Guidance for Industry and for FDA Reviewers

Guidance on Section 216 of the Food and Drug Administration Modernization Act of 1997

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U.S. Department of Health and Human Services
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Center for Devices and Radiological Health

Office of Device Evaluation

GRZAN

Preface

Public Comment

Until November 7, 2000, comments and suggestions regarding this document should be submitted to Docket No. 00D-1274, Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852. Such comments will be considered when determining whether to amend the current guidance.

After November 7, 2000 comments and suggestions may be submitted at any time for Agency consideration to: Thinh Nguyen, Center for Devices and Radiological Health, HFZ-402, 9200 Corporate Blvd., Rockville, MD 20850. Comments may not be acted upon by the Agency until the document is next revised or updated. For questions regarding the use or interpretation of this guidance contact Thinh Nguyen at 240-276-4010 or at thinh.nguyen@fda.hhs.gov.

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Guidance[1] on Section 216 of the Food and Drug Modernization Act of 1997

I. INTRODUCTION

This document provides guidance for industry and for FDA reviewers on the Food and Drug Administration's (FDA) interpretation of section 216 of the Food and Drug Administration Modernization Act of 1997 (FDAMA). The document describes how the Center for Devices and Radiological Health (CDRH) will apply the new provision and explains why FDA, through CDRH, has adopted this approach.

II. BACKGROUND

Section 216 of FDAMA establishes the six-year rule, under which:

> (4)(A)Any information contained in an application for premarket approval filed with the Secretary pursuant to section 515(c) (including information from clinical or 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-
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> (i) approving another device;
> (ii) determining whether a product development protocol has been completed under section 515 for another device;
> (iii) establishing a performance standard or special control under this Act; or
> (iv) classifying or reclassifying another device under section 513 or subsection (l)(2).
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> (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).

This provision replaced the previous section 520(h)(4) of the Food, Drug, and Cosmetic Act (FDCA), which was added by the Safe Medical Devices Act of 1990 (SMDA) and established the four-of-a-kind rule for use of data in PMA applications. Under the four-of-a-kind rule, the agency could use data contained in any filed PMA application 1 year after FDA had approved

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[1] This guidance document represents the Agency's current thinking on the interpretation of section 216 of the Food and Drug Administration Modernization Act of 1997. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

the fourth device of a kind.[2] The four-of-a-kind provision also contained detailed rules for its application to data in applications approved before SMDA's effective date. The SMDA provision replaced section 520(h)(3), which was enacted with the Medical Device Amendments of 1976 (MDA).[3] Under the MDA rule, the agency could not use data in one PMA to establish the safety or effectiveness of any device other than the one for which the data was submitted.

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[2] The use of data provision enacted with the SMDA provided:

> Any information contained in an application for premarket approval filed with the Secretary pursuant to section 515(c), including clinical and preclinical tests or studies, but excluding descriptions of methods of manufacture and product composition, that demonstrates the safety and effectiveness of a devices shall be available 1 year after the original application for the fourth devices of a kind has been approved by the Secretary, for use by the Secretary in approving devices, or determining whether a product development protocol has been completed, under section 515, establishing a performance standard under section 514, and reclassifying devices under subsections (e) and (f) of section 513, and subsection (l)(2). ...
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> (B) The Secretary, contemporaneously with the approval of the fourth device of a kind, shall publish an order in the Federal Register identifying the four devices of a kind that have been approved under section 515 and the date on which the data contained in the premarket approval applications will be available to the Secretary for use, as described in subparagraph (A).
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> (C) 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 regulatory action described in subparagraph (A).
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> (D)(i) This paragraph shall become effective--
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> (I) on November 15, 1990, for devices for which four devices of a kind were approved on or before December 31, 1987, and
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> (II) on November 15, 1991, for devices not described in subclause (I).
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> (ii) For each device described in clause (i)(I) the Secretary shall publish a notice in the Federal Register setting forth the date, which shall not be earlier than 1 year after the date of the notice, that the data identified in subparagraph (A) shall be available for the use of the Secretary.
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> (E)(i) Except as provided in clause (ii), the approval date of a device, for purposes of this paragraph, shall be the date of the letter of the Secretary to the applicant approving a device under section 515 and permitting the applicant to commercially distribute the device.
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> (ii) For each devices described in subparagraph(D)(i)(II) for which the original application for a fourth device of a kind is approved by the Secretary before November 1, 1991, the approval date of the fourth device of a kind shall be deemed to be November 15, 1991.
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> (F) Any challenge to an order under subparagraph (B) shall be made not later than 30 days after the date of the Federal Register notice referred to in such subparagraph.

[3] Section 520(h)(3), enacted with the MDA, provided:

Congress provided little explanation of the 6-year data use provision in FDAMA's legislative history. The legislative histories of the MDA and SMDA, however, each contain discussions relevant to the use of data provisions in those laws. See S. Rept. No. 513, 101st Cong., 2d Sess. 24 - 26 (1990); H. Rept. 808, 101st Cong, 2nd Sess. 27 - 28 (1990); H. Rept. No. 853, 94th Cong., 1st Sess. 50 (1976). These discussions provide a general insight: namely, that although legal rules facilitating market entry can harm fledgling industries, in strong, established markets, such rules will generally benefit both industry and consumers. In 1990, the device industry was stronger than it had been in 1976. By 1997, the industry was even stronger, see H. Rept. 307, 105th Cong., 1st Sess. 14 (1997) and better able to prosper without the aid of anti-competitive rules.

The Center never applied the SMDA four-of-a-kind provision; however, CDRH used its new FDAMA authority in its proposed reclassification of extracorporeal shock wave lithotriptors for fragmenting kidney and ureteral calculi from class III to class II. See 64 Federal Register 5987 (February 8, 1999). Although CDRH believes it had sufficient data to reclassify lithotriptors without using its authority under the new section 520(h)(4), this authority, by freeing data in five PMAs approved in 1991, provides additional support for the reclassification.

Before and since CDRH published its proposed reclassification, the Center received several letters from associations of medical device manufacturers advocating particular constructions of section 216. One association believed the provision allowed CDRH to rely on data in PMAs approved any time 6 or more years have passed; one association, which submitted a citizen's petition (see Docket Number 99P2725) outlining its views, believed the provision allowed CDRH to use only data in PMAs approved after FDAMA's effective date.

III. STATUTORY INTERPRETATION

CDRH is issuing this guidance in response to the conflicting interpretations of section 216 regulated industry has advanced. CDRH has concluded that it will apply section 216 to free data only in PMAs approved after November 28, 1990, the date of enactment of the SMDA. The agency does not intend to use data in PMAs approved before that date, other than data that would be available to the Center without the authority granted by section 216.

Several factors have led CDRH to develop this approach to application of section 216. A critical factor to consider was the language of the provision itself. CDRH believes the interpretation it has adopted is consistent with Congressional intent as expressed in section 216, but recognizes some parts of the industry believe the language supports a different interpretation,

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> Any information respecting a devices which is made available pursuant to paragraph (1) or (2) of this subsection (A) [detailed summaries of safety and effectiveness made publicly available] may not be used to establish to safety or effectiveness of another device for purposes of this Act 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.

and some believe the provision is ambiguous. CDRH discussed at length some of the legal issues raised by its interpretation of section 216 in its response to the citizen's petition on the subject, on file with FDA's Dockets Management Branch (see Docket Number 99P2725).

Another important consideration was fairness. Sponsors of applications approved before SMDA's enactment expected, at the time their applications were approved, that CDRH would not use the data they submitted to evaluate a competitor's product. This expectation was created by express language in the MDA of 1976. The four-of-a-kind rule unsettled these expectations by freeing data contained in PMAs approved before SMDA and created a new set of rules concerning data in PMAs approved after the new law. Beginning November 28, 1990, manufacturers of all as-yet unapproved medical devices had advance notice that the agency could use data contained in their approved PMA applications following approval of the third additional PMA for a device of the same kind, in accordance with the rules of the four-of-a-kind provision. Manufacturers may have anticipated that the SMDA rule would result in an extended or permanent period of protection for data contained in the applications of devices unlikely to be the subject of four or more applications. The SMDA, however, created no settled expectation of data protection on which manufacturers of such devices could reasonably rely, as medical advances, new technologies, and a variety of other market forces will affect the number of PMAs the agency receives for a device.

A third consideration was the interest of CDRH and sponsors of new submissions in access to data from earlier PMAs, an interest that seems particularly important to understanding the successive use-of-data provisions in the FDCA. Given the restrictive, contingent, and complex data use provision section 216 replaced, the purpose of the new, relatively permissive rule appears to be to facilitate informed decision-making in several areas of device regulation by allowing greater access to PMA data. Enhanced reliance on data previously reviewed by FDA is also consistent with other provisions of FDAMA that encourage the "least burdensome" pathways to product development and approval. This consideration, then, not only reflects a reasonable policy goal of the Center, but also accords with the trend in the FDCA device provisions of increasingly relaxed data-use.

A final important consideration was the need for rules that can be understood by industry and applied by the agency. This administrative consideration combined with legal, fairness, and access concerns, was included in the agency's approach to applying section 216. This approach is to use section 216 to free data in PMAs approved after November 28, 1990, in reviewing premarket submissions, classification and reclassification, and establishing special controls and performance standards for devices, but to forego use of data in PMAs approved before that date.

PROCEDURES FOR USE OF DATA FROM APPROVED PMAS

A. For what purpose can CDRH use data made available by the revised section 520(h)(4)?

Information available for use under the revised section 520(h)(4) may be used to:

1. approve another applicant's device;

2. determine whether another applicant's product development protocol has been completed;

3. establish a performance standard or special control; or

4. classify or reclassify another device under section 513 (Classification of Devices Intended for Human Use) and section 520(l)(2) (Transitional Provisions for Devices Considered as New Drugs or Antibiotic Drugs).

Information that can be used in support of the above includes data from clinical and preclinical tests or studies that were used to demonstrate the safety and effectiveness of a device. In addition, FDA may now use the publicly available detailed Summary of Safety and Effectiveness Data (SSED) required by section 520(h)(1)(A) as the evidentiary basis for any of the above four actions. FDA *may not* use information about the method of manufacture, product composition or other trade secrets found in the PMA, unless the information is otherwise publicly available to the agency. A trade secret as defined in 21 CFR 20.61 may consist of any commercially valuable plan, formula, process, or device that is used for the making, preparing, compounding, or processing of trade commodities and that can be said to be the end product of either innovation or substantial effort. There must be a direct relationship between the trade secret and the productive process.

Applicants who want CDRH to use data made available by FDAMA section 216 need to provide a detailed justification of how the information in the earlier SSED applies to the applicant's device and submission. In addition, the applicant needs to describe how the devices are similar enough to allow for the data from the earlier device to apply to the new device.

CDRH believes that, while the six-year provision may be used for 1 and 2 above, it will be most useful for CDRH and the industry when it is used as a tool to initiate reclassification, to develop a standard or special control, to develop new guidance documents for a specific device or to modify current guidance documents to reduce the burden of a specific device's data requirements. Reduction in the level of preclinical and/or clinical data requirements in a marketing application will depend on the similarities in device characteristics and performance and the intended use.

B. How will six-year data be identified?

Applicants who want to use the six year provision to support their marketing application (PMA or PDP) may identify pertinent sections of the SSED from an already approved device that they want CDRH to consider when reviewing their application for a new device. In addition, an interested person may identify information described in an SSED or other publicly available document (see "Supplements to Approved Applications for Class III Medical Devices: Use of Published Literature, Use of Previously Submitted Materials, and Priority Review" available at http://www.fda.gov/cdrh/modact/evidence.html) that they believe to be useful as a tool to implement reclassification procedures, develop a standard or special control, to develop new

guidance documents for a specific device or modify current guidance documents to reduce data requirements. An interested person should discuss the use of this provision with the appropriate ODE review division.

FDA may also, upon its own initiative, identify information available under the six-year rule for any of the uses authorized by the statute. FDA did identify such information in its proposal to downclassify lithotriptors. However, an applicant or petitioner should not rely upon FDA to identify useful data in any particular situation.

C. Does the six-year data provision mean FDA can disclose data to my competitors?

No. The six-year provision enables FDA to use certain data in taking the regulatory actions specified in 520(h)(4) of the act. It does not authorize FDA to disclose data that would otherwise be protected from disclosure. Sponsors of competitor products may be able to benefit by relying on your data 6 years after FDA approves your PMA; however, they will not gain any new rights to see your data under this provision.

D. How will I know when data in my approved PMA are used in support of an application, reclassification, or special control?

FDA plans to identify in the SSED for the new device the PMA SSED number that contained the data that were used in support of a PMA or PDP application, reclassification petition response, or FR document announcing development of a special control. The agency is interested in receiving comments and suggestions on this proposed method of notification.

E. How will use of these data affect the confidentiality of the data?

Because section 520(h)(4) does not authorize FDA to disclose data, the provision does not compromise the data's confidentiality. Use of data under this provision does not constitute disclosure of the data to a member of the public, and does not make confidential data available to the public.

FDA will train its review staff to determine what can reasonably be considered relevant and least burdensome to the applicant and the agency in accepting prior testing available under the six-year rule. FDA will also instruct staff with regard to the limits of section 520(h)(4) of the act, which expressly exclude use of methods of manufacture and product composition and other trade secrets from the kinds of data available under the six-year provision. CDRH review staff will also be trained to consult with their supervisors, the Freedom of Information Staff, and the Office of Chief Counsel, when questions arise with respect to this new provision

Interested applicants may also contact the Program Operations Staff at 301-594-2186 or the appropriate division review staff for help with the scientific review requirements related to the device and the use of the six-year provision.