

Guidance for Industry and FDA Staff

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

Document issued on: April 27, 2006

This document supersedes “Guidance on Procedures to Determine Application of Postmarket Surveillance Strategies,” and “Guidance on Procedures for Review of Postmarket Surveillance Submissions,” February 19, 1998; and “Guidance on Criteria and Approaches for Postmarket Surveillance,” November 2, 1998.

For questions regarding this document contact the Issues Management Staff at 240-276-3355.



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

Preface

Public Comment

Written comments and suggestions may be submitted at any time for Agency consideration to the Division of Dockets Management, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. When submitting comments, please refer to Docket No. 98D-0106. Comments may not be acted upon by the Agency until the document is next revised or updated.

For questions regarding the use or interpretation of this guidance contact Issues Management Staff at (240) 276-3355.

Additional Copies

Additional copies are available from the Internet at: <http://www.fda.gov/cdrh/osb/guidance/316.pdf>, or CDRH Facts-On-Demand. In order to receive this document via your fax machine, call the CDRH Facts-On-Demand system at 800-899-0381 or 301-827-0111 from a touch-tone telephone. Press 1 to enter the system. At the second voice prompt, press 1 to order a document. Enter the document number 316 followed by the pound sign (#). Follow the remaining voice prompts to complete your request.

Guidance for Industry and FDA Staff

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

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

Introduction

This guidance consolidates three separate documents pertaining to postmarket surveillance (PS)¹ into a single, comprehensive guidance document to make it easier to locate information. Since 1998, when the earlier guidances were issued, FDA has issued a regulation to implement the PS provision of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 360I. That regulation is written in Plain Language and describes the regulatory requirements for manufacturers who receive orders to conduct PS. This guidance supplements the information in that regulation and updates the earlier guidances by adding the relevant citations to the PS regulation.

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.

¹ "Guidance on Procedures to Determine Application of Postmarket Surveillance Strategies," and "Guidance on Procedures for Review of Postmarket Surveillance Submissions," February 19, 1998; and "Guidance on Criteria and Approaches for Postmarket Surveillance," November 2, 1998.

Contains Nonbinding Recommendations

The Least Burdensome Approach

We believe we should consider the least burdensome approach in all areas of medical device regulation. This guidance reflects our careful review of the relevant scientific and legal requirements and what we believe is the least burdensome way for you to comply with those requirements. However, if you believe that the information requested in the guidance is not relevant to the decision-making process or that an alternative approach would be less burdensome, please contact us so we can consider your point of view. You may send your written comments to the contact point listed in the preface to this guidance or to the CDRH Ombudsman. Comprehensive information on CDRH's Ombudsman, including ways to contact him, can be found on the Internet at <http://www.fda.gov/cdrh/ombudsman/>

Background

The act provides us with a number of tools to protect public health while continuing the availability of safe, effective medical devices. Premarket review provides information on a device's safety and effectiveness. However, there may be questions that cannot be answered in the premarket stage, or an issue may arise after the device is marketed.

The Food and Drug Administration Modernization Act of 1997 (FDAMA) modified PS requirements under section 522 of the act. Specifically, under the act, the Agency may by order:

“require a manufacturer to conduct postmarket surveillance for any device of the manufacturer which is a class II or class III device the failure of which would be reasonably likely to have serious adverse health consequences or which is intended to be-

- (1) implanted in the human body for more than one year, or
- (2) a life sustaining or life supporting device used outside a device user facility. ”

Postmarket issues may be identified through a variety of sources, including analysis of adverse event reports, a recall or corrective action, reports from other governmental authorities, or the scientific literature.

There are several areas that should be considered when establishing a postmarket strategy for a particular device or type of device. CDRH's general approach is to convene an expert review team within the Center to identify the objective, the information that is needed to achieve this objective, appropriate sources and mechanisms for obtaining this information, and necessary actions to address public health concerns. PS is one mechanism that we can use to obtain this information.

In the questions and answers below, we have tried to explain how FDA decides when PS is necessary, what the process is for notifying and involving the manufacturer, what different types of PS tools may be appropriate, how the manufacturer should conduct and report PS, and how FDA will review and follow up orders for PS.

Contains Nonbinding Recommendations

In the following questions, the term “I” refers to the reader. In the responses, the terms “we” refers to the Center for Devices and Radiological Health (CDRH) and “you” refers to the reader.

HOW DOES FDA LEARN OF POSTMARKET PROBLEMS OR ISSUES WITH A MEDICAL DEVICE?

An issue with a device may be identified at any point during the life cycle of the device, by anyone in CDRH (e.g., a reviewer in the Office of Device Evaluation (ODE), a scientist in Office of Science and Engineering Laboratories) and forwarded with the concurrence of his/her Division Director to the Director of Issues Management Staff (IMS) in the Office of Surveillance and Biometrics (OSB). Other sources, e.g., a professional association, an individual clinician, or another Center, may also identify issues.

The Director of IMS will assign an Issues Manager to work with the staff identifying the issue to develop the rationale statement for presentation to an expert review team convened for this purpose. This rationale statement will briefly summarize the hazard signal/concern, the applicable safety and effectiveness information (i.e. risks and benefits), the problem or issue, alternate strategies to resolve the concern, and the question to be addressed if PS is ordered.

HOW DOES FDA DETERMINE WHETHER TO IMPOSE POSTMARKET SURVEILLANCE UNDER SECTION 522?

The expert review team will consider whether PS is an appropriate mechanism for obtaining information to address the identified issue(s). The Issues Manager will advise the expert review team of any statutory, regulatory, or policy criteria that apply. The expert review team (or a smaller subgroup) will develop the PS question(s) and the supporting rationale that will be part of the PS order. After providing Directors of other relevant Offices a chance to comment, the Director of OSB will decide whether to order PS.

WHAT “POLICY CRITERIA” WILL FDA CONSIDER IN MAKING THIS DETERMINATION?

The most important criterion that needs to be met before we issue an order to conduct PS is the delineation of an important unanswered postmarket question about a marketed device.

While PS will not be used in lieu of adequate premarket testing, postmarket surveillance can serve to complement premarket data. Certain issues that arise during premarket evaluation of a device may be more appropriately addressed through data collection in the postmarket period rather than prior to approval or clearance for marketing. We will consider the potential to collect postmarket surveillance data to allow more rapid progress to market only when the public health will not be compromised.

Postmarket questions also may be raised about a marketed device from a variety of sources, including spontaneous reports, product complaints, and published literature. In such cases, we may issue postmarket surveillance orders to confirm the nature, severity, or frequency of suspected problems.

Contains Nonbinding Recommendations

Examples of situations that may raise postmarket questions, during both the premarket and postmarket periods, are listed below:

⇒ *New or expanded conditions of use for existing devices*

We may order postmarket surveillance to augment premarket data to obtain more experience with change from hospital use to use in the home or other environment or with new patient populations.

⇒ *Significant changes in device characteristics (technology)*

We may have questions that arise from significant or developmental changes to device technology that can be most appropriately addressed in the postmarket period. We may also have concerns that changes in the technology of a device may affect the duration of the effectiveness of the device, which could be addressed by postmarket surveillance. In these situations, postmarket surveillance, through collection of longer-term safety and effectiveness data, may augment premarket data and allow earlier marketing of new technologies without compromising the public health.

⇒ *Longer term follow-up or evaluation of rare events*

We may order postmarket surveillance to address longer term or less common safety and effectiveness issues of implantable and other devices for which the premarket testing provided only limited information. For example, premarket evaluation of the 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 during 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.

⇒ *Public health concern(s) resulting from reported or suspected problems in marketed devices*

We 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.

We may also consider the following when determining whether to issue a PS order:

- Ability of other postmarket mechanisms to address public health concerns raised by the postmarket question

We will consider whether other mechanisms may address the question, such as postapproval requirements (21 CFR 814.82), medical device reports (MDR) (21 CFR

Contains Nonbinding Recommendations

Part 803), quality systems requirements (21 CFR Part 820), field inspections, or special controls for class II devices.

- Practicality of postmarket surveillance strategies

We will consider the feasibility and timeliness of postmarket surveillance. For example, the relative value of postmarket surveillance for a given device may be influenced by the rate of device evolution. Postmarket surveillance may not be reasonable if we determine that the applicability of the results will be minimal by the time postmarket surveillance is completed.

- Priority of postmarket question, based on magnitude of risk

We will assign higher priority for postmarket surveillance where we have identified or suspect a significant risk to public health.

HOW WILL FDA NOTIFY ME THAT I AM REQUIRED TO CONDUCT POSTMARKET SURVEILLANCE OF A DEVICE?

Once we have determined that PS is an appropriate mechanism for obtaining information to address a postmarket issue, we will contact the manufacturer(s) to share our concerns (21 CFR 822.6). We generally plan to provide you with an opportunity to meet with us before we issue the order for PS. The purpose of the meeting is to:

- Give you an opportunity to provide additional information related to our postmarket concerns;
- Clarify or focus the objectives of PS;
- Identify specific surveillance methodologies that may be appropriate; and
- Determine specific reporting timeframes.

The OSB Director will generally issue the orders for postmarket surveillance under section 522 (21 CFR 822.7). In cases where postmarket surveillance requirements under section 522 have been previously established for a device category, ODE may issue the orders as part of an approval order or a substantial equivalence determination. The order will contain the rationale for imposing PS under section 522, the Center's recommendations (if any) as to the type of data collection needed to address the concern, and any other information available that may assist the manufacturer in preparing the postmarket surveillance plan. (21 CFR 822.5)

WHEN MUST I SUBMIT MY SURVEILLANCE PLAN?

You must submit your postmarket surveillance plan within 30 days from the date of the postmarket surveillance order (letter), in accordance with section 522 of the act. (21 CFR 822.8)

DOES FDA REQUIRE CONTROLLED CLINICAL TRIALS FOR PS PLANS?

Contains Nonbinding Recommendations

No. We may order PS to address a wide variety of device-related public health questions. We intend that manufacturers use the most practical, least burdensome approach to produce a scientifically sound answer to the question to be addressed in postmarket surveillance. The following examples illustrate a range of surveillance methods and situations in which they might be appropriate.

- Detailed review of complaint history and scientific literature
 - ⇒ *Example: compilation and comparison of the manufacturer's complaint files and published literature to verify frequency of reported adverse events..*
- Non-clinical testing of the device
 - ⇒ *Example: analysis of devices explanted from animal models to assess long-term effects of the body on implant materials.*
- Telephone or mail follow-up of a defined patient sample
 - ⇒ *Example: evaluation of the effectiveness of user training for a home-use device previously used only in the hospital setting; outcomes easily and reliably reportable directly by patient.*
- Use of secondary data sets (e.g., Medicare), registries (e.g, Society for Interventional Radiology stent registry), internal registries, or tracking systems.
 - ⇒ *Example: analysis of patient outcomes or device usage. (In these instances, it is important to ensure that variables of interest are included in the data set/registry).*
- Case-control study of patients implanted with or using devices
 - ⇒ *Example: comparison of cases and controls to quantify magnitude of risk posed by device exposure.*
- Consecutive enrollment studies
 - ⇒ *Example: assessment of outcomes following device exposure, to assess the frequency of problems based on clinical follow-up of patients.*
- Cross-sectional studies (multiple cohorts)
 - ⇒ *Example: assessment of device safety and/or effectiveness at designated time intervals after the initiation of the postmarket surveillance plan.*
- Non-randomized controlled cohort studies
 - ⇒ *Example: analysis of risks and benefits associated with each of several devices used to treat same disease or condition.*
- Randomized controlled trials
 - ⇒ *Example: evaluate the risk/benefit relationship for a sub-population using a device that has been approved for use with a broad indication.*

WHO WILL REVIEW THE PS SUBMISSION?

Contains Nonbinding Recommendations

During the process of determining whether to order PS, we will identify a review team for the surveillance plan. The team will consist of a review team leader from the IMS and two or more consulting reviewers from the program Offices in the CDRH. Each team will consist of, at a minimum, a statistician and/or an epidemiologist, and an ODE premarket reviewer. We will add consulting reviewers with expertise relevant to the PS question, e.g., human factors, drug elution, or engineering, as appropriate. These reviewers will typically be from the other program Offices in CDRH. On occasion, we may use staff from other Centers or Special Government Employees if they possess expertise relevant to the surveillance.

WHAT ARE THE RESPONSIBILITIES OF THE REVIEW TEAM MEMBERS?

OSB will:

- Provide document handling and tracking;
- Provide administrative services;
- Provide postmarket regulatory review;
- Make final decisions related to plan approval/disapproval, conduct of the surveillance, and evaluation of surveillance data; and
- Sign correspondence to the manufacturer related to PS. The Office Director will sign all decision letters, and the Director of IMS may sign other correspondence.

PS Review Team Leader will:

- Coordinate the review of the submission;
- Prepare the summary review for the submission, addressing comments from the consulting reviewers;
- Prepare the response to the submission for review by the team; and
- Perform an administrative review of incoming documents to determine whether the submission should be sent to the review team.
 - Examples of documents that would not be sent to the review team are: requests for extension of time to respond to a deficiency letter and submissions that are not responsive to the surveillance order or deficiency letter.
- Ensure that the manufacturer is responding in a timely manner to any deficiency letters, and determine whether interim reports are being submitted in a timely manner.

Consulting reviewers will:

- Provide technical, scientific, statistical, regulatory, and public health review and input on the proposed PS plan;
- Provide written reviews of submissions to be incorporated into the administrative record;
- Provide specific, clearly worded language for any deficiencies they identify in the plan;
- Review the decision letter to the manufacturer to ensure accurate wording of deficiencies; and
- Determine whether the PS is being conducted in accordance with the approved plan.

Contains Nonbinding Recommendations

HOW WILL FDA MAKE DECISIONS ABOUT PS PLANS?

1. The PS review team leader will review all incoming plan submissions and forward them to consulting reviewers as appropriate. All original PS plans that are administratively complete will be sent to the members of the review team.
2. All reviewers should submit written reviews to the PS team leader. Reviewers should use the PS question(s) and rationale to determine whether the plan is adequate. (21 CFR 822.16)
3. The PS review team leader will prepare the summary review and the decision letter for the submission, circulate these to the review team for review, and revise as appropriate.
4. The Director of IMS will review the decision package and initial the decision letter if he/she concurs.
5. The Director of OSB will review the decision package and sign the decision letter.

HOW LONG DOES FDA HAVE TO REVIEW MY SUBMISSION?

In accordance with section 522 of the act, we have 60 days to review and respond to your submissions. (21 CFR 822.17)

WHAT OTHER SUBMISSIONS WILL I MAKE AFTER MY PLAN IS APPROVED?

Once we have approved the PS plan, you will submit interim reports as specified in the approved plan (21 CFR 822. 38). Members of the review team will evaluate whether the manufacturer is conducting the surveillance in accordance with the approved plan and determine whether the data adequately answer the postmarket question.

WHEN IS POSTMARKET SURVEILLANCE COMPLETED?

We will consider the PS complete when the manufacturer has answered the PS question(s) specified in the surveillance order. *If* the results of the surveillance raise new issues or questions, additional actions may be required. We may, for example:

- request changes to the labeling of the device to reflect additional information learned from the postmarket surveillance;
- issue a new PS order to address a new issue; or
- consider administrative or regulatory actions if necessary to protect the public health.

WHAT HAPPENS IF THE SURVEILLANCE IS NOT CONDUCTED ACCORDING TO THE APPROVED PLAN?

If we determine that the manufacturer has not conducted the PS in accordance with the approved plan, the team will develop recommendations for appropriate enforcement strategies, taking into consideration the extent of the non-compliance. We will present the recommendations to Center

Contains Nonbinding Recommendations

staff at the appropriate levels for concurrence and implementation. We will consider whether enforcement actions, including civil money penalties, are necessary. (21 CFR 822.20)

WHAT INFORMATION WILL BE PUBLICLY AVAILABLE ABOUT MY PS PLAN?

Under the Freedom of Information Act, most of the information in your plan is subject to release. We will protect trade secret and commercial confidential information as well as any personal identifier information for patients (21 CFR 822.23).

We will also post the overall status of the surveillance, along with a brief description of the plan, on the Internet.