

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

Guidance for Industry and Food and Drug Administration Staff

GUIDANCE

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For questions regarding this document, contact the Division of Epidemiology, at 301-796-5969.



**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Office of Surveillance and Biometrics
Division of Epidemiology**

Preface

Public Comment

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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.

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Guidance for Industry and Food and Drug Administration Staff

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

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 responsible for this guidance as listed on the title page.

1. Introduction

Section 522 of the Federal Food, Drug, and Cosmetic Act (FD&C Act or the Act) provides the Food and Drug Administration (FDA) with the authority to require manufacturers to conduct postmarket surveillance of certain class II or class III devices. Postmarket surveillance is not a substitute for obtaining the necessary premarket information to support 510(k) clearance, PMA, HDE, or PDP approval, or grant of de novo order.

Congress first granted FDA the authority to require manufacturers of certain medical devices to conduct postmarket surveillance under section 522 of the Act in the Safe Medical Devices Act of 1990 (SMDA). Section 212 of the Food and Drug Modernization Act (FDAMA) of 1997 amended section 522 in part to provide that postmarket surveillance may be required by order for any Class II or Class III device the failure of which would be reasonably likely to have serious adverse health consequences, which is intended to be implanted in the human body for more than one year, or which is a life-sustaining or life-supporting device used outside a device user facility. Section 212 of FDAMA also authorized the agency to require a prospective surveillance period of up to 36 months, unless the agency determines a longer period is necessary and there is a mutual agreement between the agency and the manufacturer or, if there is no agreement, after the completion of a dispute resolution as described in section 562 of the Act, 21 U.S.C. § 360bbb-1.

Section 307 of the FDA Amendments Act of 2007 (FDAAA) further amended section 522 of the Act by adding a fourth category of class II and class III devices for which postmarket surveillance may be ordered: those devices expected to have significant use in pediatric populations. FDAAA authorized the agency to require a prospective surveillance period of more than 36 months for devices with significant use in pediatric populations and specified that postmarket surveillance may be ordered as a condition of clearance or approval for such devices.

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FDAAA also added a dispute resolution provision whereby a manufacturer may request review under section 562 of the Act of any order or condition requiring postmarket surveillance under section 522 of the Act.

Section 616 of the Food and Drug Administration Safety and Innovation Act (FDASIA) further amended section 522 by specifying that the agency may issue a postmarket surveillance order at the time of device approval or clearance or any time thereafter. It also provided that a manufacturer must commence postmarket surveillance not later than 15 months after the day the order is issued.

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

- an overview of section 522 of the Act,
- information on how to fulfill section 522 obligations,¹ and
- recommendations on the format, content, and review of postmarket surveillance plan submissions

FDA's guidance documents, including this guidance, 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 guidances means that something is suggested or recommended, but not required.

2. Legal Background

A. Statutory Criteria

Section 522 of the 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 Act);
- a class II or class III device expected to have significant use in pediatric populations (section 522(a)(1)(A)(ii) of the Act);
- a class II or class III device intended to be implanted in the human body for more than one year (section 522(a)(1)(A)(iii)(I) of the Act); or
- a class II or class III device intended to be a life-sustaining or life-supporting device used outside of a user facility (section 522(a)(1)(A)(iii)(II) of the Act)

¹ Refer to [21 CFR Part 822](#) for the full set of procedures and requirements for postmarket surveillance required under section 522 of the Act. This guidance document focuses on certain procedural requirements.

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B. Considerations Regarding Pediatric Population Provisions

Section 522(a)(1)(A)(ii) of the Act authorizes postmarket surveillance for class II and III devices that are “expected to have a significant use in pediatric populations.” This provision is not limited to devices labeled for pediatric uses. Section 522(a)(1)(B) of the Act authorizes the agency to order postmarket surveillance as a *condition* of clearance or approval for devices expected to have significant use in pediatric populations. “Pediatric populations” is not defined in section 522 of the Act. For purposes of section 522 of the Act, FDA is defining 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 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 Act at the same time as the pediatric use criterion in section 522.

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 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 <http://clinicaltrials.gov/ct2/invest>.

C. Postmarket Surveillance Duration

In general, section 522(b)(1) of the 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 Act. However, section 522(b)(2) of the Act authorizes FDA to 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 intends to work with the manufacturer to determine the appropriate time frame for a pediatric study.

D. Timing for Issuing a 522 Order And Commencement of Postmarket Surveillance

Section 522(a)(1)(A) of the Act specifies that the agency may issue a postmarket surveillance order at the time of device approval or clearance or any time thereafter. Section 522(b)(1) of the Act provides that a manufacturer must commence postmarket surveillance not later than 15 months after the day the order is issued.

3. Pre-522 Postmarket Surveillance Process

A. Identification of Issue

FDA may identify device issues that are appropriate for postmarket surveillance at any point during the life cycle of a device. 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.

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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.
- FDA may order postmarket surveillance to obtain more information on device performance associated with real-world clinical practice.
- FDA may order postmarket surveillance to 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.
- FDA may order postmarket surveillance to 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.

B. Team Review of Issue

When FDA identifies a potential issue with a device that may warrant postmarket surveillance (such as those described in Section 3.A. above), the Division of Epidemiology (DEPI), Office of Surveillance and Biometrics (OSB), Center for Devices and Radiological Health (CDRH) makes a determination regarding whether the statutory requirements for a section 522 order have been met. Next, the Division establishes a cross-Center team (i.e., pre-522 team) to review the issue in greater depth. This team may include FDA epidemiologists, clinicians, or other experts as needed to assess the issue. The pre-522 team evaluates numerous elements, as indicated below, with the ultimate goal of making a recommendation to the DEPI Division Director and OSB Director as to whether or not a 522 order should be issued to address a public health question. In addition, FDA may also choose to engage external stakeholders prior to the issuance of a 522 order.

Some of the elements discussed by FDA's pre-522 team include:

- Are the statutory criteria met?
- What is the public health question? The delineation of the public health question is the most important element discussed by the team.

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- 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 other 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, literature) or action (e.g., revised labeling, public health notice, recall), or a combination thereof, that may be used to address the public health question?
- Does another ongoing study (e.g., PMA post-approval study as described in 21 CFR 814.82(a)(2)) address the public health question?
- What types 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, what changes, if any, are being made with regard to the premarket review?

C. Issuance of 522 Order

An order for postmarket surveillance under section 522 of the Act will generally be issued by the OSB Director. The 522 order should identify the premarket submission involved (i.e., 510(k), PMA, PDP, or HDE, or de novo petition), the public health questions, the rationale for the 522 order, and postmarket surveillance design recommendations to assist the manufacturer subject to the 522 order in preparing the postmarket surveillance plan. See [21 CFR 822.5](#). If a manufacturer disagrees with any order or condition requiring postmarket surveillance under section 522 of the Act, possible recourse options are described in 21 CFR 822.7.

4. Postmarket Surveillance Plans

FDA will assign a postmarket surveillance (PS) number (i.e., PS#####) to each 522 order. Manufacturers should cite the assigned PS number when submitting a proposed postmarket surveillance plan. If there are multiple postmarket surveillance requirements in a 522 order, then a separate postmarket surveillance plan should be submitted for each requirement. FDA will confirm receipt and identify each plan submission by a unique document number. See 21 CFR 822.8. A manufacturer must submit a postmarket surveillance plan within 30 days of receipt of the 522 order (section 522(b)(1) of the Act and [21 CFR 822.8](#)) and commence surveillance not later than 15 months after the day on which FDA issues the 522 order (section 522(b)(1) of the

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Act). FDA will review all postmarket surveillance submissions and respond within 60 calendar days. Section 522(b)(1) of the Act and [21 CFR 822.17](#).

A. Elements to Include in a Postmarket Surveillance Submission

The general and specific content for a postmarket surveillance submission, including the surveillance plan, is outlined in 21 [CFR 822.9](#) and [822.10](#). The elements to include in most postmarket surveillance submissions are described in more detail, as follows:

- background (e.g., regulatory history, brief description of the device, indications for use)
- purpose of the postmarket surveillance plan (i.e., public health questions from 522 order)
- postmarket surveillance plan objectives and hypotheses
- postmarket surveillance design ([see Part D. Types of Postmarket Surveillance](#))
- patient population (including subject inclusion and exclusion criteria and definition and source of comparator group)
- sample size calculation (statistically justified and based on study hypothesis, where applicable)
- primary and secondary endpoints (including definitions for endpoints, success criteria, 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)
- length of follow-up, follow-up schedule, description of baseline, and follow-up assessments, where applicable
- description of data collection procedures (including recruitment plans, enrollment targets, plans to minimize losses to follow-up, follow-up rate targets, quality assurance, and control), where applicable²
- statistical analysis
- data collection forms, informed consent forms, and IRB approval or IRB exemption forms, where applicable
- reporting schedule for interim and final reports
- interim and final data analyses, and
- milestones/timeline elements, including (where applicable):
 - expected date of study/surveillance initiation
 - expected monthly number of study sites with IRB approvals
 - expected date of initiation of subject enrollment

² FDA notes that, where appropriate, it may be possible to meet a 522 order requirement through prospective or retrospective analysis of data from real-world data sources, such as device registries and electronic health records. In addition, if real-world data 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. FDA intends to issue separate guidance on the use of real-world evidence.

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- expected number of subjects enrolled per month
- expected date for subject enrollment completion
- 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)

B. FDA and Manufacturer Agreement on Surveillance Plan

FDA will evaluate the proposed surveillance plan to determine whether it is administratively complete and whether the plan will result in the collection of useful data that will answer the surveillance questions. See [21 CFR 822.16](#). Accordingly, FDA may issue one of the following decision letters:³

1. 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. See Appendix 1 for CDRH’s checklist for determining whether a submission is administratively complete.
2. Approval Letter – This letter indicates FDA’s approval of the proposed surveillance plan as submitted.
3. Minor Deficiency Letter – This letter cites specific minor deficiencies that must be addressed in order for the plan to be approved.
4. 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 in order for the plan to be approved.
5. 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 submission by submitting an entirely new submission that proposes a new plan intended to address the postmarket surveillance questions in the 522 order.

If a manufacturer disagrees with FDA about the content of the plan or if the plan is disapproved, possible recourse options are described in [21 CFR 822.22](#). These include requesting a meeting with the Office Director of OSB; 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.

FDA developed this guidance document, in part, to help facilitate timely discussions with manufacturers on postmarket surveillance issues and challenges. Early and ongoing interactions with FDA will afford optimal opportunities to agree on plans or other issues and will be the primary method for resolving any issues. FDA will work with manufacturers on the development of their surveillance plans, including the timelines and expectations for commencing postmarket surveillance. However, if a manufacturer does not have an approved postmarket surveillance plan within 6 months of issuance of a 522 order, the manufacturer’s plan status may be categorized as “Plan Overdue” on FDA’s website. If a manufacturer fails to meet the

³ See generally 21 CFR 822.19. FDA plans to use similar decision letters in response to supplements submitted by manufacturers proposing changes to approved surveillance plans.

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requirements for obtaining postmarket surveillance plan approval and commence postmarket surveillance within 15 months after a 522 order is issued, this would constitute a failure to comply with a requirement under section 522. Since 522 orders issued prior to the enactment of FDASIA were issued at least several years prior to the publication of this guidance, if a manufacturer in receipt of such an order has failed to commence or conduct postmarket surveillance in accordance with an approved surveillance plan by the present time, FDA would consider this to be a failure to comply with a requirement under section 522 of the Act. Failure to comply with a requirement under section 522 of the Act may result in enforcement action by FDA ([see Section 10 for further information](#)).

C. 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. [21 CFR 822.21](#) The manufacturer should not combine the request with any 522 report, but instead should submit the request and the revised postmarket surveillance plan for FDA review and approval as a standalone supplement. Any submission involving a change to an approved postmarket surveillance plan is tracked by FDA as a supplement and should be identified by the assigned PS number.

In keeping with FDA's practice of focusing review resources on complete submissions, requests to change an approved postmarket surveillance plan would first undergo acceptance review to assess whether a supplement is administratively complete in order for FDA to conduct a substantive review. 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 Minor or 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.

Unless FDA approves the revised surveillance plan, the manufacturer remains responsible for completing the approved surveillance plan. Failure to meet the milestones and timelines outlined in the approved surveillance plan may result in enforcement action by FDA.

D. Types of Postmarket Surveillance

FDA may order postmarket surveillance to address a wide variety of device-related public health questions. The table below describes different types of postmarket surveillance designs that may be used depending on the particular public health question.

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	A study in which the subjects in a defined population are followed

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Type	Design
Study	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.
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.
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, <i>passive</i> 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, <i>active</i> 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.
Comprehensive, Linked, Registry-Based Surveillance	Registry-based comprehensive surveillance with shared responsibilities leverages the national registry infrastructure that is linked with other data sources (e.g., claims data) for longitudinal assessment of device performance. Embedded in the health care delivery system, this type of surveillance is characterized by shared responsibilities of multiple stakeholders (e.g., professional societies running the registries, FDA epidemiologists performing the surveillance analytics, payers assisting with linking to administrative data, and industry supporting the registries).
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.
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. The proportions with the exposure of interest are compared.
Bench/Lab Study	A study that involves bench testing (e.g., wear testing, fatigue testing).
Animal Study	A study that involves animal testing (e.g., device or material implanted in animal).

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Type	Design
Other Design	A surveillance design that does not fit one of the other categories.

5. Interim Postmarket Surveillance Reports

An Interim Postmarket Surveillance Report is a written report to FDA on the status of the fulfillment of a postmarket surveillance requirement prior to its completion.

A. Submission of Interim Postmarket Surveillance Report

As provided at [21 CFR 822.38](#), manufacturers must submit interim and final reports as specified in an approved postmarket surveillance plan. Unless otherwise specified in the 522 order, manufacturers should submit an Interim Postmarket Surveillance 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 negotiated starting date. Manufacturers should continue this reporting schedule until the Final Postmarket Surveillance Report is submitted. FDA also recommends that the manufacturer indicates the appropriate time span on the interim report cover in bold letters (e.g., **6-Month Interim Postmarket Surveillance Report, 12-Month Interim Postmarket Surveillance Report**). FDA intends to complete the review of interim reports and respond within 60 calendar days.

B. Manufacturer's Reporting Status

Upon receipt of the interim report, FDA will determine the manufacturer's reporting status based on the agreed-upon schedule in the postmarket surveillance plan, which will be posted on the 522 Postmarket Surveillance Studies webpage (522 webpage). The reporting status categories appear in the table below.

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.

C. Evaluation of Interim Postmarket Surveillance Report

FDA epidemiologists from OSB will evaluate the Interim Postmarket Surveillance Report based on a wide range of criteria (where applicable), including:

- the completeness of the report content (especially in regard to progress towards achieving primary and secondary endpoints and performance goals, or sufficient individual endpoint data to infer progress in the case of composite endpoints)

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- the expected versus actual status of the study at the time of the report (especially timeliness in recruitment of patients and sites to the study and adherence to the agreed upon timeline)
- the causes for and solutions to delays in progress
- adherence to agreed-upon methodology and reasons for deviations from the methodology
- whether information in the reports address the public health question(s)

OSB may consult with Office of Device Evaluation (ODE) or Office of In Vitro Diagnostics and Radiological Health (OIR) and other offices as needed to ensure the data are assessed appropriately.

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 through the interactive review process and/or through a deficiency letter. If an interim report includes insufficient data or includes data that raise new concerns regarding the safety and/or effectiveness of a device, FDA may take various regulatory actions to address these issues, for example, request labeling changes, issue safety communications, or take compliance and/or enforcement action.

6. Final Postmarket Surveillance Reports

A Final Postmarket Surveillance Report is a written report of a terminated 522 order requirement or a completed postmarket surveillance.

A. Submission of Final Postmarket Surveillance Report

FDA recommends the Final Postmarket Surveillance Report be submitted no later than three months after study/surveillance completion, and should be prominently identified with **Final Postmarket Surveillance Report** at the top of the cover letter. FDA also recommends that manufacturers identify the public health question(s) for which the report is being submitted to address a particular 522 order.

B. Manufacturer's Reporting Status

As with an interim report, upon receipt of the final report, FDA will determine the manufacturer's reporting status based on the agreed-upon schedule in the postmarket surveillance plan, which will be posted on the 522 webpage.

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

FDA recommends the Final Postmarket Surveillance Report describes the methodology and results and explain how it fulfills the 522 order. The results in the final reports should meet the performance goal regarding primary and secondary endpoints. FDA epidemiologists from OSB will review the Final Postmarket Surveillance Report and determine if the manufacturer has satisfied the 522 order. OSB may consult with ODE or OIR and other offices as needed to

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ensure the data are assessed appropriately. FDA intends to complete the review of manufacturers' submissions and respond within 90 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 required. FDA may, for example:

- request changes to the labeling of the device to reflect additional information learned from the postmarket surveillance;
- issue a new postmarket surveillance order to address new issues; or
- consider administrative or regulatory actions to protect the public health (e.g., device recall or request an update to a device's indications for use statement)

7. Content and Format of Interim and Final 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 will help ensure that 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. Please note that all reports should contain the data listed below and agreed upon in the plan timeline.

A. General Information

FDA recommends this section contain:

- postmarket surveillance application number (i.e., PS#####)
- manufacturer name and contact information (name of the individual or entity holding the approved PMA, PDP or HDE, cleared 510(k), or de novo order):
 - company name/institution name
 - street address
 - city
 - state/province
 - ZIP/postal code
 - phone number (include area code)
 - fax number (include area code)
 - contact name and title

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- contact e-mail address
- date of the 522 order
- date of postmarket surveillance plan approval and, if applicable, dates of approval of any plan revisions
- device trade names
- device model numbers

B. Report Information

FDA recommends this section contain:

- date of the report
- data included in this report (choose one):
 - clinical study
 - laboratory study
 - animal study
 - other
- type of submission: (choose one):
 - interim Postmarket Surveillance Report
 - final Postmarket Surveillance Report
 - response to FDA correspondence for a deficient report or another reason (specify)

C. Postmarket Surveillance Information

FDA recommends this section contain (as applicable):

- purpose of the postmarket surveillance, including goals, objectives, and primary and secondary endpoints
- patient population being studied, including:
 - specific illness or condition
 - whether the postmarket surveillance targets subpopulations (e.g., pediatric, geriatric)
 - total number of subjects to be studied
 - schedule of subject follow-up
- 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 deadline for submission of report)

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- summary of study/surveillance progress milestones/timeline elements, where applicable:
 - date of approval of the plan
 - number of IRB approvals
 - number of clinical sites enrolled
 - number of clinical sites at which the study was initiated
 - completion date for enrollment of clinical sites
 - number of subjects enrolled (if applicable, this information should be presented for the entire subject population and for each subgroup)
 - subject accrual start date and subject accrual completion date
 - study targets: percentage of subjects reaching each designated study phase
 - comparison of target versus actual enrollment and follow-up
 - anticipated study/surveillance completion date (i.e., complete follow-up of all study participants)
- if applicable, a rationale for not meeting the milestones/timeline specified in the plan or a revised timeline⁴
- subject accountability data stratified by each follow-up time point for the entire population and for each subgroup (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:
 - subjects lost to follow-up, as well as any measure to minimize such future events
 - subject and physician-initiated discontinuations
 - any deaths, including reports from post-mortem examinations
- summary and interpretation of results
 - interim or final safety/effectiveness findings

8. Postmarket Surveillance Status Determination

FDA will determine postmarket surveillance status using the categories in the table below.

Status	Definition
Plan Pending	FDA has not approved the plan, and it has been less than 6 months since issuance of the 522 order.
Plan Overdue	FDA has not approved the plan, and it has been 6 months or more since issuance of the 522 order.
Study Pending	FDA approved the plan, but study/surveillance has not begun.
Study Progress Adequate	The study/surveillance has begun, and the progress is consistent with the plan (e.g., meeting enrollment schedule, follow-up rates, endpoints evaluated).

⁴ If a change in the study/surveillance milestones/timeline could significantly impact the outcome of the postmarket surveillance, then a device manufacturer must submit that revision as part of a 522 supplement for FDA review and approval. See 21 CFR 822.21.

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Study Progress Inadequate	The study/surveillance has begun, but the progress is inconsistent with the plan (e.g., not meeting enrollment schedule, missing time point evaluations, poor follow-up rates, not all endpoints evaluated).
Noncompliant	The study/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 study/surveillance has not commenced.
Completed	The manufacturer has fulfilled the postmarket surveillance order and FDA considers the requirement under the 522 order to be satisfied. This is a final status.
Terminated	The manufacturer has not fulfilled or cannot fulfill the postmarket surveillance order (e.g., postmarket surveillance questions are no longer relevant, dataset cannot address 522 order), and, after all appropriate efforts to fulfill the order have been exhausted, FDA has terminated the 522 order. This is a final status.
Revised/Replaced	The manufacturer has not fulfilled or cannot fulfill the 522 order. All appropriate efforts to fulfill the 522 order have been exhausted, and FDA has agreed to allow the manufacturer to revise or replace the original plan with a new plan to fulfill the 522 order. The new plan supersedes the previous plan. This is a final status.
Other	The status does not fit another category (e.g., change in ownership underway, redesigning device and need prior premarket clearance/approval to use in study, device has been cleared or approved but is not currently marketed). This is an interim status.
Consolidated	The manufacturer has requested to consolidate their multiple 522 orders for devices of a particular device type into one 522 order. FDA has agreed to have the multiple 522 orders consolidated under one order.

9. Where to Submit Postmarket Surveillance Plan Submissions

Three copies (one electronic and two paper copies) of all postmarket surveillance plan submissions should⁵ be sent to:

522 Postmarket Surveillance Program
Division of Epidemiology
Office of Surveillance and Biometrics
Center for Devices and Radiological Health
Food and Drug Administration
10903 New Hampshire Ave
WO66-4276
Silver Spring, MD 20993-0002

⁵ Section 522 is not subject to section 745A(b) of the Act, 21 U.S.C. § 379k-1(b), regarding eCopy requirements.

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As explained in the eCopy Guidance, “An electronic copy (eCopy) is defined as an exact duplicate of the paper submission, created and submitted on a compact disc (CD), digital video disc (DVD), or a flash drive... accompanied by a paper copy of the signed cover letter and the complete paper submission.” See [eCopy Program for Medical Device Submissions; Guidance for Industry and Food and Drug Administration Staff \(issued on October 10, 2013\)](#).

10. Failure to Comply with Postmarket Surveillance Requirements under Section 522

Failure or refusal to comply with a requirement under section 522, including failure to commence surveillance within 15 months of a 522 order, is a prohibited act under section 301(q)(1)(C) of the Act, 21 U.S.C. § 331(q)(1)(C), and renders the device misbranded under section 502(t)(3) of the Act, 21 U.S.C. § 352(t)(3). Please note that violations of sections 301(q)(1)(C) and 502(t)(3) may lead to enforcement actions including seizure of product, injunction, prosecution, and/or civil money penalties. See [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 comply with the 522 order. 21 CFR 822.30. 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 approved plan unless notified otherwise by the Agency. 21 CFR 822.28. Requests to terminate or modify a 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 a postmarket surveillance prior to fulfilling the postmarket surveillance commitment.

Alternatively, if FDA determines a surveillance plan will not answer or adequately address questions in an 522 order, for example because of the postmarket surveillance design or data inadequacies, or due to a discontinuation in marketing or manufacturing of the device, but the 522 order objectives remain important, FDA may initiate termination of the original surveillance plan and discuss establishing a new postmarket surveillance plan and schedule.

11. 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. See [21 CFR 822.23](#).

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

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requirements for such clinical trials. Certain information on clinical trials is publicly available on the <http://www.clinicaltrials.gov> website. Additional information on these requirements can be found at <http://clinicaltrials.gov/ct2/invest>.

In addition, to increase transparency to FDA stakeholders, including consumers, physicians, and industry, FDA posts information about postmarket surveillance on FDA's 522 webpage (<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pss.cfm>). This information is posted in compliance with applicable disclosure statutes and regulations. Postmarket surveillance details that may be posted include:

General

- postmarket surveillance application number (i.e., PS#####)
- applicant name
- device name
- medical specialty (e.g., cardiovascular, orthopedic)
- date of the 522 order
- study/surveillance name
- most recent plan approval date
- study/surveillance status

General Surveillance Plan Parameters

- postmarket surveillance design description
- data source
- comparison group
- analysis type
- patient population

Detailed Surveillance Plan Parameters, Where Applicable

- postmarket surveillance design description
- sample size: patients and sites
- patient population description
- data collection
- follow-up visits and length of follow-up

Interim Report Results

FDA may post on its website or otherwise make public postmarket surveillance interim summary data and/or FDA analyses thereof when appropriate to protect the public health, for example when interim results raise safety concerns or may otherwise impact treatment. FDA generally considers such information to be publicly releasable in accordance with applicable disclosure laws. However, if a manufacturer believes in a particular instance that interim results are prohibited from public release, for example because they constitute 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. Examples of interim report information that FDA publicly discloses include:

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

Final Report Results, Where Applicable

- actual number of patients enrolled
- actual number of sites enrolled
- patient follow-up rate
- final safety/effectiveness findings and results
- study/surveillance strengths and weaknesses

Reporting Information

- interim and final report schedule
- due date for interim and final report (based on agreed upon schedule)
- FDA receipt date of interim and final report
- status category of interim and final report

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

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APPENDIX 1:

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

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 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
(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 procedure 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