Draft Guidance for Industry and FDA Staff

Annual Reports for Approved Premarket Approval Applications (PMA)

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.
Document issued on: October 26, 2006

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Alternatively, electronic comments may be submitted to http://www.fda.gov/dockets/ecomments. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this document contact Laura Byrd at 240-276-4040 or Laura.Byrd@fda.hhs.gov. For questions regarding the application of this guidance to devices regulated by the Center for Biologics Evaluation and Research (CBER), contact Leonard Wilson at 301-827-0373 or by email at leonard.wilson@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration

Center for Devices and Radiological Health

Center for Biologics Evaluation and Research

Preface

Additional Copies

Additional copies are available from the Internet at: http://www.fda.gov/cdrh/ode/1585.pdf, or 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 (**1585**) followed by the pound sign (#). Follow the remaining voice prompts to complete your request.

Table of Contents

Draft Guidance for Industry and FDA Staff

Annual Reports for Approved Premarket Approval Applications (PMA)

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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.

1. Introduction

Devices subject to premarket approval under section 515 of the Federal Food, Drug, and Cosmetic Act (the act) are also subject to periodic reports imposed by the PMA approval order (21 CFR 814.82(a), 21 CFR 814.84(b)). We typically specify that you submit a report one year from the date of approval of the original PMA and annually thereafter. Therefore, the periodic report is usually referred to as an annual report. Although this guidance addresses "annual reports," there may be circumstances where FDA specifies more frequent periodic reports. We believe this guidance will also be relevant to the more frequent reports.

This guidance document describes the information required by 21 CFR 814.84(b), additional information requirements that may be imposed by approval order under 21 CFR 814.82, and our recommendations for the level of detail you should provide in your annual report. It also identifies the steps FDA staff generally takes when reviewing annual reports, the resources available to assist staff in their reviews, and the actions they may recommend in their conclusions. This guidance document is intended to help ensure your annual reports are complete and that the actions of CDRH and CBER staff are consistent.

In our efforts to bring safe and effective products to market as quickly as possible, CDRH needs to be able to rely on a variety of postmarket controls that will assure continuing safety and effectiveness after a medical device is widely distributed. We believe that data and information gathered in the postmarket setting is critical to our continued confidence in the

safety and effectiveness of the marketed device. Annual reports are one of the important tools that FDA relies upon to gather information about the device in its post-approval setting. Annual reports currently contain a variety of information, including information about manufacturing changes, design changes, and labeling changes that were made during the preceding year for the PMA product. This guidance recommends that this and other information be analyzed and presented in a way that will be most useful to both the company and the FDA. For example, the guidance recommends that you describe in detail the rationale for changes made to your device, including whether the changes were the result of product complaints and adverse events. This will give us a more complete picture of the post-market safety profile of the device. The guidance also recommends that you include a summary of all changes that were made to your device during the reporting period, including those that were the subject of a PMA supplement. Having the information submitted in this way will help ensure that limited agency resources are devoted to assessing meaningful information rather than sifting through vast amounts of data that has not been systematically reviewed by the firm.

FDA believes that the types of information that we are requesting in this guidance and the types of review, summary, and analysis we are recommending are already part of the quality system practices of companies that comply with GMP regulations. For example, design controls already require the type of look back and assessment that we are suggesting be part of the annual report.

Annual reports that contain well developed and meaningful information will be an important tool for the agency and the industry to assure postmarket safety and protect the public. When manufacturers prepare the type of analysis this guidance describes and provide this information to FDA in annual reports, industry and FDA will be better positioned to recognize and address possible safety signals.

The Least Burdensome Approach

This draft guidance document reflects our careful review of what we believe are the relevant issues related to annual reports and what we believe would be the least burdensome way of addressing these issues. If you have comments on whether there is a less burdensome approach, however, please submit your comments as indicated on the cover of this document.

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. Background

In the PMA approval order, FDA requires that PMA sponsors submit post-approval periodic reports, i.e., annual reports to FDA, in accordance with 21 CFR 814.82(a)(7) and 814.84(b). Section 21 CFR 814.84(b) describes the information required:

Unless FDA specifies otherwise, a periodic report must:

1. Identify changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).
2. Contain a summary and bibliography of the following information not previously submitted as part of the PMA:
    i. Unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices and known to or that reasonably should be known to the applicant.
    ii. Reports in the scientific literature concerning the device and known to or that reasonably should be known to the applicant. If, after reviewing the summary and bibliography, FDA concludes that the agency needs a copy of the unpublished or published reports, FDA will notify the applicant that copies of such reports shall be submitted.

You are primarily responsible for determining whether changes to your device, labeling, or manufacturing processes impact safety or effectiveness and, thus, require a PMA Supplement or 30-Day Notice.[1] This guidance is not intended to define when you should submit a new original PMA or any type of PMA Supplement.

In accordance with 21 CFR 814.84(a), you must also comply with **Medical Device Reporting** (MDR) requirements, 21 CFR Part 803, and any requirements made applicable by other regulations or by order approving the device, including:

- **Post Approval Study Reports**, if FDA has imposed continuing evaluation (post-approval study) requirements on your device in the PMA approval order, 21 CFR 814.82(a)(2)
- **Adverse Reaction Reports and Device Defect Reports**, if imposed in the PMA approval order, 21 CFR 814.82(a)(9), but only to the extent such reports do not duplicate MDR reporting requirements.

[1]We recommend that you carefully assess whether a change requires a PMA Supplement, 21 CFR 814.39(a) or 30-Day Notice, 21 CFR 814.39(e). The list of examples in 21 CFR 814.39(a) illustrates the kind of changes that require a PMA Supplement; however, it is not an exhaustive list.

3. Post-Approval Study Reports

As provided by 21 CFR 814.82(a)(2), FDA may require continuing evaluation (post-approval study) and periodic reporting on the safety, effectiveness, and reliability of your device (post-approval study report), in addition to requiring annual reports under 21 CFR 814.82(a)(7). If your approval order identifies post-approval studies you must conduct, the order will describe the purpose of the studies and how frequently you must submit post-approval study reports.

We recommend that you submit your annual report and post-approval study report separately, even if they are due at the same time. This will facilitate FDA's review because different Offices in CDRH review the post-approval study report and the annual report.[2] If you choose to provide a separate report as recommended, please include the date that you submitted your post-approval study report in your annual report.

If you choose to include your post-approval study report along with your annual report, we recommend that you create a separate section of the annual report for the post-approval study report.

4. Contents of an Annual Report

A complete annual report should include all of the information described below. If your annual report is complete, we can review your annual report more efficiently and it is more likely that we will not request additional information from you.

Cover Letter for an Annual Report

We recommend that you include a cover letter to your PMA annual report. Your cover letter should include:

PMA Number

Device Name (including any model names and numbers)

Company Name

Date of Report

Reporting Period (i.e., the dates the reporting period begins and ends)

[2]See the draft guidance, **Procedures for Handling Post-Approval Studies Imposed by PMA Order**, issued for comment on September 15, 2005 at http://www.fda.gov/cdrh/osb/guidance/1561.html. (When final, the internet address will link to the guidance issued for implementation.)

Approval Date (dates original PMA and any PMA Supplements were approved)

Manufacturing, Design, and Labeling Changes

To facilitate our review of your annual report, we recommend dividing your report into separate sections for manufacturing, design, and labeling changes.

As described below, each of the three sections should identify all changes made during the reporting period[3], including those that were submitted in a PMA supplement or 30-Day Notice and those changes that you have not already reported in a PMA Supplement or 30-Day Notice.[4]

Identification of the Changes

For each change in your summary, we recommend you identify:

- the change made;
- the rationale for making the change;
- a listing of any validation or other testing that was performed, including a description of the method and acceptance criteria (but not the data itself); and
- the implementation date.

For changes that are the subject of an approved or pending PMA Supplement or 30-Day Notice, we recommend that you also identify the document number assigned by FDA and, if approved, the approval date.

We recommend that you provide separate tables for manufacturing changes, design changes, and labeling changes. An example of a design changes table is provided below. We recommend that you include similar tables for manufacturing changes and labeling changes.

Design Changes Table

[3] Please note that simple changes related to the device documentation or manufacturing process documentation, such as rewording or expanding for clarification, translating from one language to another, correcting typographical errors, and moving component characteristics from an engineering drawing note to a different document, such as an SOP, do not need to be reported in the annual report. In general, such changes do not affect the design, performance, labeling or processing of the device, only how the characteristics are documented.

[4] In accordance with 21 CFR 814.39(b), you may change your approved device without submitting a PMA Supplement, if the change does not affect the device's safety or effectiveness and you report the change to FDA in your annual report.

Change	Rationale for Change	Summary of Validation Activities	Implementation Date	PMA Supplement Type & Number Assigned by FDA, if applicable	Approval Date, if applicable

Examples of rationales for device changes we recommend you specify include whether the change was:

- made as a result of a problem that resulted in an MDR (if so, we recommend that you provide the applicable MDR number(s));
- made as a result of an adverse event, device defect, or failure reported to you or identified in the literature;
- associated with any recall or corrective action (see also 21 CFR 820.100);
- in response to any customer complaint, request, or suggestion;
- related to any public disclosure or communication on your part, i.e., "Dear Doctor" or "Dear Patient" letters or Technical bulletins;
- related to an FDA Safety Alert, Public Health Notification or warning letter.

If any change that you have made is associated with any written communications to practitioners or patients, we recommend you include a copy of the communication in your annual report.

Detailed Description of Changes Not Reported in Existing Supplements

For changes not reported in a PMA Supplement or a 30-Day Notice, we recommend that you describe the changes and the scientific and/or regulatory rationale basis for concluding that the change had no impact on safety or effectiveness. The description and rationale should provide sufficient detail to allow FDA to determine that the changes did not require a PMA Supplement or 30-Day Notice. It may be helpful to link together the summary data in the Tables with the detailed data by some means such as unique enumeration. That is, you may wish to number the items in the Tables and then refer to those numbers in the detailed descriptions.

As part of your rationale for the changes you are reporting, we also recommend that you include a brief summary of the risk analysis performed to assess the effect of the changes

made during the reporting period that were not already described in PMA supplements or 30-Day Notices. If you did not conduct system-level testing of the cumulative changes, your risk analysis should also assess whether incremental testing was adequate to assure continued safety and effectiveness of your device in the absence of system level testing. If you performed the risk analysis in conformance to any consensus standards, these should be identified.

If any changes to the design, manufacturing, or labeling you have made during the reporting period (that did not require submission of a PMA supplement or 30 Day notice) are associated with MDRs, failures or recalls of any kind, corrective actions (21 CFR 820.100), complaints, or in response to FDA warning letters or inspection findings ("FDA Form 483"), we recommend you:

- describe your investigation of the cause or source of the problem
- explain your decision to change your device design, labeling or manufacturing process by describing how the changes have corrected the problem and mitigated harm[5]

Summary and Bibliography of Reports of Scientific Investigations and Literature

You are required to provide a summary and bibliography of reports in the scientific literature that are known, or that reasonably should be known to you, and that were not previously submitted as part of your PMA application (21 CFR 814.84(b)(2)(ii)). If there are reports or scientific literature on clinical or nonclinical studies of similar devices, we recommend that you include them in your summary and bibliography.

The summary and bibliography must also include unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving your device or related devices that are known, or that reasonably should be known to you (21 CFR 814.84(b)(2)(i)).

Your summary should include a discussion of how the results and conclusions in the reports and literature could impact the known safety and effectiveness profile of your device. If, as a result of reviewing the reports and literature, you determine that changes to your device or its labeling are necessary, we recommend that you inform us of your plan for submitting a PMA supplement or 30-Day Notice for these changes or explain why you believe such a submission is not appropriate.

[5] Please note, any information supplied in this report related to corrective actions will be evaluated with the purpose of understanding the reason for the change to your device design, labeling or manufacturing process. The information will not be evaluated for adequacy with respect to compliance with 21 CFR 820.100.

If, after reviewing your annual report, we conclude that we need an actual copy of a published or unpublished report, we will notify you. You must submit a copy in response, as required by 21 CFR 814.84(b)(2)(ii). However, if you anticipate that we will need a copy of any of these reports, you may, on your own initiative, provide it in your annual report.

Information on Devices Shipped or Sold

To help FDA assess the public health impact of the previously requested information, we are also asking that you provide us with data about the number of devices shipped or sold during the reporting period. For device implants, data regarding the number of devices actually implanted should be provided, if it is available.

Posting of Reports and Option to Submit a Redacted Copy

The confidentiality of information in a PMA file, which includes information in annual reports, is governed by 21 CFR § 814.9. Consistent with this regulation and with 21 CFR Part 20, we intend to publicly post a redacted copy of your annual report on our website. FDA will not make public any confidential commercial or financial information or trade secrets[6] or any information the disclosure of which might cause an unwarranted invasion of personal privacy.[7] You may, on your own initiative, include a redacted copy of your annual report for this purpose.

5. FDA's Review of Your Annual Report

FDA's review of annual reports will allow the agency to assess several important issues related to post-market safety of approved devices. These issues include the nature and adequacy of reported modifications and the adequacy of report documentation. If, after reviewing your annual report, we need additional information, or if we believe the device modifications you have reported require a PMA Supplement or a 30-Day Notice, we will notify you in writing.

Several FDA offices may work in partnership in reviewing your annual report. In CDRH, the Office of Device Evaluation (ODE) or the Office of In Vitro Diagnostics (OIVD),

[6] See 21 CFR 20.61.

[7] See, for example, 21 C.F.R. 20.63(a), "The names or other information which would identify patients or research subjects in any medical or similar report, test, study or other research project shall be deleted before the record is made available for public disclosure."

depending on the device type, has the primary responsibility for reviewing the scientific information, including design and labeling changes. Generally, The Office of Compliance (OC) and ODE or OIVD review the manufacturing information. As necessary, the Office of Surveillance and Biometrics (OSB) may also perform a search of the MAUDE database to further evaluate MDRs submitted during the reporting period. The review memo will include the findings from each Office.

FDA intends to review most annual reports within 90 days of receipt. In general, our review memos follow the format described below.

Reported Changes and Rationale for the Changes

Our review memo will summarize the changes described in the annual report and our evaluation of those changes. Our review memo will also describe our understanding of your rationale for the changes and our assessment of your rationale. The memo will clearly indicate whether we believe the changes you described are appropriate for an annual report or should have been described in a PMA Supplement or a 30-Day Notice.

Device Change Information

ODE or OIVD, in consultation with other Offices within CDRH, as appropriate, will evaluate your summary of the changes made to your device. As appropriate, we also plan to search the MAUDE database and review other FDA records to assess the post-market safety profile of your device.

We will evaluate the information on the changes made to the device and the rationale for the changes, along with information you submitted from published and unpublished reports, and literature to determine if the safety and effectiveness profile of your device has changed. We can then determine whether any action (e.g., labeling change) is necessary to ensure the continued safety and effectiveness of your device.

6. FDA's Recommendations

Generally, our review memo will conclude with one of the following recommendations described below.

Acknowledgement of Complete Annual Report

If we determine that the annual report fulfills the requirements of 21 CFR 814.84, we will issue a letter or send an e-mail to inform you that the annual report is complete.

Request Additional Information

If you have not provided all the information required for an annual report, or we find that the information provided is not sufficient to allow a complete review, we plan to request

additional information by letter or e-mail. If we only need clarification of an issue, we will either telephone or email you, whichever we believe will be the most expeditious.

Changes Not Appropriate for an Annual Report

If we determine that a change made to the device required a PMA Supplement or 30-Day Notice under 21 CFR 814.39, and you did not meet this requirement, we will notify you in writing. In general, we will issue a letter notifying you that a PMA Supplement or 30-Day Notice is required for the change and requesting that you provide the appropriate submission within a specified timeframe. However, there may also be instances when OC will review to determine if any additional regulatory actions are warranted.