Contains Nonbinding Recommendations

Postmarket Surveillance Under Section 522 of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry and Food and Drug Administration Staff

Document issued October 7, 2022.

The draft of this document was issued on May 27, 2021.

This document supersedes "Postmarket Surveillance Under Section 522 of the Federal Food, Drug, and Cosmetic Act", issued on May 16, 2016.

For questions about this document, contact OPEQ: Office of Product Evaluation and Quality / OCEA: Office of Clinical Evidence and Analysis / Division of Clinical Science and Quality via email at MandatedStudiesPrograms@fda.hhs.gov.



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

GRZAN

Preface

Public Comment

You may submit electronic comments and suggestions at any time for Agency consideration to https://www.regulations.gov. Submit written comments to the Dockets Management Staff, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852. Identify all comments with the docket number FDA-2011-D-0514. Comments may not be acted upon by the Agency until the document is next revised or updated.

Additional Copies

Additional copies are available from the Internet. You may also send an e-mail request to CDRH-Guidance@fda.hhs.gov to receive a copy of the guidance. Please include the document number 19042 and complete title of the guidance in the request.

Table of Contents

I. Introduction 4

II. Pre-522 Postmarket Surveillance Process 5
A. Legal Background 5
B. Identification of Issue 6
C. Team Review of Issue 6
D. Considerations Regarding Pediatric Population Provisions 7
E. Issuance of 522 Order 8

III. Postmarket Surveillance Plans 9
A. General Information 9
B. Elements to Include in a Postmarket Surveillance Plan 9
C. FDA and Manufacturer Agreement on Surveillance Plan 11
D. Changes to an Approved Postmarket Surveillance Plan 13
E. Types of Postmarket Surveillance 14

IV. When and How to Submit Postmarket Surveillance Reports 16

V. Content and Format of Postmarket Surveillance Reports 17
A. General Information 17
B. Postmarket Surveillance Enrollment Reports 18
C. Interim Postmarket Surveillance Status Report 19
D. Final Postmarket Surveillance Reports 20

VI. Evaluation of Interim Postmarket Surveillance Reports 20

VII. Evaluation of Postmarket Surveillance Final Reports and Possible FDA Actions After 522 Order Completion 21

VIII. Manufacturer's Reporting Status 22

IX. Postmarket Surveillance Status 23

X. Failure to Comply with Postmarket Surveillance Requirements under Section 522 of the FD&C Act 25

XI. Public Disclosure of Postmarket Surveillance Plan Information and Reports 26
A. FDA Website 26

APPENDIX 1: Section 522 Administrative Checklist Review (Per 21 CFR 822.9 & 822.10) 29

Postmarket Surveillance Under Section 522 of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry and Food and Drug Administration Staff

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction

Section 522 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) provides the Food and Drug Administration (FDA) with the authority to require manufacturers to conduct postmarket surveillance at the time of approval or clearance or at any time thereafter of certain class II or class III devices. Postmarket surveillance is the active, systematic, scientifically valid collection, analysis, and interpretation of data or other information about a marketed device.[1] The data collected under a surveillance order help to address important public health questions on the safety and effectiveness of a device.

This guidance document will assist manufacturers of devices subject to section 522 postmarket surveillance orders (522 orders) by providing:

- an overview of section 522 of the FD&C Act;
- information on how to fulfill section 522 obligations,[2] including:
    - when postmarket surveillance should be considered commenced;
    - recommendations for achieving an approved postmarket surveillance plan in a timely manner; and
    - recommendations for enrollment schedules to help achieve timely completion of postmarket surveillance;

[1] 21 CFR 822.3(i).

[2] *See* 21 CFR Part 822 for the full set of procedures and requirements for postmarket surveillance under section 522 of the FD&C Act.

- recommendations on the format, content, and review of postmarket surveillance plan and report submissions, including revised FDA review times for postmarket surveillance-related submissions; and
- updated surveillance status categories to better reflect progress.

This guidance document also aims to increase transparency to stakeholders on FDA's approach to the issuance and tracking of 522 orders, and expectations for timely study completion. Our initiative to increase transparency includes posting the manufacturers' progress on addressing 522 orders on FDA's website.[3]

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance means that something is suggested or recommended, but not required.

II. Pre-522 Postmarket Surveillance Process

A. Legal Background

When FDA identifies a potential issue with a device that could warrant postmarket surveillance (such as those described in Section II.B below), the associated review team may assess whether a 522 order is appropriate and falls within the statutory criteria.

Section 522 of the FD&C Act, 21 U.S.C. § 360l, authorizes FDA to require postmarket surveillance in the following instances:

- a class II or class III device for which failure of the device would be reasonably likely to have a serious adverse health consequence (section 522(a)(1)(A)(i) of the FD&C Act);
- a class II or class III device expected to have significant use in pediatric populations (section 522(a)(1)(A)(ii) of the FD&C Act);
- a class II or class III device that is intended to be implanted in the human body for more than one year (section 522(a)(1)(A)(iii)(I) of the FD&C Act); or
- a class II or class III device that is intended to be a life-sustaining or life-supporting device used outside of a device user facility (section 522(a)(1)(A)(iii)(II) of the FD&C Act).

[3] 522 Postmarket Surveillance Studies Database webpage: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pss.cfm.

B. Identification of Issue

FDA may identify device issues that are appropriate for postmarket surveillance at any point during the life cycle of a class II or III device, which meets statutory criteria identified in section 522(a)(1)(A) of the FD&C Act. Such issues may be identified through a variety of sources including analysis of adverse event reports, a recall or corrective action, post-approval data, review of premarket data, reports from other governmental authorities, or review of scientific literature.

Examples of situations that may raise postmarket questions, during both the premarket and postmarket periods, are listed below. FDA may order postmarket surveillance to:

- better understand the nature, severity, or frequency of suspected problems reported in adverse event reports or in the published literature.
- obtain more information on device performance associated with real-world clinical practice.
- address long term or infrequent safety and effectiveness issues for implantable and other devices for which the premarket testing provided more limited information. For example, premarket evaluation of a device may have been based on surrogate markers. Once the device is actually marketed, postmarket surveillance may be appropriate to assess the effectiveness of the device in detecting or treating the disease or condition, rather than the surrogate. Data collected through postmarket surveillance may include rates of malfunction or failure of a device intended for long-term use or incidents of latent sequelae resulting from device use.
- better define the association between problems and devices when unexpected or unexplained serious adverse events occur after a device is marketed, if there is a change in the nature of serious adverse events (e.g., severity), or if there is an increase in the frequency of serious adverse events.

C. Team Review of Issue

In assessing the appropriateness of issuing a 522 order, multiple elements are considered, as indicated below, with the goal of making a determination as to whether or not postmarket surveillance for a class II or class III device should be ordered. In addition, FDA may also engage external stakeholders prior to the issuance of a 522 order, when appropriate.

Some of the elements considered by FDA in deciding whether to issue a 522 order include:

- Are the statutory criteria of section 522 of the FD&C Act met?
- What is the public health question? The delineation of the public health question is the most important element discussed by the team.
- What is the public health question based on? It should be based on FDA's evaluation of

currently available data. Examples include but are not limited to scientific/medical concern from the review of a premarket submission and/or observed issues from the premarket data, a recall, medical device reports (MDRs), case studies, literature, or another source.

- Is the public health issue device-specific or device type-specific?

- For a device for which a condition of clearance or approval is being considered, can and should the public health question be addressed premarket rather than as part of a 522 order?

- Is there any other source of data (e.g., MDR review, published literature, real-world data (RWD) sources) or action (e.g., revised labeling, public health notice, recall), or a combination thereof, that may be used to address the public health question, instead of a 522 order?

- Does another ongoing study (e.g., premarket approval application (PMA) post-approval study as described in 21 CFR 814.82(a)(2) and 21 CFR 814.82(a)(9)) address the public health question?

- What type(s) of 522 postmarket surveillance design(s) should be recommended? Feasibility and timeliness of the different types of postmarket surveillance should be considered.

- What combination of efforts should be considered to address the public health question? In addition, when applicable, what changes, if any, are being made with regard to the premarket review?

D. Considerations Regarding Pediatric Population Provisions

As noted above, the statute authorizes postmarket surveillance for class II and III devices that are "expected to have a significant use in pediatric populations" and also authorizes the Agency to order postmarket surveillance as a condition of clearance or approval for devices expected to have significant use in pediatric populations.[4,5] These provisions are not limited to devices labeled for pediatric uses, and therefore specific consideration is given to devices with anticipated pediatric use.

Note that section 402(j)(1)(A)(ii) of the Public Health Service Act (PHS Act) (42 U.S.C. § 282(j)(1)(A)(ii)) also states that any "pediatric postmarket surveillance required under section

[4] Sections 522(a)(1)(A)(ii) and 522(a)(1)(B)

[5] Since "pediatric populations" is not defined in section 522 of the FD&C Act, for the purposes of 522 orders, FDA interprets pediatric populations to mean patients who are 21 years of age or younger at the time of diagnosis or treatment, that is, from birth through the twenty-first year of life, up to, but not including the patient's twenty-second birthday. This definition is consistent with the definition of "pediatric patients" under section 520(m)(6)(E)(i) of the FD&C Act, which was added to the FD&C Act at the same time as the pediatric use criterion in section 522.

522" is considered to be an "applicable device clinical trial." As such, the pediatric postmarket surveillance must be in compliance with the registration and results submission requirements of section 402(j) of the PHS Act (42 U.S.C. § 282(j)). Additional information on these requirements can be found at https://clinicaltrials.gov/.

FDA intends to work with the manufacturer to help FDA determine the appropriate timeframe for a pediatric 522 postmarket surveillance study.

E. Issuance of 522 Order

The 522 order will specify the device(s) subject to the surveillance order and the reason that we are requiring postmarket surveillance (i.e., the public health question(s)).[6] The order will also typically include any general or specific guidance that is available to assist the manufacturer subject to the 522 order in preparing the postmarket surveillance plan.[7] FDA intends to identify the premarket submission involved (i.e., premarket notification [510(k)], PMA, humanitarian device exemption (HDE) application, or De Novo request) in the 522 order. A 522 order could also include timelines for certain surveillance plan milestones such as subject enrollment, data accrual, and submission of the final report, depending on the plan and timing of the order. If a manufacturer disagrees with any order or condition requiring postmarket surveillance under section 522 of the FD&C Act, a manufacturer may request review under section 562 of the FD&C Act (see section 522(c) of the FD&C Act) and other options are further described in 21 CFR 822.7.

Section 522(a)(1)(A) of the FD&C Act specifies that the Agency may issue a postmarket surveillance order at the time of device approval or clearance or any time thereafter. When a 522 order is being considered for issuance at the time of market authorization, FDA may advise the manufacturer of the potential 522 order and the surveillance plan schedule, when appropriate. Pursuant to section 522(b)(1) each manufacturer must develop and submit for FDA approval a postmarket surveillance plan within 30 days[8] of receiving the order (see also 21 C.F.R. 822.9 and 822.10). Section 522(b)(1) of the FD&C Act provides that a manufacturer must commence postmarket surveillance not later than 15 months after the day the order is issued. FDA typically considers postmarket surveillance to have commenced when the first subject is enrolled as outlined in the approved surveillance plan. For plans that do not involve enrollment of subjects (e.g., non-clinical studies), FDA considers postmarket surveillance to have commenced when data accrual has started as outlined in the approved surveillance plan.[9]

In FDA's experience, surveillance plans that require enrolling subjects in a prospectively-targeted manner are more likely to achieve timely completion by following the recommended schedule below ***from the date of issuance of the 522 order***.

- Study commenced within 15 months

[6] 21 CFR 822.5.
[7] *Ibid*
[8] Use of the term "days" or "calendar days" throughout this guidance is intended to refer to calendar days and distinguish calendar days from working days (as specified in 21 CFR 822.34).
[9] For non-clinical surveillance/studies data, accrual milestone reports may be used to track progress.

- 20% of subjects enrolled within 18 months
- 50% of subjects enrolled within 21 months
- 100% of subjects enrolled within 24 months

III. Postmarket Surveillance Plans

FDA will assign a postmarket surveillance (PS) order number (i.e., PS######) to each 522 order. Manufacturers should cite the assigned PS order number when submitting a proposed postmarket surveillance plan. Surveillance plans are reviewed under the assigned PS order number. If there are multiple postmarket surveillance questions in a 522 order that require different methodologies to address each question, then a separate postmarket surveillance plan should be submitted for each question, and it is tracked as an individual requirement under the PS order number. FDA will confirm receipt and identify each plan submission by a unique document number.[10]

A manufacturer must submit a postmarket surveillance plan within 30 calendar days of receipt of the 522 order.[11] Per Section 522(b)(1) of the FD&C Act and 21 CFR 822.17, FDA will review postmarket surveillance plans and respond within 60 calendar days of receipt. FDA intends to promptly review postmarket surveillance plans and work interactively with the manufacturer in order to issue a decision within 30 calendar days of receiving the plan. The manufacturer should prioritize resolution of any surveillance plan deficiencies identified by the Agency and work interactively with the FDA to facilitate that a full surveillance plan review can be achieved within 60 calendar days from the issuance of the 522 order date.

A. General Information

The general content and format of a postmarket surveillance submission is outlined in 21 CFR 822.9. See Appendix 1 for FDA's internal checklist for determining whether a submission is administratively complete in accordance with 21 CFR 822.9.

B. Elements to Include in a Postmarket Surveillance Plan

As outlined in 21 CFR 822.10, the following sections must be included in your postmarket surveillance plan:

- postmarket surveillance plan objectives addressing the surveillance question(s)[12]
- postmarket surveillance approach (i.e., design) or methodology to be used[13] (see Section III.E. of this guidance); we recommend including the hypothesis(es) and success criteria

[10] *See* 21 CFR 822.8.
[11] Section 522(b)(1) of the FD&C Act and 21 CFR 822.8.
[12] 21 CFR 822.10(a)
[13] 21 CFR 822.10(d)

- the subject of the study,[14] e.g., the patient population (may include subject inclusion and exclusion criteria and definition, source of comparator group, and targets for ensuring diversity with respect to sex,[15] age, race, and ethnicity[16], as appropriate)
- the variables and endpoints for assessing the surveillance question(s),[17] such as the primary and secondary endpoints; we recommend including definitions for endpoints, a list of expected adverse events/complications, an agreement to collect unexpected adverse events, and a plan to assess relatedness of endpoints with the device and/or the procedure
- sample size;[18] we recommend including sample size calculation that is statistically justified and based on study hypothesis, where applicable
- description of the data source (e.g., hospital records, registry data);[19] we recommend including description of the data source relevance (e.g., does it capture information to address the surveillance question(s) in the order?) and of its reliability (e.g., data quality)
- description of data collection plan[20] (such as procedures, including data management and quality control where applicable[21])
- data collection forms,[22] informed consent forms,[23] and Institutional Review Board (IRB) approval or IRB exemption documentation,[24] where applicable
- patient follow-up plan or schedule;[25] we recommend including length of follow-up, a plan to minimize losses to follow-up assessments, estimated follow-up rate, as well as a description of baseline and follow-up assessments
- all data analyses and statistical tests planned[26] (such as statistical analysis plan)
- investigators agreement, if applicable[27]

---

[14] 21 CFR 822.10(b)
[15] *See* FDA guidance, "Evaluation of Sex-Specific Data in Medical Device Clinical Studies" (available at https://www.fda.gov/media/82005/download).
[16] *See* FDA guidance, "Evaluation and Reporting of Age-, Race-, and Ethnicity-Specific Data in Medical Device Clinical Studies" (available at https://www.fda.gov/media/98686/download).
[17] 21 CFR 822.10(c)
[18] 21 CFR 822.10(e)
[19] 21 CFR 822.10(g)
[20] 21 CFR 822.10(h)
[21] FDA notes that, where appropriate, it may be possible to meet a 522 order requirement through prospective or retrospective analysis of data from RWD sources, such as device registries and electronic health records. In addition, if RWD already exist that are of sufficient relevance and reliability and a prospective analysis will be timely performed by a device manufacturer, FDA may decide not to issue a 522 order. For additional information on the use of real-world evidence for medical devices, *see* FDA Guidance, "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-real-world-evidence-support-regulatory-decision-making-medical-devices.
[22] 21 CFR 822.10(h)
[23] 21 CFR 822.10(i)
[24] 21 CFR 822.10(j)
[25] 21 CFR 822.10(k)
[26] 21 CFR 822.10(n)
[27] 21 CFR 822.10(f)

- procedures for monitoring conduct and progress of the surveillance,[28] and estimate of the duration of the surveillance,[29] such as plan milestones/timeline elements, we recommend including (where applicable):
    - expected monthly number of study sites with IRB approvals
    - expected dates for achieving enrollment milestones (e.g., first subject, 20%, 50%, and 100%)
    - expected date to complete follow-up of all study participants, and
    - if applicable, information related to intermediate milestones (e.g., evaluation of surrogate endpoints in a study that also measures clinical benefits)

  FDA expects for manufacturers to meet elements set forth in and committed to in the postmarket surveillance plan.[30] The milestones identified in the postmarket surveillance plan will be the milestones which FDA intends to use to assess study status (see Sections III.D., IV, V, IX, and X for additional details related to reports and postmarket surveillance status).

- The content and timing of the Postmarket Surveillance Reports[31]

In addition to the items above, FDA also recommends the postmarket surveillance plan include the following:

- an interim data release plan (include frequency of interim analyses, type of analysis, data endpoints that will be assessed, content (i.e., endpoints to be posted), and proposed frequency of posting on the FDA's 522 Postmarket Surveillance Studies Database webpage).
- a background section (e.g., a brief description of the device, the regulatory history, the indications for use), and enrollment and recruitment plan.

In general, section 522(b)(1) of the FD&C Act authorizes FDA to order prospective postmarket surveillance for duration of up to 36 months unless the manufacturer and FDA agree to extend that timeframe or, if there is no agreement, after the completion of a dispute resolution as described in section 562 of the FD&C Act. Further, under section 522(b)(2) of the FD&C Act, FDA 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 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. FDA may work interactively with the manufacturer to help FDA determine the appropriate time frame for a pediatric 522 postmarket surveillance study.

C. FDA and Manufacturer Agreement on Surveillance Plan

FDA will evaluate the proposed surveillance plan to determine whether it is administratively

[28] 21 CFR 822.10(l)
[29] 21 CFR 822.10(m)
[30] 21 CFR 822.20
[31] 21 CFR 822.10(o)

complete, whether 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 and will answer the surveillance question(s).[32] Accordingly, FDA may issue one of the following letters:[33]

- **Not Acceptable Letter** – This letter is issued when a submission is found to be administratively incomplete because it does not include the items required by 21 CFR 822.9 and 822.10 to allow for a substantive review. See Appendix 1 for FDA's internal checklist for determining whether a submission is administratively complete.
- **Approval Letter** – This letter indicates FDA's approval of the proposed surveillance plan as submitted, along with any specific requirements or recommendations related to the surveillance plan.
- **Major Deficiency Letter** – This letter cites serious deficiencies relating to whether the plan will result in the collection of useful data that will answer the surveillance questions. The manufacturer must address these deficiencies and/or requests for specific information within the specified timeframe before the surveillance plan can be approved.[34]
- **Disapproval Letter** – This letter indicates FDA's disapproval of the plan submitted because FDA has determined it is not likely to result in the collection of useful data that will address the postmarket surveillance questions in the 522 order. The letter directs the manufacturer to revise its surveillance plan by submitting an entirely new submission within the specified timeframe that proposes a new surveillance plan intended to address the postmarket surveillance questions in the 522 order.

If a manufacturer disagrees with FDA about the content of the surveillance plan or if the surveillance plan is disapproved, possible recourse options are described in 21 CFR 822.22. These include seeking internal review of FDA's decision under 21 CFR 10.75; requesting an informal hearing under 21 CFR Part 16; or requesting review by the Medical Devices Dispute Resolution Panel of the Medical Devices Advisory Committee. A manufacturer may also request a meeting with the FDA employee that has signed the 522 order. During the pendency of such review, FDA does not intend to take enforcement action except as indicated in Section X.

FDA developed this guidance document, in part, to help facilitate timely discussions with manufacturers on postmarket surveillance plans, issues and challenges. Early and ongoing

[32] *See* 522(b)(1) of the FD&C Act and 21 CFR 822.16.
[33] *See* 21 CFR 822.19. FDA plans to use similar decision letters for supplements submitted by manufacturers proposing changes to approved surveillance plans.
[34] Consistent with FDA's approach to least burdensome provisions as outlined in the guidance "Developing and Responding to Deficiencies in Accordance with the Least Burdensome Provisions" (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/developing-and-responding-deficiencies-accordance-least-burdensome-provisions) if only minor deficiencies are identified, FDA intends to resolve such outstanding issues interactively.

interactions with FDA should be the primary method to ensure the adequacy of 522 surveillance plans and to resolve any issues. FDA intends to work with manufacturers on the development of their surveillance plans, including the timelines and expectations for commencing and progress of the postmarket surveillance, and plan for posting of any interim data that may be supplied on FDA's website. However, if FDA is unable to complete the review of the postmarket surveillance plan within 60 calendar days of issuance of a 522 order due to outstanding deficiencies that the manufacturer needs to address, we intend for the postmarket surveillance to be categorized as "Plan Overdue" on FDA's website.[35] Moreover, once the Secretary issues an order under section 522 requiring a manufacturer to conduct postmarket surveillance, if a manufacturer fails to submit a plan within 30 calendar days of the 522 order, fails to have an approved postmarket surveillance plan, or fails to commence postmarket surveillance within 15 months of the 522 order, this would constitute a failure to comply with a requirement under section 522. Failure to comply with a requirement under section 522 of the FD&C Act may result in enforcement action by FDA, as appropriate (See Section X.)

D. Changes to an Approved Postmarket Surveillance Plan

If a manufacturer wishes to propose a change to an approved postmarket surveillance plan that will affect the nature or validity of the data collected, the manufacturer must obtain FDA approval in writing before making such changes.[36] Examples of changes to an approved postmarket surveillance plan that FDA may consider to affect the nature or validity of the data collected could include changes to sample size, endpoints, follow-up assessments, etc. The manufacturer should not combine such a surveillance plan change with any 522 reports, but instead should submit a supplement to the PS order number (PS######) with the request and the revised postmarket surveillance plan for FDA review. Changes in the postmarket surveillance plan that will not affect the nature or validity of the data collected in accordance with the plan must be reported in the next interim report as required by the order.[37]

FDA understands that study delays sometimes may occur, however, FDA generally does not intend for manufacturers to routinely modify the postmarket surveillance plan to adjust study milestones. Manufacturers may request changes to the original enrollment milestones and FDA intends to consider each request on a case-by-case basis. An example of where a change to the original study milestone could be appropriate might be when new information indicates that the original study enrollment milestones were impractical at the time of the postmarket surveillance plan approval. However, based on its past experience, FDA expects that revisions to the original study milestones in the surveillance plan may only be appropriate in limited circumstances and the agency intends to determine the postmarket surveillance progress and to designate its status (e.g., as pending, ongoing, overdue, delayed, or non-compliant) based on the milestones as specified in the approved surveillance plan. See Section IV and Section V.C for recommendations regarding the communication of anticipated or occurring study delays in status reports. See Section VI for considerations for mitigating study delays.

[35] 522 Postmarket Surveillance Studies Database webpage: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pss.cfm
[36] *See* 21 CFR 822.21.
[37] *Ibid.*

In keeping with FDA's practice of focusing review resources on complete submissions, requests to change an approved postmarket surveillance plan will first undergo acceptance review to assess whether a supplement is administratively complete for FDA to conduct a substantive review.[38] If a supplement does not include the items listed in Appendix 1, a Not Acceptable letter may be issued identifying the missing items, which the manufacturer would need to provide in order for FDA to conduct a substantive review of the supplement.

Once accepted for substantive review, FDA may also find other deficiencies with a supplement, and issue a Major Deficiency letter identifying those issues that the manufacturer would need to address in order to receive approval. Or, if FDA determines that a proposed modification to an approved plan is not likely to result in the collection of useful data that will address the postmarket surveillance question, FDA will issue a Disapproval letter identifying the reasons for disapproval.[39]

Unless FDA approves the revised surveillance plan, the manufacturer remains responsible for completing the postmarket surveillance following the previously approved surveillance plan. Failure to meet the milestones and timelines outlined in the approved surveillance plan may result in enforcement action by FDA (see Section X).

E. Types of Postmarket Surveillance

FDA may order postmarket surveillance to address a wide variety of device-related public health questions. When developing a surveillance plan, FDA and the manufacturer should consider a least burdensome approach that is scientifically appropriate to address the surveillance question(s).[40] A 522 order may include multiple public health questions. If more than one postmarket surveillance study is needed to address the postmarket questions, each is tracked as a unique requirement under the 522 order. FDA also notes that, where appropriate, it may be possible to meet a 522 order requirement through prospective or retrospective analysis of data from RWD sources, such as device registries and electronic health records.[41]

Table 1 below describes different types of postmarket surveillance designs that could be used depending on the particular public health question.

Table 1. Types of Postmarket Surveillance Designs

[38] *See* 21 CFR 822.16.
[39] *See* 21 CFR 822.19.
[40] *See* FDA Guidance, "Least Burdensome Provisions: Concept and Principles", available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/least-burdensome-provisions-concept-and-principles.
[41] *See* FDA Guidance, "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-real-world-evidence-support-regulatory-decision-making-medical-devices.

Type	Design
Randomized Clinical Trial	Prospective study comparing the effects of one or more intervention(s) against a control group. Subjects are assigned randomly to one of the study groups.
Prospective Cohort Study	A study in which the subjects in a defined population are followed prospectively in time to assess the occurrence of outcomes of interest as they occur. Such studies can include one or more groups defined in terms of their exposure to a device. There is no randomization of treatment assignment.
Retrospective Cohort Study	A study in which the subjects in a defined population are followed forward in time; however, unlike a prospective cohort study, the data records documenting the device exposure and outcomes have been collected in the past relative to the time when the study is initiated. Such studies can include one or more groups defined in terms of their exposure to a device. There is no randomization of treatment assignment.
Cross-Sectional Study	A study in which the presence or absence of an exposure and health outcome are assessed at the same point in time.
Enhanced Surveillance	Continued monitoring of the distribution and trends in the incidence of adverse events through ongoing, *passive,* but systematic collection, analysis, and interpretation of data. A passive approach to surveillance means that the organization conducting the surveillance does not contact potential reporters and leaves the initial reporting to others. The surveillance may be designed to collect information on events that are both MDR-reportable and MDR non-reportable adverse events or device complaints.
Active Surveillance	Continued monitoring of the distribution and trends in the incidence of adverse events through ongoing, *active* systematic collection, analysis, and interpretation of data. An active approach means that the organization conducting the surveillance initiates procedures to obtain reports. The surveillance may be designed to collect information on events that are both MDR-reportable and MDR non-reportable adverse events or device complaints.
Meta-Analysis	Systematic review that combines the results of several studies that address a set of related research hypotheses. This is normally done by identification of a common measure of effect size, which is modeled using a form of meta-regression of the published or unpublished study data.
Prospective & Retrospective Study	A hybrid cohort study in which data are collected both retrospectively and prospectively. There is no randomization of the treatment assignment.
Case Control Study	Study in which subjects are identified on the basis of the presence of an outcome (cases) and compared to an appropriate comparison group (non-cases). The proportions with the exposure of interest are compared and Odds Ratios for the outcome(s) of interest are calculated.

Type	Design
Non-Clinical Study	A study that involves testing on the bench or laboratory setting (e.g., wear testing, fatigue testing).
Animal Study[42]	A study that involves animal testing (e.g., device or material implanted in animal).
Other Design	A surveillance methodology that does not fit one of the other categories.

IV. When and How to Submit Postmarket Surveillance Reports

Per 21 CFR 822.38, manufacturers must submit interim and final reports as specified in the postmarket surveillance plan. A 522 order can include the timing of reports. FDA recommends submitting two types of interim reports: "Enrollment Reports" and "Interim Postmarket Surveillance Status Reports." An Enrollment Report provides the progress towards meeting the enrollment milestones specified in the postmarket surveillance plan. For Enrollment Reports, the timing can be based on the expected completion dates for those enrollment milestones. An Interim Postmarket Surveillance Status Report includes subject accountability as well as device performance data. There may be instances in which the timing for submission of an Enrollment Report coincides with the timing for an Interim Postmarket Surveillance Status Report. In such instances, a manufacturer can submit one report labeled as "Enrollment and Interim Postmarket Surveillance Status Report."

The Final Postmarket Surveillance Report is a written report of a postmarket surveillance requirement that has been completed or terminated.

Unless alternative timeframes are specified in the 522 order, for each postmarket surveillance requirement, manufacturers should submit an Interim Postmarket Surveillance Status Report every 6 months for the first 2 years of the postmarket surveillance and annually, thereafter, from the date of the 522 postmarket surveillance plan approval or other agreed-upon starting date, separately for each unique requirement. Manufacturers should continue this reporting schedule, for each unique requirement, until the Final Postmarket Surveillance Report(s) are submitted. In accordance with the 522 order, the Final Postmarket Surveillance Report should be submitted no later than three months after study/surveillance completion for the particular postmarket surveillance requirement, which FDA considers to have occurred when the last data point is collected during the surveillance period (e.g., when the last subject completes the last follow-up visit).[43]

[42] FDA supports the principles of the "3Rs," to reduce, refine, and replace animal use in testing when feasible. We encourage manufacturers to consult with us if they wish to use a non-animal testing method they believe is suitable, adequate, validated, and feasible. We will consider if such an alternative method could be assessed for equivalency to an animal test method.

[43] For non-clinical surveillance/studies submission of final report is expected no later than three months from the date the last datapoint was captured.

In order to ensure proper review, the manufacturer should indicate the type of report and the time span on the report cover letter in **bold** letters (e.g., **Enrollment Report**, **6-Month Interim Postmarket Surveillance Status Report**, **12-Month Interim Postmarket Surveillance Status Report, Final Postmarket Surveillance Report**). For final reports, FDA also recommends that manufacturers clearly identify the postmarket surveillance requirement (i.e., public health question(s)) for which the report is being submitted.

Section 522 is not subject to section 745A(b) of the FD&C Act [21 U.S.C. § 379k-1(b)], regarding electronic copy (eCopy) requirements. However, submission of an eCopy is recommended for all postmarket surveillance plan submissions. If you choose to submit an eCopy, the eCopy should be accompanied by a paper copy of your signed cover letter and should be sent to the current address displayed on the eCopy Program webpage http://www.fda.gov/cdrhsubmissionaddress. Refer to FDA Guidance, "eCopy Program for Medical Device Submissions", for additional information on the eCopy program.[44]

V. Content and Format of Postmarket Surveillance Reports

FDA's ability to adequately track and evaluate postmarket surveillance depends on the quality and timeliness of information provided. The recommendations in this section are intended to help ensure that Postmarket Surveillance Reports contain adequate information for the Agency to identify the device being studied, the specific postmarket surveillance being conducted, the status of that postmarket surveillance, and, if applicable, the reasons for any delays or failures to complete the postmarket surveillance.

FDA recommends that Postmarket Surveillance Reports (interim and final) include the information listed below, clearly identified, and in separate sections. All reports should contain the data listed below and submitted per the timeline in the postmarket surveillance plan.

A. General Information

FDA recommends all reports include a section that contains the following general information:

- Postmarket surveillance tracking number (i.e., PS######)
- Manufacturer name and contact information (name of the individual or entity holding the approved PMA, or HDE, cleared 510(k), or De Novo order):
    - Company Name/Institution Name
    - Street Address
    - City
    - State/Province

[44] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/ecopy-program-medical-device-submissions

    - ZIP/Postal Code
    - Phone Number (include area code)
    - Contact name and title
    - Contact e-mail address
- Date of issuance of the 522 order
- Date of postmarket surveillance plan approval and, if applicable, dates of approval of any plan revisions
- Device trade name(s), subject to the 522 order
- Device model number(s), subject to the 522 order
- Report information:
    - Date of the report
    - Description of the data included in the report, including:
        - Enrollment data
        - Clinical study data
        - Non-clinical data (e.g., bench/laboratory)
        - Animal[45] study data
        - Other
- Type of submission:
    - Enrollment Report
    - Interim Postmarket Surveillance Status Report
    - Final Postmarket Surveillance Report
    - Response to FDA correspondence for a deficient report or another reason (specify)

B. Postmarket Surveillance Enrollment Reports

FDA intends to review Enrollment Reports to assess progress towards the surveillance plan milestones. If the postmarket surveillance plan involves new enrollment of subjects,[46] FDA may request a manufacturer to submit Enrollment Reports until enrollment is completed. The Enrollment Reports should include sufficient information to allow FDA and the manufacturer to track progress towards the enrollment milestones specified in the postmarket surveillance plan, including:

- Begin and end dates of period covered by the report
- Start and completion dates for clinical site(s) recruitment
- Number of IRB approvals and number of clinical sites at which the surveillance was initiated
- Subject-enrollment start date and expected completion date
- Number of subjects enrolled (if applicable, this information should be presented for the

[45] FDA supports the principles of the "3Rs," to reduce, refine, and replace animal use in testing when feasible. We encourage manufacturers to consult with us if they wish to use a non-animal testing method they believe is suitable, adequate, validated, and feasible. We will consider if such an alternative method could be assessed for equivalency to an animal test method.

[46] For non-clinical surveillance data, accrual milestone reports may be used to track progress.

entire subject population and for each subgroup, including sex,[47] age, race, and ethnicity[48], as appropriate)
- Comparison of target versus actual enrollment dates based on enrollment milestones specified in the postmarket surveillance plan

C. Interim Postmarket Surveillance Status Report

FDA recommends Interim Postmarket Surveillance Status Reports include (as applicable):

- purpose of the postmarket surveillance, including goals, objectives, and primary and secondary endpoints
- begin and end dates of period covered by the report
- date of database closure for the report (should not exceed three months prior to the submission of report)
- if clinical study:
    - description of the patient population being studied, including:
        - specific illness or condition
        - whether the postmarket surveillance targets subpopulations (e.g., pediatric, geriatric), and targets for ensuring diversity with respect to sex,[49] age, race, and ethnicity[50], as appropriate
        - total number of subjects to be studied
        - schedule of subject follow-up
    - subject accountability (e.g., enrolled, randomized, completed, withdrawn, lost to follow-up) at each follow-up timepoint for the entire population and broken down by subgroups, if applicable. To limit the potential bias in safety and effectiveness data, manufacturers should make every effort to reduce the number of subjects lost to follow-up.
    - if applicable, an explanation for:
        - delays in enrollment and plans to address challenges and meet enrollment milestones specified in the postmarket surveillance plan
        - subjects lost to follow-up, as well as any measure to minimize such future events
        - subject and healthcare provider-initiated discontinuations
        - any deaths, including reports from post-mortem examinations
- summary and interpretation of interim safety/effectiveness findings, as specified in the postmarket surveillance plan
- proposed interim summary data to be posted on FDA's 522 Postmarket Surveillance

[47] *See* FDA guidance, "Evaluation of Sex-Specific Data in Medical Device Clinical Studies" (available at https://www.fda.gov/media/82005/download).
[48] *See* FDA guidance, "Evaluation and Reporting of Age-, Race-, and Ethnicity-Specific Data in Medical Device Clinical Studies" (available at https://www.fda.gov/media/98686/download).
[49] *See* FDA guidance, "Evaluation of Sex-Specific Data in Medical Device Clinical Studies" (available at https://www.fda.gov/media/82005/download).
[50] *See* FDA guidance, "Evaluation and Reporting of Age-, Race-, and Ethnicity-Specific Data in Medical Device Clinical Studies" (available at https://www.fda.gov/media/98686/download).

Studies Database webpage[51]

D. Final Postmarket Surveillance Reports

FDA recommends Final Postmarket Surveillance Reports include (as applicable):

- purpose of the postmarket surveillance, including goals, objectives, and primary and secondary endpoints
- begin and end dates of period covered by the final report
- date of database closure for the final report
- if clinical study:
    - patient population being studied, including:
        - specific illness or condition
        - whether the postmarket surveillance targets subpopulations (e.g., pediatric, geriatric), and targets for ensuring diversity with respect to sex,[52] age, race, and ethnicity[53], as appropriate
        - total number of subjects to be studied
        - schedule of subject follow-up
    - final accountability of enrolled subjects, compared to target
    - final accountability of number of subjects (e.g., enrolled, randomized, completed, withdrawn, lost to follow-up) at each follow-up timepoint, for the entire population and broken down by subgroups, if applicable
    - if applicable, an explanation for:
        - subjects lost to follow-up, if known
        - subject and healthcare provider-initiated discontinuations
        - any deaths, including reports from post-mortem examinations
        - assessment of potential bias introduced by losses to follow-up (e.g., are subjects lost to follow-up different from those that remain under surveillance? Is the loss to follow-up differential by study group?) and impact on interpretation of results
- summary and interpretation of final safety/effectiveness findings
- proposed summary data to be posted on FDA's 522 Postmarket Surveillance Studies Database webpage[54]

VI. Evaluation of Interim Postmarket Surveillance Reports

FDA intends to consider multiple factors when evaluating an Interim Postmarket Surveillance Study Report, including:

- the completeness of the report content (especially in regard to progress towards

[51] FDA will make the final determination of what information is posted on the 522 Postmarket Surveillance Studies Database webpage based on the totality of our review and consistent with applicable disclosure laws.
[52] *See* FDA guidance, "Evaluation of Sex-Specific Data in Medical Device Clinical Studies" (available at https://www.fda.gov/media/82005/download).
[53] *See* FDA guidance, "Evaluation and Reporting of Age-, Race-, and Ethnicity-Specific Data in Medical Device Clinical Studies" (available at https://www.fda.gov/media/98686/download).
[54] *Ibid.*

achieving primary and secondary endpoints and performance goals, or sufficient individual endpoint data to infer progress in the case of composite endpoints)
- adherence to methodology in the postmarket surveillance plan and reasons for deviations from the methodology
- whether information in the reports address the public health question(s)
- the expected versus actual status of the study at the time of the report (especially timeliness in recruitment of subjects and sites to the study and adherence to the timeline in the postmarket surveillance plan)
- the causes for delays in postmarket surveillance progress or failure to meet enrollment milestones approved in the postmarket surveillance plan, and plan to address challenges and meet established milestones
    - When a sponsor fails to meet those enrollment milestones, FDA expects sponsors to act with due diligence to mitigate continued study delays. FDA intends to consider the sponsors' mitigations to address study delays. Mitigation efforts FDA may consider include, but are not limited to the following:

        - current and past enrollment recovery efforts;
        - evaluation of slow enrollment;
        - device availability on the market;
        - measures taken to initiate study sites;
        - measures taken to incentivize study subjects;
        - outreach to study investigators and potential subjects; and
        - plans to remove barriers to site and subject participation.

Although it is recommended that the manufacturer identify any missed milestones as part of postmarket surveillance reports, the manufacturer should communicate circumstances which are impacting their ability to meet the milestones in the postmarket surveillance plan to FDA as soon as possible.

FDA intends to review Interim Postmarket Surveillance Reports within 30 calendar days from submission receipt. If FDA has questions regarding the data provided in the report, or believes that the data are incomplete or insufficient, FDA will generally request additional information interactively and/or through a deficiency letter. If an interim report includes insufficient data or the manufacturer failed to meet established enrollment milestones or timelines, FDA ultimately may take enforcement actions to ensure compliance with the 522 order, as appropriate (see Section X). Additionally, if the data raise new concerns regarding the safety and/or effectiveness of a device, FDA may consider taking actions, which may include issuing a Safety Communication to provide recommendations on patient management, as appropriate.

VII. Evaluation of Postmarket Surveillance Final Reports and Possible FDA Actions After 522 Order Completion

FDA recommends the Final Postmarket Surveillance Report describe the methodology and results and explain how it fulfills the public health questions identified in the 522 order.

FDA will consider several factors in its evaluation of the Final Postmarket Surveillance Report, including:

- the completeness of the report content;
- adherence to methodology in the postmarket surveillance plan and reasons for deviations from the methodology;
- evaluation of information in the report to assess the performance of the device; and
- evaluation of fulfillment of the 522 order (i.e., have the public health questions been addressed).

FDA intends to complete its review of a manufacturer's Final Postmarket Surveillance Report submission and respond within 60 calendar days. If FDA concludes that the manufacturer has fulfilled the obligations in the 522 order, FDA will send a letter to the manufacturer reflecting that decision. However, if the results of the postmarket surveillance raise new issues or questions, additional actions may be warranted. In such circumstances, FDA could, for example:

- request changes to the labeling of the device to reflect additional information learned from the postmarket surveillance;
- issue a new 522 order to address new issues;
- consider other actions to protect the public health (e.g., request an update to a device's indications for use statement); or
- consider clinical recommendations to guide patient management (e.g., Safety Communication), as appropriate.

VIII. Manufacturer's Reporting Status

Upon receipt of an Interim or Final Postmarket Surveillance Report, FDA determines your reporting status based on the schedule in the postmarket surveillance plan. The reporting status categories are included in Table 2 below. The reporting status for each postmarket surveillance study is posted in the 522 Postmarket Surveillance Studies Database webpage.[55]

Table 2. Reporting Status Categories

Status	Definition
Report on Time	FDA has received the scheduled Interim or Final Postmarket Surveillance Report by the due date set in the agreed-upon schedule.
Report Overdue	FDA has not received the Interim or Final Postmarket Surveillance Report by the due date set in the agreed-upon schedule.
Report Overdue/Received	FDA has received the Interim or Final Postmarket Surveillance Report, although receipt was after the due date set in the agreed-upon schedule.

[55] https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pss.cfm

IX. Postmarket Surveillance Status

After the review of a supplement with a postmarket surveillance plan, or of an interim[56] or final report, FDA will consider the manufacturer's progress with completing the postmarket surveillance. Factors in considering the postmarket surveillance status include, as applicable:

1. Assessing the status of surveillance plan approval
2. After surveillance plan approval, assessing the following:
    a. Whether the surveillance plan milestones are met
    b. Progress with data accrual
    c. Submission of a final report

Based on the above, FDA will review the potential progress categories (see Table 3 below) and consider the appropriate progress status to be posted on the 522 Postmarket Surveillance Studies Database webpage.[57, 58] Information regarding study status is typically communicated to sponsors prior to updates on the 522 webpage. Of note, there may be circumstances in which a postmarket surveillance requirement may be put on a temporary hold, be redesigned, or terminated. A manufacturer's progress status is considered based on current information available to the agency and may be revised accordingly based on the availability of new information. Each of these status categories are described in Table 3 below.

Table 3. Postmarket Surveillance Status Categories

Overall Status	Description
Plan Pending	FDA has not received the postmarket surveillance plan or is reviewing the manufacturer's proposed postmarket surveillance plan, and it has been less than 60 calendar days since issuance of the 522 order.
Plan Overdue	FDA is unable to complete its review of the proposed postmarket surveillance plan due to outstanding deficiencies that the manufacturer needs to address, and it has been more than 60 calendar days since issuance of the 522 order.
Surveillance Pending	This status category is used from the time the postmarket surveillance plan is approved to the completion of the review of the first Interim Postmarket Surveillance Report.
Ongoing	The surveillance is proceeding according to, or is ahead of, the approved schedule. The FDA considers the surveillance to be ongoing until a final report is submitted to the FDA, as long as the activities are proceeding according to the approved

[56] *See* Section IV for types of Postmarket Surveillance Reports
[57] https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pss.cfm
[58] FDA updates the 522 Postmarket Surveillance Studies Database on a weekly basis. FDA encourages manufacturers to review the status of their postmarket surveillance to ensure its accuracy and if not, contact MandatedStudiesPrograms@fda.hhs.gov with questions.

Overall Status	Description
	surveillance plan.
Delayed	The progression of the surveillance is behind the approved schedule. For example, the enrollment of subjects (or data accrual) may or may not have started but the projected date for completion of that milestone has passed. Delays can occur in any phase of the surveillance, including subject enrollment, analysis of data, or submission of the final report to the FDA. While the milestones in the postmarket surveillance plan serve as the basis for defining the surveillance as delayed, each phase of the surveillance will be considered on its own right. If the manufacturer has one delayed phase, but gets back on schedule during the next phase, the delayed status will no longer apply.
Non-compliant	The surveillance fails to comply with a requirement under section 522, e.g., it has been more than 15 months since the 522 order date and the surveillance has not commenced.
Completed	The manufacturer has fulfilled the postmarket surveillance requirement(s) and FDA considers the requirement(s) under the 522 order to be satisfied.
Terminated	The manufacturer has not fulfilled or cannot fulfill the postmarket surveillance requirement identified in the 522 order (i.e., postmarket surveillance questions are no longer relevant, dataset cannot address public health question(s) in 522 order), and after all appropriate efforts to fulfill the requirement have been exhausted, FDA has terminated the postmarket surveillance requirement.
Redesigned/Replaced	The manufacturer has not fulfilled or cannot fulfill the surveillance requirement in the 522 order as designed and approved. All appropriate efforts to fulfill the postmarket surveillance requirement have been exhausted, and FDA has agreed to allow the manufacturer to redesign or replace the approved postmarket surveillance plan with a new surveillance plan to address the public health question(s) in the 522 order. The new plan supersedes the previous plan.
Hold	This status reflects when a postmarket surveillance requirement has been placed on a hold temporarily. Examples of situations when a postmarket surveillance requirement might be temporarily paused include the following examples: • while a change in ownership is completed, a pending separate study is being used to address the public health

Overall Status	Description
	question(s) in the 522 order, • redesigning the device and it needs prior premarket authorization to use in study, • device has been authorized for marketing in US, but is not currently marketed by manufacturer, • ceased device sales, but regulatory submission that received the 522 order has not been withdrawn. When the circumstances supporting the hold have resolved, the manufacturer is responsible for implementing the surveillance plan. The progress is assessed against the milestones approved in the postmarket surveillance plan and time since issuance of the revised 522 order.
Consolidated	The manufacturer has requested to consolidate multiple 522 orders for devices of a particular device type into one consolidated 522 order. FDA has agreed to have the multiple 522 orders consolidated under one 522 order.

X. Failure to Comply with Postmarket Surveillance Requirements under Section 522 of the FD&C Act

Failure or refusal to comply with a requirement under section 522 of the FD&C Act, including failure to commence surveillance within 15 months of a 522 order, is a prohibited act under section 301(q)(1)(C) of the FD&C Act, 21 U.S.C. § 331(q)(1)(C), and renders the device misbranded under section 502(t)(3) of the FD&C Act, 21 U.S.C. § 352(t)(3). Note that violations of sections 301(q)(1)(C) or misbranding under section 502(t)(3) may lead to enforcement actions including seizure of product, injunction, prosecution, and/or civil money penalties, as appropriate.[59]

Furthermore, the "failure to have an approved postmarket surveillance plan or failure to conduct postmarket surveillance in accordance with the approved plan" could also be the basis of enforcement action, as appropriate, because such constitutes failure to comply with section 522 of the FD&C Act, which is a prohibited act under section 301(q)(1)(C) of the FD&C Act and the device would be misbranded under section 502(t)(3) of the FD&C Act (21 CFR 822.20).

There may be instances in which it is impossible or inappropriate for a manufacturer to complete a particular postmarket surveillance order, and manufacturers may request exemption from the requirement to conduct postmarket surveillance for their devices, which FDA will consider under 21 CFR 822.30. Unless an exemption is granted, manufacturers must

[59] 21 CFR 822.20

comply with the 522 order.[60] If a manufacturer stops marketing the device subject to the postmarket surveillance order, it still must continue to conduct postmarket surveillance in accordance with the postmarket surveillance plan unless notified otherwise by the Agency.[61] Requests to terminate or modify postmarket surveillance in such instances will be decided on a case-by-case basis but are less likely to be granted for devices that are implanted long-term. FDA recommends that manufacturers initiate early communication with FDA if they intend to terminate postmarket surveillance prior to fulfilling the postmarket surveillance commitment.

Alternatively, if FDA determines a surveillance plan will no longer answer or adequately address questions in a 522 order, for example, because of the postmarket surveillance design, or due to a discontinuation in marketing or manufacturing of the device, but the 522 order objectives remain important, FDA intends to discuss the establishment of a new postmarket surveillance plan and schedule with the manufacturer.

XI. Public Disclosure of Postmarket Surveillance Plan Information and Reports

After approval of the manufacturer's plan, FDA may disclose the contents of the original submission and any amendments, supplements, or reports, in accordance with applicable disclosure laws, such as the Freedom of Information Act. When FDA discloses such information, FDA will continue to protect any trade secret or confidential commercial information, as well as any personal privacy information of patients.[62]

Any postmarket surveillance study that is an "applicable device clinical trial" as defined in section 402(j)(1)(A)(ii) of the PHS Act must comply with registration and results submission requirements for such clinical trials. Certain information on clinical trials is publicly available on the Clinical Trials webpage. Additional information on these requirements can be found at https://clinicaltrials.gov/ct2/manage-recs/background.

A. FDA Website

To increase transparency to FDA stakeholders, including consumers, healthcare providers, and industry, FDA posts information about postmarket surveillance (e.g., study description, status, and interim or final study results, see details below) on the FDA 522 Postmarket Surveillance Studies Database webpage.[63] As noted above, this information is posted in compliance with applicable disclosure statutes and regulations. Postmarket surveillance details that may be posted include:

General Information

- postmarket surveillance application number (i.e., PS########)

[60] 21 CFR 822.30
[61] 21 CFR 822.28
[62] 21 CFR 822.23
[63] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pss.cfm

- manufacturer name
- device name
- medical specialty (e.g., cardiovascular, orthopedic)
- date of issuance of the 522 order
- study/surveillance name
- most recent surveillance plan approval date
- study/surveillance plan overall status (see Section IX, Table 3 of this guidance)

General Surveillance Plan Parameters

- postmarket surveillance design
- data source(s)
- comparison group
- analysis type
- patient population

Detailed Surveillance Plan Parameters (where applicable)

- description of the postmarket surveillance design
- surveillance milestones in the approved surveillance plan
- sample size (number of subjects and sites)
- description of study population
- description of study endpoint(s)
- follow-up visits and length of follow-up

Interim Postmarket Surveillance Status Report Information

FDA intends to post on its website, or otherwise make public, postmarket surveillance interim results consistent with the interim data release plan in the postmarket surveillance plan. When interim data includes additional information that may be beneficial for public awareness that is not specified in the interim release plan, FDA may also include these data on the 522 Postmarket Surveillance Studies Database webpage. If the postmarket surveillance plan does not include an interim data release plan, FDA intends to post postmarket surveillance interim summary data and/or FDA's analyses thereof when appropriate to protect the public health, for example, when interim results raise safety concerns, serves to provide critical device performance information, or may otherwise impact treatment. FDA generally considers such information to be publicly releasable in accordance with applicable disclosure laws, such as the Freedom of Information Act. When sharing information appropriate to protect public health, FDA will consider the benefits of sharing the information, as well as other considerations on the study conduct. Examples of interim report information that FDA publicly discloses include:

- number of subjects enrolled
- number of sites enrolled
- interim safety/effectiveness findings

However, if a manufacturer believes in a particular instance that interim results are prohibited from public release; for example, because they constitute personal identifying information, trade secrets, or confidential commercial information, they should notify FDA of this in the

interim report containing the results and explain why they believe disclosure of the data is prohibited.

Final Postmarket Surveillance Report Results (where applicable)

- actual number of subjects enrolled
- actual number of sites enrolled
- subject follow-up rate
- final safety/effectiveness findings and results
- FDA's interpretation and summation of the study/surveillance strengths and weaknesses

Reporting Information

- Interim and Final Postmarket Surveillance Report(s) schedule
- due date(s) for Interim and Final reports (based on postmarket surveillance plan)
- FDA receipt date(s) of Interim and Final Postmarket Surveillance Report(s)
- receipt status category for Interim and Final Postmarket Surveillance Report(s)

Additional elements may be posted on FDA's website, as permitted by applicable disclosure statutes and regulations.

APPENDIX 1: Section 522 Administrative Checklist Review (Per 21 CFR 822.9 & 822.10)

The following is an internal checklist for use by FDA staff to determine whether a postmarket surveillance submission is administratively complete. The checklist can be used by manufacturers as a reference when preparing their postmarket surveillance submissions.

Items required	Circle Yes or No or N/A
21 CFR 822.9 – The submission must include:	
(a) Organizational/administrative information	
(1) Name and address	**Yes or No or N/A**
(2) Generic and trade names of the device	**Yes or No or N/A**
(3) Name and address of the contact person for the submission	**Yes or No or N/A**
(4) Premarket application/submission number and device identifiers for the device	**Yes or No or N/A**
(5) Table of contents identifying page numbers for each section of the submission	**Yes or No or N/A**
(6) Description of the device (this may be incorporated by reference to the appropriate premarket application/submission)	**Yes or No or N/A**
(7) Product codes and list of all relevant model numbers	**Yes or No or N/A**
(8) Indications for use and claims for the device	**Yes or No or N/A**
(b) Postmarket surveillance plan	**Yes or No or N/A**
(c) Designated person information	
(1) Name, address, and telephone number	**Yes or No or N/A**
(2) Experience and qualifications	**Yes or No or N/A**
21 CFR 822.10 – The surveillance plan must include:	
(a) The plan objective(s) addressing the surveillance questions identified in the 522 order	**Yes or No or N/A**
(b) The subject of the study, e.g., patients, the device, animals	**Yes or No or N/A**
(c) The variables and endpoints that will be used to answer the surveillance question, e.g., clinical parameters or outcomes	**Yes or No or N/A**
(d) The surveillance approach or methodology to be used	**Yes or No or N/A**
(e) Sample size and units of observation	**Yes or No or N/A**
(f) The investigator agreement, if applicable	**Yes or No or N/A**
(g) Sources of data, e.g., hospital records	**Yes or No or N/A**
(h) The data collection plan and forms	**Yes or No or N/A**
(i) The consent document, if applicable	**Yes or No or N/A**

Items required	Circle Yes or No or N/A
(j) Institutional review board information, if applicable	**Yes or No or N/A**
(k) The patient follow-up plan, if applicable	**Yes or No or N/A**
(l) The procedures for monitoring conduct and progress of the surveillance	**Yes or No or N/A**
(m) An estimate of the duration of surveillance, e.g., timeline for milestones	**Yes or No or N/A**
(n) All data analysis and statistical test planned	**Yes or No or N/A**
(o) The content and timing of reports, e.g., reporting schedule	**Yes or No or N/A**