing of product at the package level, including the standardized numerical identifier, or package security features; and

(iii) ensure the protection of confidential commercial information and trade secrets.

(B) Procedure

In issuing the guidance under subparagraph (A), and in revising such guidance, if applicable, the Secretary shall follow the procedure set forth in paragraph (5).

(4) Standards for interoperable data exchange

(A) In general

In order to enhance secure tracing of a product at the package level, the Secretary, not later than 18 months after conducting a public meeting on the interoperable standards necessary to enhance the security of the pharmaceutical distribution supply chain, shall update the guidance issued pursuant to subsection (a)(2), as necessary and appropriate, and finalize such guidance document so that the guidance document—

(i) identifies and makes recommendations with respect to the standards necessary for adoption in order to support the secure, interoperable electronic data exchange among the pharmaceutical distribution supply chain that comply with a form and format developed by a widely recognized international standards development organization;

(ii) takes into consideration standards established pursuant to subsection (a)(2) and section 355e of this title;

(iii) facilitates the creation of a uniform process or methodology for product tracing; and

(iv) ensures the protection of confidential commercial information and trade secrets.

(B) Procedure

In issuing the guidance under subparagraph (A), and in revising such guidance, if applicable, the Secretary shall follow the procedure set forth in paragraph (5).

(5) Procedure

In issuing or revising any guidance issued pursuant to this subsection or subsection (g), except the initial guidance issued under paragraph (2)(A), the Secretary shall—

(A) publish a notice in the Federal Register for a period not less than 30 days announcing that the draft or revised draft guidance is available;

(B) post the draft guidance document on the Internet Web site of the Food and Drug Administration and make such draft guidance document available in hard copy;

(C) provide an opportunity for comment and review and take into consideration any comments received;

(D) revise the draft guidance, as appropriate;

(E) publish a notice in the Federal Register for a period not less than 30 days announcing that the final guidance or final revised guidance is available;

(F) post the final guidance document on the Internet Web site of the Food and Drug Administration and make such final guidance document available in hard copy; and

(G) provide for an effective date of not earlier than 1 year after such guidance becomes final.

(i) Public meetings

(1) In general

The Secretary shall hold not less than 5 public meetings to enhance the safety and security of the pharmaceutical distribution supply chain and provide for comment. The Secretary may hold the first such public meeting not earlier than 1 year after November 27, 2013. In carrying out the public meetings described in this paragraph, the Secretary shall—

(A) prioritize topics necessary to inform the issuance of the guidance described in paragraphs (3) and (4) of subsection (h); and

(B) take all measures reasonable and practicable to ensure the protection of confidential commercial information and trade secrets.

(2) Content

Each of the following topics shall be addressed in at least one of the public meetings described in paragraph (1):

(A) An assessment of the steps taken under subsections (b) through (e) to build capacity for a unit-level system, including the impact of the requirements of such subsections on—

(i) the ability of the health care system collectively to maintain patient access to medicines;

(ii) the scalability of such requirements, including as it relates to product lines; and

(iii) the capability of different sectors and subsectors, including both large and small businesses, to affix and utilize the product identifier.

(B) The system attributes necessary to support the requirements set forth under subsection (g), including the standards necessary for adoption in order to support the secure, interoperable electronic data exchange among sectors within the pharmaceutical distribution supply chain.

(C) Best practices in each of the different sectors within the pharmaceutical distribution supply chain to implement the requirements of this section.

(D) The costs and benefits of the implementation of this section, including the impact on each pharmaceutical distribution supply chain sector and on public health.

(E) Whether electronic tracing requirements, including tracing of product at the package level, are feasible, cost effective, and needed to protect the public health.

(F) The systems and processes needed to utilize the product identifiers to enhance tracing of product at the package level, including allowing for verification, aggregation, and inference, as necessary.

(G) The technical capabilities and legal authorities, if any, needed to establish an interoperable, electronic system that provides for tracing of product at the package level.

(H) The impact that such additional requirements would have on patient safety, the drug supply, cost and regulatory burden, and timely patient access to prescription drugs.

(I) Other topics, as determined appropriate by the Secretary.

(j) Pilot projects

(1) In general

The Secretary shall establish 1 or more pilot projects, in coordination with authorized manufacturers, repackagers, wholesale distributors, and dispensers, to explore and evaluate methods to enhance the safety and security of the pharmaceutical distribution supply chain. Such projects shall build upon efforts, in existence as of November 27, 2013, to enhance the safety and security of the pharmaceutical distribution supply chain, take into consideration any pilot projects conducted prior to November 27, 2013, including any pilot projects that use aggregation and inference, and inform the draft and final guidance under paragraphs (3) and (4) of subsection (h).

(2) Content

(A) In general

The Secretary shall ensure that the pilot projects under paragraph (1) reflect the diversity of the pharmaceutical distribution supply chain and that the pilot projects, when taken as a whole, include participants representative of every sector, including both large and small businesses.

(B) Project design

The pilot projects under paragraph (1) shall be designed to—

(i) utilize the product identifier for tracing of a product, which may include verification of the product identifier of a product, including the use of aggregation and inference;

(ii) improve the technical capabilities of each sector and subsector to comply with systems and processes needed to utilize the product identifiers to enhance tracing of a product;

(iii) identify system attributes that are necessary to implement the requirements established under this section; and

(iv) complete other activities as determined by the Secretary.

(k) Sunset

The following requirements shall have no force or effect beginning on the date that is 10 years after November 27, 2013:

(1) The provision and receipt of transaction history under this section.

(2) The requirements set forth for returns under subsections (b)(4)(E), (c)(1)(B)(i), (d)(1)(C)(i), and (e)(4)(E).

(3) The requirements set forth under subparagraphs (A)(v)(II) and (D) of subsection (c)(1), as applied to lot level information only.

(*l*) Rule of construction

The requirements set forth in subsections (g)(4), (i), and (j) shall not be construed as a condition, prohibition, or precedent for precluding or delaying the provisions becoming effective pursuant to subsection (g).

(m) Requests for information

On the date that is 10 years after November 27, 2013, the timeline for responses to requests for information from the Secretary, or other appropriate Federal or State official, as applicable, under subsections (b)(1)(B), (c)(1)(C), and (e)(1)(C) shall be not later than 24 hours after receiving the request from the Secretary or other appropriate Federal or State official, as applicable, or in such other reasonable time as determined by the Secretary based on the circumstances of the request.

(June 25, 1938, ch. 675, § 582, as added and amended Pub. L. 113–54, title II, §§ 202, 203, Nov. 27, 2013, 127 Stat. 605, 623.)

Editorial Notes

AMENDMENTS

2013—Subsecs. (g) to (m). Pub. L. 113–54, § 203, added subsecs. (g) to (m).

§ 360eee–2. National standards for prescription drug wholesale distributors

(a) In general

The Secretary shall, not later than 2 years after November 27, 2013, establish by regulation standards for the licensing of persons under section 353(e)(1) of this title, including the revocation, reissuance, and renewal of such license.

(b) Content

For the purpose of ensuring uniformity with respect to standards set forth in this section, the standards established under subsection (a) shall apply to all State and Federal licenses described under section 353(e)(1) of this title and shall include standards for the following:

(1) The storage and handling of prescription drugs, including facility requirements.

(2) The establishment and maintenance of records of the distributions of such drugs.

(3) The furnishing of a bond or other equivalent means of security, as follows:

(A)(i) For the issuance or renewal of a wholesale distributor license, an applicant that is not a government owned and operated wholesale distributor shall submit a surety bond of $100,000 or other equivalent means of security acceptable to the State.

(ii) For purposes of clause (i), the State or other applicable authority may accept a surety bond in the amount of $25,000 if the annual gross receipts of the previous tax year for the wholesaler is $10,000,000 or less.

(B) If a wholesale distributor can provide evidence that it possesses the required bond in a State, the requirement for a bond in another State shall be waived.

(4) Mandatory background checks and fingerprinting of facility managers or designated representatives.

(5) The establishment and implementation of qualifications for key personnel.

(6) The mandatory physical inspection of any facility to be used in wholesale distribution within a reasonable time frame from the initial application of the facility and to be conducted by the licensing authority or by the State, consistent with subsection (c).

(7) In accordance with subsection (d), the prohibition of certain persons from receiving or maintaining licensure for wholesale distribution.

(c) Inspections

To satisfy the inspection requirement under subsection (b)(6), the Federal or State licensing authority may conduct the inspection or may accept an inspection by the State in which the facility is located, or by a third-party accreditation or inspection service approved by the Secretary or the State licensing such wholesale distributor.

(d) Prohibited persons

The standards established under subsection (a) shall include requirements to prohibit a person from receiving or maintaining licensure for wholesale distribution if the person—

(1) has been convicted of any felony for conduct relating to wholesale distribution, any felony violation of subsection (i) or (k) of section 331 of this title, or any felony violation of section 1365 of title 18 relating to product tampering; or

(2) has engaged in a pattern of violating the requirements of this section, or State requirements for licensure, that presents a threat of serious adverse health consequences or death to humans.

(e) Requirements

The Secretary, in promulgating any regulation pursuant to this section, shall, notwithstanding section 553 of title 5—

(1) issue a notice of proposed rulemaking that includes a copy of the proposed regulation;

(2) provide a period of not less than 60 days for comments on the proposed regulation; and

(3) provide that the final regulation take effect on the date that is 2 years after the date such final regulation is published.

(June 25, 1938, ch. 675, § 583, as added Pub. L. 113–54, title II, § 204(a)(5), Nov. 27, 2013, 127 Stat. 634.)

Statutory Notes and Related Subsidiaries

EFFECTIVE DATE

Section effective Jan. 1, 2015, see section 204(c) of Pub. L. 113–54, set out as an Effective Date of 2013 Amendment note under section 353 of this title.

§ 360eee–3. National standards for third-party logistics providers

(a) Requirements

No third-party logistics provider in any State may conduct activities in any State unless each facility of such third-party logistics provider—

(1)(A) is licensed by the State from which the drug is distributed by the third-party logistics provider, in accordance with the regulations promulgated under subsection (d); or

(B) if the State from which the drug distributed by the third-party logistics provider has not established a licensure requirement, is licensed by the Secretary, in accordance with the regulations promulgated under subsection (d); and

(2) if the drug is distributed interstate, is licensed by the State into which the drug is distributed by the third-party logistics provider if such State licenses third-party logistics providers that distribute drugs into the State and the third-party logistics provider is not licensed by the Secretary as described in paragraph (1)(B).

(b) Reporting

Beginning 1 year after November 27, 2013, a facility of a third-party logistics provider shall report to the Secretary, on an annual basis pursuant to a schedule determined by the Secretary—

(1) the State by which the facility is licensed and the appropriate identification number of such license; and

(2) the name and address of the facility and all trade names under which such facility conducts business.

(c) Costs

(1) Authorized fees of Secretary

If a State does not establish a licensing program for a third-party logistics provider, the Secretary shall license the third-party logistics provider located in such State and may collect a reasonable fee in such amount necessary to reimburse the Secretary for costs associated with establishing and administering the licensure program and conducting periodic inspections under this section. The Secretary shall adjust fee rates as needed on an annual basis to generate only the amount of revenue needed to perform this service. Fees authorized under this paragraph shall be collected and available for obligation only to the extent and in the amount provided in advance in appropriations Acts. Such fees are authorized to remain available until expended. Such sums as may be necessary may be transferred from the Food and Drug Administration salaries and expenses appropriation account without fiscal year limitation to such appropriation account for salaries and expenses with such fiscal year limitation.

(2) State licensing fees

(A) State established program

Nothing in this chapter shall prohibit a State that has established a program to license a third-party logistics provider from collecting fees from a third-party logistics provider for such a license.

(B) No State established program

A State that does not establish a program to license a third-party logistics provider in accordance with this section shall be prohibited from collecting a State licensing fee from a third-party logistics provider.

(d) Regulations

(1) In general

Not later than 2 years after November 27, 2013, the Secretary shall issue regulations regarding the standards for licensing under subsection (a), including the revocation and reissuance of such license, to third-party logistics providers under this section.

(2) Content

Such regulations shall—

(A) establish a process by which a third-party accreditation program approved by the Secretary shall, upon request by a third-party logistics provider, issue a license to each third-party logistics provider that meets the requirements set forth in this section;

(B) establish a process by which the Secretary shall issue a license to each third-party logistics provider that meets the requirements set forth in this section if the Secretary is not able to approve a third-party accreditation program because no such program meets the Secretary's requirements necessary for approval of such a third-party accreditation program;

(C) require that the entity complies with storage practices, as determined by the Secretary for such facility, including—

(i) maintaining access to warehouse space of suitable size to facilitate safe operations, including a suitable area to quarantine suspect product;

(ii) maintaining adequate security; and

(iii) having written policies and procedures to—

(I) address receipt, security, storage, inventory, shipment, and distribution of a product;

(II) identify, record, and report confirmed losses or thefts in the United States;

(III) correct errors and inaccuracies in inventories;

(IV) provide support for manufacturer recalls;

(V) prepare for, protect against, and address any reasonably foreseeable crisis that affects security or operation at the facility, such as a strike, fire, or flood;

(VI) ensure that any expired product is segregated from other products and returned to the manufacturer or repackager or destroyed;

(VII) maintain the capability to trace the receipt and outbound distribution of a product, and supplies and records of inventory; and

(VIII) quarantine or destroy a suspect product if directed to do so by the respective manufacturer, wholesale distributor, dispenser, or an authorized government agency;

(D) provide for periodic inspection by the licensing authority, as determined by the Secretary, of such facility warehouse space to ensure compliance with this section;

(E) prohibit a facility from having as a manager or designated representative anyone convicted of any felony violation of subsection (i) or (k) of section 331 of this title or any violation of section 1365 of title 18, relating to product tampering;

(F) provide for mandatory background checks of a facility manager or a designated representative of such manager;

(G) require a third-party logistics provider to provide the applicable licensing authority, upon a request by such authority, a list of all product manufacturers, wholesale distributors, and dispensers for whom the third-party logistics provider provides services at such facility; and

(H) include procedures under which any third-party logistics provider license—

(i) expires on the date that is 3 years after issuance of the license; and

(ii) may be renewed for additional 3-year periods.

(3) Procedure

In promulgating the regulations under this subsection, the Secretary shall, notwithstanding section 553 of title 5—

(A) issue a notice of proposed rulemaking that includes a copy of the proposed regulation;

(B) provide a period of not less than 60 days for comments on the proposed regulation; and

(C) provide that the final regulation takes effect upon the expiration of 1 year after the date that such final regulation is issued.

(e) Validity

A license issued under this section shall remain valid as long as such third-party logistics provider remains licensed consistent with this section. If the Secretary finds that the third-party accreditation program demonstrates that all applicable requirements for licensure under this section are met, the Secretary shall issue a license under this section to a third-party logistics provider receiving accreditation, pursuant to subsection (d)(2)(A).

(June 25, 1938, ch. 675, § 584, as added Pub. L. 113–54, title II, § 205, Nov. 27, 2013, 127 Stat. 636.)

§ 360eee–4. Uniform national policy

(a) Product tracing and other requirements

Beginning on November 27, 2013, no State or political subdivision of a State may establish or continue in effect any requirements for tracing products through the distribution system (including any requirements with respect to statements of distribution history, transaction history, transaction information, or transaction statement of a product as such product changes ownership in the supply chain, or verification, investigation, disposition, notification, or recordkeeping relating to such systems, including paper or electronic pedigree systems or for tracking and tracing drugs throughout the distribution system) which are inconsistent with, more stringent than, or in addition to, any requirements applicable under section 353(e) of this title or this part (or regulations issued thereunder), or which are inconsistent with—

(1) any waiver, exception, or exemption pursuant to section 360eee or 360eee–1 of this title; or

(2) any restrictions specified in section 360eee–1 of this title.

(b) Wholesale distributor and third-party logistics provider standards

(1) In general

Beginning on November 27, 2013, no State or political subdivision of a State may establish or continue any standards, requirements, or regulations with respect to wholesale prescription drug distributor or third-party logistics provider licensure that are inconsistent with, less stringent than, directly related to, or covered by the standards and requirements applicable under section 353(e) of this title, in the case of a wholesale distributor, or section 360eee–3 of this title, in the case of a third-party logistics provider.

(2) State regulation of third-party logistics providers

No State shall regulate third-party logistics providers as wholesale distributors.

(3) Administration fees

Notwithstanding paragraph (1), a State may administer fee collections for effectuating the wholesale drug distributor and third-party logistics provider licensure requirements under sections 353(e), 360eee–2, and 360eee–3 of this title.

(4) Enforcement, suspension, and revocation

Notwithstanding paragraph (1), a State—

(A) may take administrative action, including fines, to enforce a requirement promulgated by the State in accordance with section 353(e) of this title or this part;

(B) may provide for the suspension or revocation of licenses issued by the State for violations of the laws of such State;

(C) upon conviction of violations of Federal, State, or local drug laws or regulations, may provide for fines, imprisonment, or civil penalties; and

(D) may regulate activities of licensed entities in a manner that is consistent with product tracing requirements under section 360eee–1 of this title.

(c) Exception

Nothing in this section shall be construed to preempt State requirements related to the distribution of prescription drugs if such requirements are not related to product tracing as described in subsection (a) or wholesale distributor and third-party logistics provider licensure as described in subsection (b) applicable under section 353(e) of this title or this part (or regulations issued thereunder).

(June 25, 1938, ch. 675, § 585, as added Pub. L. 113–54, title II, § 205, Nov. 27, 2013, 127 Stat. 638.)

PART I—NONPRESCRIPTION SUNSCREEN AND OTHER ACTIVE INGREDIENTS

TERMINATION OF PART

This part ceased to be effective at the end of fiscal year 2022, see section 360fff–8 of this title.

§ 360fff. Definitions

In this part—

(1) the term ''Advisory Committee'' means the Nonprescription Drug Advisory Committee of the Food and Drug Administration or any successor to such Committee;

(2) the term ''final sunscreen order'' means an order published by the Secretary in the Federal Register containing information stating that a nonprescription sunscreen active ingredient or combination of nonprescription sunscreen active ingredients—

(A) is GRASE and is not misbranded if marketed in accordance with such order; or

(B) is not GRASE and is misbranded;

(3) the term ''GRASE'' means generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling of a drug as described in section 321(p) of this title;

(4) the term ''GRASE determination'' means, with respect to a nonprescription active ingredient or a combination of nonprescription active ingredients, a determination of whether such ingredient or combination of ingredients is GRASE;

(5) the term ''nonprescription'' means not subject to section 353(b)(1) of this title;

(6) the term ''pending request'' means each request with respect to a nonprescription sunscreen active ingredient submitted under section 330.14 of title 21, Code of Federal Regulations (as in effect on November 26, 2014) for consideration for inclusion in the over-the-counter drug monograph system—

(A) that was determined to be eligible for such review by publication of a notice of eligibility in the Federal Register prior to November 26, 2014; and

(B) for which safety and effectiveness data have been submitted to the Secretary prior to November 26, 2014;

(7) the term ''proposed sunscreen order'' means an order containing a tentative determination published by the Secretary in the Federal Register containing information proposing that a nonprescription sunscreen active ingredient or combination of nonprescription sunscreen active ingredients—

(A) is GRASE and is not misbranded if marketed in accordance with such order;

(B) is not GRASE and is misbranded; or

(C) is not GRASE and is misbranded because the data are insufficient to classify such ingredient or combination of ingredients as GRASE and not misbranded and additional information is necessary to allow the Secretary to determine otherwise;

(8) the term ''sponsor'' means the person that submitted—

(A) a request under section 360fff–1 of this title;

(B) a pending request; or

(C) any other application subject to this part;

(9) the term ''sunscreen'' means a drug containing one or more sunscreen active ingredients; and

(10) the term ''sunscreen active ingredient'' means an active ingredient that is intended for application to the skin of humans for purposes of absorbing, reflecting, or scattering ultraviolet radiation.

(June 25, 1938, ch. 675, § 586, as added Pub. L. 113–195, § 2(a), Nov. 26, 2014, 128 Stat. 2035.)

Statutory Notes and Related Subsidiaries

CONSTRUCTION

Pub. L. 113–195, § 2(b), Nov. 26, 2014, 128 Stat. 2045, provided that: ''Nothing in the amendment made by this section [enacting this section and sections 360fff–1 to [former] 360fff–5 of this title] shall be construed to—

''(1) limit the right of a sponsor (as defined in section 586(8) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360fff(8)], as added by subsection (a)) to request that the Secretary of Health and Human Services convene an advisory committee; or

''(2) limit the authority of the Secretary of Health and Human Services to meet with a sponsor (as defined in section 586(8) of the Federal Food, Drug, and Cosmetic Act, as added by subsection (a)).''

§ 360fff–1. Submission of requests

Any person may submit a request to the Secretary for a determination of whether a nonprescription sunscreen active ingredient or a combination of nonprescription sunscreen active ingredients, for use under specified conditions, to be prescribed, recommended, or suggested in the labeling thereof (including dosage form, dosage strength, and route of administration) is GRASE and should be included in part 352 of title 21, Code of Federal Regulations (or any successor regulations) concerning nonprescription sunscreen.

(June 25, 1938, ch. 675, § 586A, as added Pub. L. 113–195, § 2(a), Nov. 26, 2014, 128 Stat. 2036.)

§ 360fff–2. Eligibility determinations; data submission; filing

(a) Eligibility determinations

(1) In general

Not later than 60 calendar days after the date of receipt of a request under section 360fff–1 of this title, the Secretary shall—

(A) determine, in accordance with paragraph (2), whether the request is eligible for further review under subsection (b) and section 360fff–3 of this title;

(B) notify the sponsor of the determination of the Secretary; and

(C) make such determination publicly available in accordance with paragraph (3) and subsection (b)(1).

(2) Criteria for eligibility

(A) In general

To be eligible for review under subsection (b) and section 360fff–3 of this title, a request

shall be for a nonprescription sunscreen active ingredient or combination of nonprescription sunscreen active ingredients, for use under specified conditions, to be prescribed, recommended, or suggested in the labeling thereof, that—

(i) is not included in part 352 of title 21, Code of Federal Regulations (or any successor regulations) concerning nonprescription sunscreen; and

(ii) has been used to a material extent and for a material time under such conditions, as described in section 321(p)(2) of this title.

(B) Establishment of time and extent

A sponsor shall include in a request under section 360fff–1 of this title the information required under section 330.14 of title 21, Code of Federal Regulations (or any successor regulations) to meet the standard described in subparagraph (A)(ii).

(3) Public availability

(A) Redactions for confidential information

If a nonprescription sunscreen active ingredient or combination of nonprescription sunscreen active ingredients is determined under paragraph (1)(A) to be eligible for further review, the Secretary shall make the request publicly available, with redactions for information that is treated as confidential under section 552(b) of title 5, section 1905 of title 18, or section 331(j) of this title.

(B) Identification of confidential information by sponsor

At the time that a request is made under section 360fff–1 of this title, the sponsor of such request shall identify any information that such sponsor considers to be confidential information described in subparagraph (A).

(C) Confidentiality during eligibility review

The information contained in a request under section 360fff–1 of this title shall remain confidential during the Secretary's consideration under this section of whether the request is eligible for further review consistent with section 330.14 of title 21, Code of Federal Regulations (or any successor regulations).

(b) Data submission and filing of requests

(1) In general

In the case of a request under section 360fff–1 of this title that is determined to be eligible under subsection (a) for further review under this section and section 360fff–3 of this title, the Secretary shall, in notifying the public under subsection (a)(1)(C) of such eligibility determination, post the eligibility determination on the Internet website of the Food and Drug Administration, invite the sponsor of such request and any other interested party to submit comments, and provide a period of not less than 45 calendar days for comments in support of or otherwise relating to a GRASE determination, including published and unpublished data and other information related to the safety and efficacy of such request.

(2) Filing determination

Not later than 60 calendar days after the submission of data and other information described in paragraph (1) by the sponsor, the Secretary shall determine whether the data and other information submitted by the sponsor under this section are sufficiently complete, including being formatted in a manner that enables the Secretary to determine the completeness of such data and information, to enable the Secretary to conduct a substantive review under section 360fff–3 of this title with respect to such request. Not later than 60 calendar days after the submission of data and other information described in paragraph (1) by the sponsor, if the Secretary determines—

(A) that such data and other information are sufficiently complete, the Secretary shall—

(i) issue a written notification to the sponsor of the determination to file such request, and make such notification publicly available; and

(ii) file such request made under section 360fff–1 of this title; or

(B) that such data and other information are not sufficiently complete, the Secretary shall issue a written notification to the sponsor of the determination to refuse to file the request, which shall include the reasons for the refusal, including why such data and other information are not sufficiently complete, and make such notification publicly available.

(3) Refusal to file a request

(A) Request for meetings; submission of additional data or other information

If the Secretary refuses to file a request made under section 360fff–1 of this title, the sponsor may—

(i) within 30 calendar days of receipt of written notification of such refusal, request, in writing, a meeting with the Secretary regarding the filing determination; and

(ii) submit additional data or other information.

(B) Meetings

(i) In general

If a sponsor seeks a meeting under subparagraph (A)(i), the Secretary shall convene the meeting within 30 calendar days of the request for such meeting.

(ii) Actions after meeting

Following any meeting held under clause (i)—

(I) the Secretary may file the request within 60 calendar days;

(II) the sponsor may submit additional data or other information; or

(III) if the sponsor elects, within 120 calendar days, to have the Secretary file the request (with or without amendments to correct any purported deficiencies to the request)—

(aa) the Secretary shall file the request over protest, not later than 30 calendar days after the sponsor makes such election;

(bb) at the time of filing, the Secretary shall provide written notification of such filing to the sponsor; and

(cc) the Secretary shall make such notification publicly available.

(iii) Requests filed over protest

The Secretary shall not require the sponsor to resubmit a copy of the request for purposes of filing a request filed over protest, as described in clause (ii)(III).

(C) Submissions of additional data or other information

Within 60 calendar days of any submission of additional data or other information under subparagraph (A)(ii) or (B)(ii)(II), the Secretary shall reconsider the previous determination made under paragraph (2) with respect to the applicable request and make a new determination in accordance with paragraph (2).

(4) Public availability

(A) Redactions for confidential information

After the period of confidentiality described in subsection (a)(3)(C), the Secretary shall make data and other information submitted in connection with a request under section 360fff–1 of this title publicly available, with redactions for information that is treated as confidential under section 552(b) of title 5, section 1905 of title 18, or section 331(j) of this title.

(B) Identification of confidential information by sponsor

A person submitting information under this section shall identify at the time of such submission the portions of such information that the person considers to be confidential information described in subparagraph (A).

(June 25, 1938, ch. 675, §586B, as added Pub. L. 113–195, §2(a), Nov. 26, 2014, 128 Stat. 2036.)

§360fff–3. GRASE determination

(a) Review of new request

(1) Proposed sunscreen order

In the case of a request under section 360fff–1 of this title, not later than 300 calendar days after the date on which such request is filed under subsection (b)(2)(A) or (b)(3)(B)(ii)(III) of section 360fff–2 of this title, the Secretary—

(A) may convene a meeting of the Advisory Committee to review such request; and

(B) shall complete the review of such request and issue a proposed sunscreen order with respect to such request.

(2) Proposed sunscreen order by Commissioner

If the Secretary does not issue a proposed sunscreen order under paragraph (1)(B) within such 300-day period, the sponsor of such request may notify the Office of the Commissioner of such request and request review by the Office of the Commissioner. If such sponsor so notifies the Office of the Commissioner, the Commissioner shall, not later than 60 calendar days after the date of notification under this paragraph, issue a proposed sunscreen order with respect to such request.

(3) Public comment period

A proposed sunscreen order issued under paragraph (1)(B) or (2) with respect to a request shall provide for a period of 45 calendar days for public comment.

(4) Meeting

A sponsor may request, in writing, a meeting with respect to a proposed sunscreen order issued under this subsection and described in subparagraph (B) or (C) of section 360fff(7) of this title, not later than 30 calendar days after the Secretary issues such order. The Secretary shall convene a meeting with such sponsor not later than 45 calendar days after such request for a meeting.

(5) Final sunscreen order

With respect to a proposed sunscreen order under paragraph (1)(B) or (2)—

(A) the Secretary shall issue a final sunscreen order—

(i) in the case of a proposed sunscreen order described in subparagraph (A) or (B) of section 360fff(7) of this title, not later than 90 calendar days after the end of the public comment period under paragraph (3); or

(ii) in the case of a proposed sunscreen order described in subparagraph (C) of section 360fff(7) of this title, not later than 210 calendar days after the date on which the sponsor submits the additional information requested pursuant to such proposed sunscreen order; or

(B) if the Secretary does not issue such final sunscreen order within such 90- or 210-calendar-day period, as applicable, the sponsor of such request may notify the Office of the Commissioner of such request and request review by the Office of the Commissioner.

(6) Final sunscreen order by Commissioner

The Commissioner shall issue a final sunscreen order with respect to a proposed sunscreen order subject to paragraph (5)(B) not later than 60 calendar days after the date of notification under such paragraph.

(b) Review of pending requests

(1) In general

The review of a pending request shall be carried out by the Secretary in accordance with this subsection.

(2) Inapplicability of sections 360fff–1 and 360fff–2 of this title

Sections 360fff–1 and 360fff–2 of this title shall not apply with respect to any pending request.

(3) Feedback letters as proposed sunscreen order

Notwithstanding the requirements of section 360fff(7) of this title, a letter issued pursuant to section 330.14(g) of title 21, Code of Federal Regulations before November 26, 2014, with respect to a pending request, shall be deemed to be a proposed sunscreen order and displayed on the Internet website of the Food and Drug Administration. Notification of the avail-

ability of such letter shall be published in the Federal Register not later than 45 calendar days after November 26, 2014.

(4) Proposed sunscreen order

In the case of a pending request for which the Secretary has not issued a letter pursuant to section 330.14(g) of title 21, Code of Federal Regulations before November 26, 2014, the Secretary shall complete review of such request and, not later than 90 calendar days after November 26, 2014, issue a proposed sunscreen order with respect to such request.

(5) Proposed sunscreen order by Commissioner

If the Secretary does not issue a proposed sunscreen order under paragraph (4), or the Secretary does not publish a notification of the availability of a letter under paragraph (3), as applicable, the sponsor of such request may notify the Office of the Commissioner of such request and request review by the Office of the Commissioner. The Commissioner shall, not later than 60 calendar days after the date of notification under this paragraph, issue a proposed order with respect to such request.

(6) Public comment period

A proposed sunscreen order issued under paragraph (4) or (5), or a notification of the availability of a letter under paragraph (3), with respect to a pending request shall provide for a period of 45 calendar days for public comment.

(7) Meeting

(A) In general

A sponsor may request, in writing, a meeting with respect to a proposed sunscreen order issued under this subsection, including a letter deemed to be a proposed sunscreen order under paragraph (3), not later than 30 calendar days after the Secretary issues such order or the date upon which such feedback letter is deemed to be a proposed sunscreen order, as applicable. The Secretary shall convene a meeting with such sponsor not later than 45 calendar days after the date of such request for a meeting.

(B) Confidential meetings

A sponsor may request one or more confidential meetings with respect to a proposed sunscreen order, including a letter deemed to be a proposed sunscreen order under paragraph (3), to discuss matters relating to data requirements to support a general recognition of safety and effectiveness involving confidential information and public information related to such proposed sunscreen order, as appropriate. The Secretary shall convene a confidential meeting with such sponsor in a reasonable time period. If a sponsor requests more than one confidential meeting for the same proposed sunscreen order, the Secretary may refuse to grant an additional confidential meeting request if the Secretary determines that such additional confidential meeting is not reasonably necessary for the sponsor to advance its proposed sunscreen order, or if the request for a confidential meeting fails to include sufficient information upon which to base a substantive discussion. The Secretary shall publish a post-meeting summary of each confidential meeting under this subparagraph that does not disclose confidential commercial information or trade secrets. This subparagraph does not authorize the disclosure of confidential commercial information or trade secrets subject to 552(b)(4)[1] of title 5 or section 1905 of title 18.

(8) Advisory Committee

In the case of a proposed sunscreen order under paragraph (3), (4), or (5), an Advisory Committee meeting may be convened for the purpose of reviewing and providing recommendations regarding the pending request.

(9) Final sunscreen order

In the case of a proposed sunscreen order under paragraph (3), (4), or (5)—

(A) the Secretary shall issue a final sunscreen order with respect to the request—

(i) in the case of a proposed sunscreen order described in subparagraph (A) or (B) of section 360fff(7) of this title, not later than 90 calendar days after the end of the public comment period under paragraph (6); or

(ii) in the case of a proposed sunscreen order described in subparagraph (C) of section 360fff(7) of this title—

(I) if the Advisory Committee is not convened under paragraph (8), not later than 210 calendar days after the date on which the sponsor submits the additional information requested pursuant to such proposed sunscreen order, which shall include a rationale for not convening such Advisory Committee; or

(II) if the Advisory Committee is convened under paragraph (8), not later than 270 calendar days after the date on which the sponsor submits such additional information; or

(B) if the Secretary does not issue such final sunscreen order within such 90-, 210-, or 270-calendar-day period, as applicable, the sponsor of such request may notify the Office of the Commissioner about such request and request review by the Office of the Commissioner.

(10) Final sunscreen order by Commissioner

The Commissioner shall issue a final sunscreen order with respect to a proposed sunscreen order subject to paragraph (9)(B) not later than 60 calendar days after the date of notification under such paragraph.

(c) Advisory Committee

The Secretary shall not be required to—

(1) convene the Advisory Committee—

(A) more than once with respect to any request under section 360fff–1 of this title or any pending request; or

(B) more than twice in any calendar year with respect to the review under this section; or

(2) submit more than a total of 3 requests under section 360fff–1 of this title or pending

[1] So in original. Probably should be preceded by ''section''.

requests to the Advisory Committee per meeting.

(d) No delegation

Any responsibility vested in the Commissioner by subsection (a)(2), (a)(6), (b)(5), or (b)(10) shall not be delegated.

(e) Effect of final sunscreen order

(1) In general

(A) Sunscreen active ingredients determined to be GRASE

Upon issuance of a final sunscreen order determining that a nonprescription sunscreen active ingredient or combination of nonprescription sunscreen active ingredients is GRASE and is not misbranded, a sunscreen containing such ingredient or combination of ingredients shall be permitted to be introduced or delivered into interstate commerce for use under the conditions described in such final sunscreen order, in accordance with all requirements applicable to drugs not subject to section 353(b)(1) of this title, for so long as such final sunscreen order remains in effect.

(B) Sunscreen active ingredients determined not to be GRASE

Upon issuance of a final sunscreen order determining that a nonprescription sunscreen active ingredient or combination of nonprescription sunscreen active ingredients is not GRASE and is misbranded, a sunscreen containing such ingredient or combination of ingredients shall not be introduced or delivered into interstate commerce, for use under the conditions described in such final sunscreen order, unless an application is approved pursuant to section 355 of this title with respect to a sunscreen containing such ingredient or combination of ingredients, or unless conditions are later established under which such ingredient or combination of ingredients is later determined to be GRASE and not misbranded under the over-the-counter drug monograph system.

(2) Amendments to final sunscreen orders

(A) Amendments at initiative of Secretary

In the event that information relevant to a nonprescription sunscreen active ingredient or combination of nonprescription sunscreen active ingredients becomes available to the Secretary after issuance of a final sunscreen order, the Secretary may amend such final sunscreen order by issuing a new proposed sunscreen order under subsection (a)(1) and following the procedures set forth in this section.

(B) Petition to amend final order

Any interested person may petition the Secretary to amend a final sunscreen order under section 10.30, title 21 Code of Federal Regulations (or any successor regulations). If the Secretary grants any petition under such section, the Secretary shall initiate the process for amending a final sunscreen order by issuing a new proposed sunscreen order under subsection (a)(1) and following the procedures set forth in this section.

(C) Applicability of final orders

Once the Secretary issues a new proposed sunscreen order to amend a final sunscreen order under subparagraph (A) or (B), such final sunscreen order shall remain in effect and paragraph (3) shall not apply to such final sunscreen order until the Secretary has issued a new final sunscreen order or has determined not to amend the final sunscreen order.

(3) Relationship to orders under section 355h of this title

A final sunscreen order shall be deemed to be a final order under section 355h of this title.

(f) Exclusivity

(1) In general

A final sunscreen order shall have the effect of authorizing solely the order requestor (or the licensees, assignees, or successors in interest of such requestor with respect to the subject of such request and listed under paragraph (5)) for a period of 18 months, to market a sunscreen ingredient under this section incorporating changes described in paragraph (2) subject to the limitations under paragraph (4), beginning on the date the requestor (or any licensees, assignees, or successors in interest of such requestor with respect to the subject of such request and listed under paragraph (5)) may lawfully market such sunscreen ingredient pursuant to the order.

(2) Changes described

A change described in this paragraph is a change subject to an order specified in paragraph (1) that permits a sunscreen to contain an active sunscreen ingredient not previously incorporated in a marketed sunscreen listed in paragraph (3).

(3) Marketed sunscreen

The marketed sunscreen ingredients described in this paragraph are sunscreen ingredients—

(A) marketed in accordance with a final monograph for sunscreen drug products set forth at part 352 of title 21, Code of Federal Regulations (as published at 64 Fed. Reg. 27687); or

(B) marketed in accordance with a final order issued under this section.

(4) Limitations on exclusivity

Only one 18-month period may be granted per ingredient under paragraph (1).

(5) Listing of licensees, assignees, or successors in interest

Requestors shall submit to the Secretary at the time when a drug subject to such request is introduced or delivered for introduction into interstate commerce, a list of licensees, assignees, or successors in interest under paragraph (1).

(June 25, 1938, ch. 675, § 586C, as added Pub. L. 113–195, § 2(a), Nov. 26, 2014, 128 Stat. 2039; amended Pub. L. 116–136, div. A, title III, § 3854(b)(1)–(3), Mar. 27, 2020, 134 Stat. 455, 456.)

Editorial Notes

AMENDMENTS

2020—Subsec. (b)(7). Pub. L. 116–136, § 3854(b)(2), designated existing provisions as subpar. (A), inserted heading, and added subpar. (B).

Subsec. (e)(3). Pub. L. 116–136, § 3854(b)(1), amended par. (3) generally. Prior to amendment, par. (3) related to inclusion of ingredients that are subjects of final orders in the sunscreen monograph.

Subsec. (f). Pub. L. 116–136, § 3854(b)(3), added subsec. (f).

Statutory Notes and Related Subsidiaries

REVIEW OF NONPRESCRIPTION SUNSCREEN ACTIVE INGREDIENTS

Pub. L. 116–136, div. A, title III, § 3854(a), Mar. 27, 2020, 134 Stat. 454, provided that:

''(1) APPLICABILITY OF SECTION 505G FOR PENDING SUBMISSIONS.—

''(A) IN GENERAL.—A sponsor of a nonprescription sunscreen active ingredient or combination of nonprescription sunscreen active ingredients that, as of the date of enactment of this Act [Mar. 27, 2020], is subject to a proposed sunscreen order under section 586C of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360fff–3) may elect, by means of giving written notification to the Secretary of Health and Human Services within 180 calendar days of the enactment of this Act, to transition into the review of such ingredient or combination of ingredients pursuant to the process set out in section 505G of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355h], as added by section 3851 of this subtitle.

''(B) ELECTION EXERCISED.—Upon receipt by the Secretary of Health and Human Services of a timely notification under subparagraph (A)—

''(i) the proposed sunscreen order involved is deemed to be a request for an order under subsection (b) of section 505G of the Federal Food, Drug, and Cosmetic Act, as added by section 3851 of this subtitle; and

''(ii) such order is deemed to have been accepted for filing under subsection (b)(6)(A)(i) of such section 505G.

''(C) ELECTION NOT EXERCISED.—If a notification under subparagraph (A) is not received by the Secretary of Health and Human Services within 180 calendar days of the date of enactment of this Act, the review of the proposed sunscreen order described in subparagraph (A)—

''(i) shall continue under section 586C of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360fff–3); and

''(ii) shall not be eligible for review under section 505G, added by section 3851 of this subtitle.

''(2) DEFINITIONS.—In this subsection, the terms 'sponsor', 'nonprescription', 'sunscreen active ingredient', and 'proposed sunscreen order' have the meanings given to those terms in section 586 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360fff).''

§ 360fff–4. Guidance; other provisions

(a) Guidance

(1) In general

(A) Draft guidance

Not later than 1 year after November 26, 2014, the Secretary shall issue draft guidance on the implementation of, and compliance with, the requirements with respect to sunscreen under this part, including guidance on—

(i) the format and content of information submitted by a sponsor in support of a request under section 360fff–1 of this title or a pending request;

(ii) the data required to meet the safety and efficacy standard for determining whether a nonprescription sunscreen active ingredient or combination of nonprescription sunscreen active ingredients is GRASE and is not misbranded;

(iii) the process by which a request under section 360fff–1 of this title or a pending request is withdrawn; and

(iv) the process by which the Secretary will carry out section 360fff–3(c) of this title, including with respect to how the Secretary will address the total number of requests received under section 360fff–1 of this title and pending requests.

(B) Final guidance

The Secretary shall finalize the guidance described in subparagraph (A) not later than 2 years after November 26, 2014.

(C) Inapplicability of Paperwork Reduction Act

Chapter 35 of title 44 shall not apply to collections of information made for purposes of guidance under this subsection.

(2) Submissions pending issuance of final guidance

Irrespective of whether final guidance under paragraph (1) has been issued—

(A) persons may, beginning on November 26, 2014, make submissions under this part; and

(B) the Secretary shall review and act upon such submissions in accordance with this part.

(b) Rules of construction

(1) Currently marketed sunscreens

Nothing in this part shall be construed to affect the marketing of sunscreens that are marketed in interstate commerce on or before November 26, 2014, except as otherwise provided in this part.

(2) Ensuring safety and effectiveness

Nothing in this part shall be construed to alter the authority of the Secretary with respect to prohibiting the marketing of a sunscreen that is not safe and effective or is misbranded, or with respect to imposing restrictions on the marketing of a sunscreen to ensure safety and effectiveness, except as otherwise provided in this part, including section 360fff–3(e) of this title.

(3) Other drugs

Except as otherwise provided in section 360fff–6 of this title, nothing in this part shall be construed to affect the authority of the Secretary under this chapter or the Public Health Service Act (42 U.S.C. 201 et seq.) with respect to a drug other than a nonprescription sunscreen.

(4) Effect on drugs otherwise approved

Nothing in this part shall affect the marketing of a drug approved under section 355 of this title or section 351 of the Public Health Service Act [42 U.S.C. 262].

(c) Timelines

The timelines for the processes and procedures under paragraphs (1), (2), (5), and (6) of section

360fff–3(a) of this title shall not apply to any requests submitted to the Secretary under section 360fff–1 of this title after the date that is 6 years after November 26, 2014.

(June 25, 1938, ch. 675, § 586D, as added Pub. L. 113–195, § 2(a), Nov. 26, 2014, 128 Stat. 2044.)

Editorial Notes

REFERENCES IN TEXT

The Public Health Service Act, referred to in subsec. (b)(3), is act July 1, 1944, ch. 373, 58 Stat. 682, which is classified generally to chapter 6A (§ 201 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 201 of Title 42 and Tables.

§ 360fff–5. Repealed. Pub. L. 116–136, div. A, title III, § 3854(b)(5), Mar. 27, 2020, 134 Stat. 456

Section, June 25, 1938, ch. 675, § 586E, as added Pub. L. 113–195, § 2(a), Nov. 26, 2014, 128 Stat. 2045, related to sunscreen monograph.

§ 360fff–6. Non-sunscreen time and extent applications

(a) Pending time and extent applications

(1) In general

(A) Request for framework for review

If, prior to November 26, 2014, an application was submitted pursuant to section 330.14 of title 21, Code of Federal Regulations for a GRASE determination for a drug other than a nonprescription sunscreen active ingredient or combination of nonprescription sunscreen active ingredients and such drug was found to be eligible to be considered for inclusion in the over-the-counter drug monograph system pursuant to section 330.14 of title 21, Code of Federal Regulations, the sponsor of such application may request that the Secretary provide a framework under paragraph (2) for the review of such application.

(B) Request requirements

A request for a framework for review of an application made under subparagraph (A) shall be made within 180 calendar days of November 26, 2014, and shall include the preference of such sponsor as to whether such application is reviewed by the Secretary in accordance with—

(i) the processes and procedures set forth for pending requests under section 360fff–3(b) of this title, except that specific timelines shall be determined in accordance with other applicable requirements under this section;

(ii) the processes and procedures set forth under part 330 of title 21, Code of Federal Regulations (or any successor regulations);

(iii) an initial filing determination under the processes and procedures described in section 360fff–2(b) of this title and the processes and procedures set forth for pending requests under section 360fff–3(b) of this title, except that specific timelines shall be determined in accordance with other applicable requirements under this section; or

(iv) an initial filing determination under the processes and procedures described in section 360fff–2(b) of this title and the processes and procedures set forth under part 330 of title 21, Code of Federal Regulations (or any successor regulations).

(C) No request

If a sponsor described in subparagraph (A) does not make such request within 180 calendar days of November 26, 2014, such application shall be reviewed by the Secretary in accordance with the timelines of the applicable regulations when such regulations are finalized under subsection (b).

(2) Framework

Not later than 1 year after November 26, 2014, the Secretary shall provide, in writing, a framework to each sponsor that submitted a request under paragraph (1). Such framework shall set forth the various timelines, in calendar days, with respect to the processes and procedures for review under clauses (i), (ii), (iii), and (iv) of paragraph (1)(B) and—

(A) such timelines shall account for the considerations under paragraph (5); and

(B) the timelines for the various processes and procedures shall not be shorter than the timelines set forth for pending requests under sections 360fff–2(b) and 360fff–3(b) of this title, as applicable.

(3) Governing processes and procedures for review

(A) Election

Not later than 60 calendar days after the Secretary provides a framework to a sponsor under paragraph (2), such sponsor may provide an election to the Secretary regarding the processes and procedures for review under clause (i), (ii), (iii), or (iv) of paragraph (1)(B). If such sponsor makes such election, the Secretary shall review the application that is the subject of such election pursuant to the processes and procedures elected by such sponsor and the applicable timelines in calendar days set forth under such framework, which the Secretary shall confirm in writing to the sponsor not later than the date upon which the Secretary provides a report under paragraph (4). If such sponsor does not make such election, such application shall be reviewed by the Secretary in accordance with the timelines of the applicable regulations when such regulations are finalized under subsection (b).

(B) Different processes and procedures

At any time during review of an application, the Secretary may review such application under different processes and procedures under clause (i), (ii), (iii), or (iv) of paragraph (1)(B) than the processes and procedures the sponsor elected in accordance with subparagraph (A), so long as the Secretary proposes, in writing, the change and the sponsor agrees, in writing, to such change.

(C) Inclusion of ingredients in monographs

If the sponsor elects to use the processes and procedures for review in accordance

with clause (i) or (iii) of paragraph (1)(B), the Secretary may incorporate any resulting final order into a regulation addressing the conditions under which other drugs in the same therapeutic category are GRASE and not misbranded, including through direct final rulemaking, and the final order so incorporated shall cease to be effective on the effective date of the final regulation that addresses such drug.

(4) Letter regarding pending applications

Not later than 18 months after November 26, 2014, the Secretary shall report to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives, in writing, regarding all pending applications subject to paragraph (1). In such letter, the Secretary shall provide a report on the review of such applications, including the timelines, in calendar days, for the review and GRASE determination for each application. Such timelines shall account for the considerations under paragraph (5).

(5) Timelines

The timelines in calendar days established by the Secretary pursuant to this subsection—

(A) may vary based on the content, complexity, and format of the application submitted to the Secretary; and

(B) shall—

(i) reflect the public health priorities of the Food and Drug Administration, including the potential public health benefits posed by the inclusion of additional drugs in the over-the-counter drug monograph system;

(ii) take into consideration the resources available to the Secretary for carrying out such priorities and the processes and procedures described in paragraphs (1)(B) and (2); and

(iii) be reasonable, taking into consideration the requirements described in clauses (i) and (ii).

(b) New time and extent applications

(1) In general

Not later than 18 months after November 26, 2014, the Secretary shall issue proposed regulations establishing timelines for the review of applications for GRASE determinations for drugs other than nonprescription sunscreen active ingredients or combinations of nonprescription sunscreen active ingredients that are submitted to the Secretary after November 26, 2014, under section 330.14 of title 21, Code of Federal Regulations (or any successor regulations), and that are found to be eligible to be considered for inclusion in the over-the-counter drug monograph system pursuant to section 330.14 of title 21, Code of Federal Regulations (or any successor regulations), or that are subject to this subsection pursuant to paragraph (1) or (3) of subsection (a), as applicable, providing—

(A) timely and efficient completion of evaluations of applications under section 330.14 of title 21, Code of Federal Regulations (or any successor regulations) for drugs other than sunscreens; and

(B) timely and efficient completion of the review of the safety and effectiveness submissions pursuant to such applications, including establishing—

(i) reasonable timelines, in calendar days, for the applicable proposed and final regulations for applications of various content, complexity, and format, and timelines for internal procedures related to such processes; and

(ii) measurable metrics for tracking the extent to which the timelines set forth in the regulations are met.

(2) Timelines

The timelines in calendar days established in the regulations under paragraph (1)—

(A) may vary based on the content, complexity, and format of the application submitted to the Secretary; and

(B) shall—

(i) reflect the public health priorities of the Food and Drug Administration, including the potential public health benefits posed by the inclusion of additional drugs in the over-the-counter drug monograph system;

(ii) take into consideration the resources available to the Secretary for carrying out such priorities and the processes and procedures described in paragraph (1); and

(iii) be reasonable, taking into consideration the requirements described in clauses (i) and (ii).

(3) Procedure

In promulgating regulations under this subsection, the Secretary shall issue a notice of proposed rulemaking that includes a copy of the proposed regulation, provide a period of not less than 60 calendar days for comments on the proposed regulation, and publish the final regulation not less than 30 calendar days before the effective date of the regulation.

(4) Restrictions

Notwithstanding any other provision of law, the Secretary shall promulgate regulations implementing this section only as described in paragraphs (1), (2), and (3).

(5) Final regulations

The Secretary shall finalize the regulations under this section not later than 27 months after November 26, 2014.

(June 25, 1938, ch. 675, § 586F, as added Pub. L. 113–195, § 3, Nov. 26, 2014, 128 Stat. 2046.)

Statutory Notes and Related Subsidiaries

TREATMENT OF NON-SUNSCREEN TIME AND EXTENT APPLICATIONS

Pub. L. 116–136, div. A, title III, § 3854(d), Mar. 27, 2020, 134 Stat. 457, provided that:

''(1) IN GENERAL.—Any application described in section 586F of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360fff–6) that was submitted to the Secretary pursuant to section 330.14 of title 21, Code of Federal Regulations, as such provisions were in effect immediately prior to the date of enactment date of this Act [Mar. 27, 2020], shall be extinguished as of such date of enactment, subject to paragraph (2).

''(2) ORDER REQUEST.—Nothing in paragraph (1) precludes the submission of an order request under section

505G(b) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355h(b)], as added by section 3851 of this subtitle, with respect to a drug that was the subject of an application extinguished under paragraph (1).''

§ 360fff–7. Report

(a) In general

(1) In general

Not later than 18 months after November 26, 2014, and on the dates that are 2 and 4 years thereafter, the Secretary shall issue a report to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives describing actions taken under this part.

(2) Contents

The reports under this subsection shall include—

(A) a review of the progress made in issuing GRASE determinations for pending requests, including the number of pending requests—

(i) reviewed and the decision times for each request, measured from the date of the original request for an eligibility determination submitted by the sponsor;

(ii) resulting in a determination that the nonprescription sunscreen active ingredient or combination of nonprescription sunscreen active ingredients is GRASE and is not misbranded;

(iii) resulting in a determination that the nonprescription sunscreen active ingredient or combination of nonprescription sunscreen active ingredients is not GRASE and is misbranded and the reasons for such determinations; and

(iv) for which a determination has not been made, and an explanation for the delay, a description of the current status of each such request, and the length of time each such request has been pending, measured from the date of original request for an eligibility determination by the sponsor;

(B) a review of the progress made in issuing GRASE determinations for requests not included in the reporting under subparagraph (A), including the number of such requests—

(i) reviewed and the decision times for each request;

(ii) resulting in a determination that the nonprescription sunscreen active ingredient, combination of nonprescription sunscreen active ingredients, or other ingredient is GRASE and is not misbranded;

(iii) resulting in a determination that the nonprescription sunscreen active ingredient, combination of nonprescription sunscreen active ingredients, or other ingredient is not GRASE and is misbranded and the reasons for such determinations; and

(iv) for which a determination has not been made, and an explanation for the delay, a description of the current status of each such request, and the length of time each such request has been pending, measured from the date of original request for an eligibility determination by the sponsor;

(C) an annual accounting (including information from years prior to November 26, 2014, where such information is available) of the total number of requests submitted, pending, or completed under this part, including whether such requests were the subject of an advisory committee convened by the Secretary;

(D) a description of the staffing and resources relating to the costs associated with the review and decisionmaking pertaining to requests under this part;

(E) a review of the progress made in meeting the deadlines with respect to processing requests under this part; and

(F) to the extent the Secretary determines appropriate, recommendations for process improvements in the handling of requests under this part, including the advisory committee review process.

(b) Method

The Secretary shall publish the reports under subsection (a) in the manner the Secretary determines to be the most effective for efficiently disseminating the report, including publication of the report on the Internet website of the Food and Drug Administration.

(June 25, 1938, ch. 675, § 586G, as added Pub. L. 113–195, § 4(c), Nov. 26, 2014, 128 Stat. 2050.)

§ 360fff–8. Sunset

This part shall cease to be effective at the end of fiscal year 2022.

(June 25, 1938, ch. 675, § 586H, as added Pub. L. 116–136, div. A, title III, § 3854(b)(4), Mar. 27, 2020, 134 Stat. 456.)

SUBCHAPTER VI—COSMETICS

§ 361. Adulterated cosmetics

A cosmetic shall be deemed to be adulterated—

(a) If it bears or contains any poisonous or deleterious substance which may render it injurious to users under the conditions of use prescribed in the labeling thereof, or under such conditions of use as are customary or usual, except that this provision shall not apply to coal-tar hair dye, the label of which bears the following legend conspicuously displayed thereon: ''Caution—This product contains ingredients which may cause skin irritation on certain individuals and a preliminary test according to accompanying directions should first be made. This product must not be used for dyeing the eyelashes or eyebrows; to do so may cause blindness.'', and the labeling of which bears adequate directions for such preliminary testing. For the purposes of this paragraph and paragraph (e) the term ''hair dye'' shall not include eyelash dyes or eyebrow dyes.

(b) If it consists in whole or in part of any filthy, putrid, or decomposed substance.

(c) If it has been prepared, packed, or held under insanitary conditions whereby it may