Guidance for Industry and FDA Staff

User Fees and Refunds for Premarket Approval Applications

Document Issued on: November 24, 2003

For questions regarding this document, contact Thinh Nguyen (CDRH) at 240-276-4010 or by email at thinh.nguyen@fda.hhs.gov or Sayah Nedjar (CBER) at (301) 827-3524 or by email at nedjar@cber.fda.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

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. Alternatively, electronic comments may be submitted to http://www.fda.gov/dockets/ecomments. Please identify your comments with the docket number listed in the notice of availability that publishes in the *Federal Register* announcing the availability of this guidance document. Comments may not be acted upon by the Agency until the document is next revised or updated.

Additional Copies

Additional copies are available from the Internet at: http://www.fda.gov/cdrh/mdufma/guidance/1224.pdf or http://www.fda.gov/cber/mdufma/mdufma.htm, or by phone at (301) 827-2000 or (800) 835-4709, 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 (**1224**) followed by the pound sign (#). Follow the remaining voice prompts to complete your request.

Contains Nonbinding Recommendations

Table of Contents

Guidance for Industry and FDA Staff

User Fees and Refunds for Premarket Approval Applications

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.

I. Purpose

The purpose of this guidance document is to:

- outline the various types of premarket approval (PMA) applications,
- discuss the fees associated with each type, and
- identify industry or FDA actions on submissions that may result in refunds of fees that have been paid.

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.

II. Background

The Medical Device User Fee and Modernization Act of 2002 (MDUFMA) (P.L. 107-250) amends the Federal Food, Drug, and Cosmetic Act (the act) to provide FDA new responsibilities and resources. One significant provision of MDUFMA, Section 738[1], requires FDA to collect user fees for certain premarket applications received on or after October 1, 2002. The new law establishes user fee rates that vary depending on the type of application submitted. There are, however, several types of PMA submissions that are not subject to user fees because they are expressly excluded from fees under MDUFMA

[1] All references to sections 737 and 738 in this guidance refer to sections 737 and 738 of MDUFMA.

(e.g., 30 day Notices/135 day Supplement, Special PMA Supplement – Changes Being Affected).

III. What Types of Original PMA Applications Are Subject to User Fees?

In accordance with section 738(a)(1)(A), all types of original PMA applications submitted on or after October 1, 2002 are subject to user fees, as discussed below. The types of original PMA applications are:

- Traditional PMAs
- Modular PMAs
- Licensing Agreement PMAs.

A. Traditional PMAs

A traditional PMA is one in which all elements required under 21 CFR 814.20 are submitted at the same time in a single application. FDA will assess the user fee in effect at the time of the submission (e.g., $206,811 in FY 04).[2]

B. Modular PMAs

As discussed in the guidance document entitled, "Premarket Approval Application Modular Review," a modular PMA is a compilation of sections or "modules" that are submitted at different times that together become a complete application. FDA uses the term module to identify a set of elements, tests, information, etc., that addresses a selected aspect of the device application, such as manufacturing or animal testing. This approach allows an applicant to submit discrete sections of the PMA to FDA for review soon after completing the testing and analysis. Additionally, the modular approach allows the applicant to potentially resolve any deficiencies noted by FDA earlier in the review process than would occur with a traditional PMA application.[3]

For a modular PMA with a module submitted before October 1, 2002, FDA will not assess a fee. For a modular PMA with the first module submitted on or after October 1, 2002, FDA will assess the full fee for an original PMA.[4] This fee is due when the applicant submits the first module.[5]

C. Licensing Agreement PMAs

---

[2] See 68 FR 45246, August 1, 2003; Section 738(a)(1)(A)(i).

[3] For more information on the modular PMA process, see the guidance entitled, "Premarket Approval Application Modular Review" on the web at: [Insert website when posted].

[4] See Section 738(a)(1)(A).

[5] See Section 738(a)(1)(C).

A PMA holder (hereafter referred to as a licensor) may enter into a licensing agreement with another party (hereafter referred to as a licensee) to provide that party with permission to reference the data in its PMA. The licensee, in submitting the licensing agreement PMA to FDA, requests FDA to approve its own device, by referencing the information that was used as a basis for approval of the licensor's device. Upon receiving FDA's approval, the licensee assumes all the responsibilities of a PMA holder, including the manufacture and distribution of a device that is identical to the licensor's. In addition, following approval of the licensing agreement, licensees may choose to make changes to their product. As for all PMA holders, such changes may require the submission of a PMA supplement.

Under the MDUFMA user fee provisions, there is no distinction with respect to fee amounts for PMAs based on licensing agreements and those based on original data.[6] Therefore, PMAs based on licensing agreements are subject to the same fees as submissions based on original data. Similarly, certain PMA supplements submitted to a licensee's PMA would be subject to a user fee just as such supplements to a licensor's PMA would be subject to fees.

Appendix I summarizes the user fees associated with the different types of original PMAs.

IV. What Types of PMA Supplements Are Subject to User Fees?

In accordance with MDUFMA, three types of PMA supplements are subject to user fees, as discussed below.[7] The PMA supplements subject to user fees are:

- panel-track supplements
- 180-day supplements
- real-time supplements.[8]

A. Panel-Track PMA Supplements

Similar to a traditional PMA, a panel-track PMA supplement submitted on or after October 1, 2002, will be assessed the user fee in effect at the time of submission (e.g., $206,811 for FY 04).[9]

---

[6] See Sections 737 and 738(a)(1)(A).
[7] See Sections 738(a)(1)(A)(iii), (iv), and (v).
[8] For definitions of panel-track, 180-day, and real-time supplements, see the guidance entitled, "Assessing User Fees; PMA Supplements Definitions, Modular PMA Fees, BLA and Efficacy Supplement Definitions, Bundling Multiple Devices in a Single Application, and Fees for Combination Products: at: www.fda.gov/cdrh/mdufma/guidance/1201.html. (Hereafter this guidance will be referred to as the Assessing User Fee guidance.)
[9] See Section 738(a)(1)(A)(iii) and 68 FR 45246, August 1, 2003.

B. 180-Day Supplements and Real-Time Supplements

Under MDUFMA, 180-day supplements and real-time supplements submitted on or after October 1, 2002, will be assessed the user fee in effect at the time of the submission (e.g., $44,464 (21.5% of an original PMA fee) and $14,890 (7.2% of an original PMA fee), respectively, for FY 04).[10]

V. Are There Any Exceptions to the Above Fees for Original PMAs or PMA Supplements?

Yes. Under MDUFMA, any original PMA or PMA supplement that is intended solely for a pediatric population is exempt from user fees.[11] If, however, after approval of the original PMA, the PMA holder proposes conditions of use for an adult population, the supplement is subject to the fee in effect at the time of submission.[12]

In addition, MDUFMA provides an exception for PMAs or PMA supplements submitted by a state or federal government entity "unless the device involved is to be distributed commercially."[13] While permitted by statute, FDA does not anticipate that many PMAs will be submitted under these circumstances.

VI. What Types of PMA Supplements or Submissions Are Not Subject to User Fees?

There are other types of supplemental applications, defined in the regulation (21 CFR 814.39) and discussed below, that are not subject to user fees. Because the changes submitted in the supplements identified below are not reviewed jointly with the applicant, FDA does believe that these supplements fall within MDUFMA's definition of a real-time supplement.[14] Therefore, the submissions listed below are not subject to user fees.

---

[10] See Sections 738(a)(1)(A)(iv) and (v).

[11] See Section 738(a)(1)(B)(v)(I). In addition, there may be situations, which upon review of the device and its intended population, FDA determines that the application qualified for the pediatric exemption although the applicant did not request a waiver. In such a case, FDA intends to refund the user fee.

[12] See Section 738(a)(1)(B)(v)(II).

[13] See Section 738(a)(1)(B)(iii).

[14] According to Section 737(4)(D), a real-time supplement "requests a minor change to the device, such as a minor change to the design of the device, software, manufacturing, sterilization, or labeling, and for which the applicant has requested and the agency has granted a meeting or similar forum to jointly review and determine the status of the supplement."

- Special PMA Supplements – Changes Being Affected and 30 day Notices/135 day Supplements
- Manufacturing site changes, including Express PMA Supplements
- Private label distributor
- Trade name change
- Post approval protocol
- Modifying the post approval protocol
- Post approval study results.

These types of submissions are briefly described in the following sections. You should refer to the regulation cited, however, for complete descriptions of the types of changes that are appropriate for these types of submissions.

A. Special PMA Supplements – Changes Being Affected and 30 Day Notices/135 Day Supplements

In a Special PMA Supplement – Changes Being Affected, the PMA holder may effect any change "that enhances the safety of the device or the safety in the use of the device" such as: a) "labeling changes that add or strengthen a contraindication, warning, precaution, or information about an adverse reaction, or b) "changes in quality controls or manufacturing process that add a new specification or test method, or otherwise provide additional assurance of the purity, identify, strength, or reliability of a device" prior to the receipt of a written FDA order approving the supplement.

In addition, "modifications to the manufacturing procedures or methods of manufacture that affect the safety and effectiveness of a device" may be submitted under the 30 Day Notice/135 Day Supplement provision of the PMA regulation.[15]

B. Manufacturing Site Changes

A manufacturing site change supplement is one in which the applicant is requesting to move the manufacturing site to another location or to add an additional site.[16]

C. Private Label Distributor

In a private label distributor supplement, a PMA holder enters into an agreement with another party to permit that party to distribute the approved device under its own

[15] See 21 CFR 814.39 (d) (Special PMA Supplement - Changes Being Affected) and (f) (30 day notices/135 day supplements).
[16] See 21 CFR 814.39(a)(3).

private label. The holder of the original PMA must submit a PMA supplement requesting FDA approval of the agreement.[17]

D. Trade Name Change

In this type of supplement, the PMA holder requests a change in the trade name of its approved device.[18]

E. Post Approval Protocol

FDA may require a PMA applicant, as a condition of approval of the original PMA, to conduct a post approval study to look at specific safety concerns or to assess the long-term safety and effectiveness of the device.[19] As such, a PMA holder must request approval of the post approval study protocol, as required by the Conditions of Approval for the PMA.

F. Modifying the Post Approval Protocol

During the course of the post approval study, the PMA holder may wish to request approval for a modification of the post approval protocol (e.g., to reduce the number of subjects in the study due to slow enrollment).

G. Post Approval Study Results

Upon completion of a post approval study, the PMA holder may need to update the device labeling to reflect the results of the study. These results are submitted for agency review as a PMA supplement.[20]

Appendix II summarizes the user fees associated with the different types of PMA supplements and submissions.

VII. Will FDA Refund User Fees When an Applicant Submits a PMA for a Product That We Determine is Not a Device?

Prior to a PMA filing review, FDA determines whether the product is a device as defined in section 201(h) of the act. If FDA determines that the product is not a device, the agency notifies the applicant in writing of its decision (i.e, a PMA application is not required). In this situation, FDA plans to refund the full fee to the applicant.

[17] See 21 CFR 814.39(a).
[18] See 21 CFR 814.39(a).
[19] See 21 CFR 814.82(a)(2).
[20] See 21 CFR 814.39 (a).

VIII. Will FDA Refund User Fees When We Refuse to File an Application?

If a traditional PMA or panel-track supplement is refused for filing, FDA will refund 75% of the fee paid.[21] When the applicant resubmits the PMA with the additional information necessary to file the PMA, however, FDA intends to assess the full fee.

IX. Will FDA Refund User Fees When an Applicant Withdraws a PMA Application?

Generally, the amount of the fee that FDA may refund for a PMA depends on the type of application (i.e., original or supplement) and when the applicant submits the request to withdraw the application, as discussed below.

A. Refunds when an applicant requests withdrawal of a traditional PMA or panel-track supplement before filing

If an applicant requests withdrawal of a traditional PMA or panel-track supplement before FDA makes the filing decision, we will refund 75% of the fee.[22]

B. Refunds when an applicant requests a refund after FDA has filed the traditional PMA or panel-track supplement, but before FDA takes a first action

FDA has the discretion to refund fees if an applicant withdraws its PMA or panel-track supplement *after* FDA has filed it, but *before* we have taken a first action.[23] First actions may be the issuance of a major deficiency letter, a not approvable letter, an approvable letter, an approval order, or a withdrawal letter.[24] FDA will base any refund after filing, but before the first action is taken, on the "level of effort already expended on the review," as required by MDUFMA.[25] FDA believes that, in most instances, our level of effort can be appropriately assessed by the *number of days* that an application was under review. This approach permits FDA to calculate and process refunds much more efficiently than if we were to attempt to estimate factors on a case-by-case basis, such as the amount of time each member of the review team spent on the review and the significance and complexity of the scientific, medical, technical, and regulatory issues examined during the course of the review. For these reasons, FDA generally intends to make refunds by referring to the following guidelines for traditional PMAs and panel-track supplements:

---

[21] See Section 738(a)(1)(D)(i).
[22] See Section 738(a)(1)(D)(ii).
[23] See Section 738(a)(1)(D)(iii).
[24] See the guidance entitled, "FDA and Industry Actions of Premarket Approval Applications (PMAs): Effect on FDA Review Clock and Performance Assessment" at www.fda.gov/cdrh/mdufma/guidance/1218.html.
[25] See Section 738(a)(1)(D)(iii).

- when withdrawn between the date of the filing decision and day 90, a 50% refund of the fee
- when withdrawn between day 91 and day 135, a 25% refund of the fee
- when withdrawn after day 135, no refund.

FDA recognizes, however, that when there are unusual circumstances, the number of days that an application was under review may not provide a complete picture. Under such unusual circumstances, FDA may take additional factors other than the number of days under review into consideration.

C. Refunds after FDA has taken a first action on a traditional PMA or panel-track supplement

In accordance with MDUFMA, if an applicant requests withdrawal of a traditional PMA or panel-track supplement at any time after FDA has taken its first action, regardless of when the action is taken, FDA will not refund any portion of the fee.[26]

D. Refunds for 180-day and Real-Time Supplements

For 180-day and real-time supplements, FDA considers the application filed upon receipt. The fees for these types of supplements are significantly less than those required for original PMAs, and generally, the reviews are conducted over a shorter period of time. Therefore, in accordance with FDA's authority under section 738(a)(1)(D)(iii) of MDUFMA to base the refund on the amount of effort expended, FDA does not intend to refund any amount of the fee for these types of supplements after they have been filed.

X. What Refunds Are There for Modular PMAs?

For a modular PMA, the applicant is required by statute to pay a full fee for an original PMA when the "first portion" of the application is submitted.[27] The filing decision for a modular PMA, however, is not made until the last module is submitted.[28] If FDA does not file the modular PMA application, the agency will refund 75% of the fee in accordance with MDUFMA.[29]

---

[26] Section 738(a)(1)(D)(iii) does not provide FDA with authority to refund any portion of fees after the agency has taken a first action on an application.

[27] See Section 738(a)(1)(C).

[28] See "Premarket Approval Application Modular Review" for a complete discussion of the modular PMA review program at [Insert website when posted]. As detailed in this guidance, the last module generally is the clinical module, and FDA bases its filing decision on this last module.

[29] See Section 738(a)(1)(D)(i).

In addition, applicants who withdraw their modular PMAs can expect refunds in the same manner as other original PMAs:

- when withdrawn prior to FDA's filing decision, a 75% refund of the fee[30]
- when withdrawn after the filing decision but before a first action, FDA will follow the guidelines presented in Section IX. B.
- when withdrawn after first action, no refund.[31]

XI. What Refunds Are There for Licensing Agreement PMAs?

Licensing Agreement PMAs are considered filed upon receipt. In those cases where an applicant submitted a licensing agreement PMA that included new manufacturing procedures and/or a new manufacturing facility and requests withdrawal before FDA takes its first action, we intend to apply the refund policy discussed above (see Section IX. B.) for traditional PMAs. If, however, the licensing agreement PMA incorporates by authorized reference all the information required by 21 CFR 814.20, including the same manufacturing procedures and facilities, and an applicant requests withdrawal before first action (generally an approval order), FDA plans to refund the full fee.

XII. How Does an Applicant Request a Refund?

FDA considers your written request to withdraw a PMA or panel-track supplement to be an automatic request for a refund. Withdrawal requests should be submitted to:[32]

PMA Document Mail Center, HFZ-401
Office of Device Evaluation
Center for Devices and Radiological Health
9200 Corporate Blvd.
Rockville, MD 20850

XIII. Is There a Deadline to Request a Refund?

Yes. To request a refund, an applicant must submit the request to FDA no later than 180 days after the fee was due.[33]

[30] See Section 738(a)(1)(D)(ii).
[31] See Section 738(a)(1)(D)(iii).
[32] See Section 738(j).
[33] See Section 738(j).

XIV. Are FDA's Decisions on Refunds Reviewable by a Court?

No. Although you may request that FDA reconsider its decision about a refund,[34] you may not appeal FDA's decision to a court. MDUFMA provides that any refund decision that FDA makes with respect to a PMA is not reviewable.[35]

[34] See the guidance entitled, "Resolving Disputes that Affect the Payment or Refund of Medical Device User Fees" at [Insert website when available].
[35] See Section 738(a)(1)(D)(iii).

Appendix I. User Fees for Original PMAs

Types of Original PMAs	Fee Due at the Time of Submission[A]
Traditional Submitted on or after Oct. 1, 2002	Fee in effect at the time of submission
Modular First module submitted before Oct. 1, 2002	$ 0.0
Modular First module submitted on or after Oct. 1, 2002	Fee in effect at the time of submission
Licensing Agreement Submitted on or after Oct. 1, 2002	Fee in effect at the time of submission

[A] In accordance with section 738(c) of MDUFMA, FDA will adjust the fees each year to account for inflation, changes in workload, and other factors. FDA will announce the new fees for the next fiscal year in a Federal Register notice no later than 60 days before the start of that fiscal year, and post these fees on our website at www.fda.gov/cdrh/mdufma/index.html.

Appendix II. User Fees for PMA Supplements or Submissions

Types of PMA Supplements or Submissions	Fee Due at the Time of Submission[A]
Panel-Track	Fee in effect at time of submission
180-Day	Fee in effect at time of submission
Real-Time	Fee in effect at time of submission
Special PMA Supplement – Changes Being Affected	$ 0.0
30 Day Notice/135 Day Supplement	$ 0.0
Manufacturing site change, including Express PMA Supplement	$ 0.0
Private Label Distributor	$ 0.0
Trade Name Change	$ 0.0
Submission of post approval protocol as a Condition of Approval for the original PMA	$ 0.0
Submission of a request to modify post approval protocol	$ 0.0
Submission of the results of post approval study to change the device labeling	$ 0.0

[A] In accordance with section 738(c) of MDUFMA, FDA will adjust the fees each year to account for inflation, changes in workload, and other factors. FDA will announce the new fees for the next fiscal year in a Federal Register notice no later than 60 days before the start of that fiscal year. FDA will also post these fees on our website at www.fda.gov/cdrh/mdufma/index.html.