Draft Guidance for Industry and FDA Staff

User Fees and Refunds for Premarket Approval Applications

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.
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For questions regarding the interpretation of this document in the review of PMAs, please contact the PMA Staff at (240) 276-4040. For questions regarding the interpretation of this document in the review of PMA devices regulated by CBER, please contact the Office of Communication, Training and Manufacturers Assistance, Division of Manufacturers Assistance and Training at 800-835-4709 or 301-827-1800.

When final, this document will supersede "User Fees and Refunds for Premarket Approval Applications" dated November 24, 2003.

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 Center for Devices and Radiological Health (CDRH) through the Internet at http://www.fda.gov/cdrh/ode/guidance/1681.pdf. You may also send an e-mail request to dsmica@fda.hhs.gov to receive an electronic copy of the guidance or send a fax request to 240-276-3151 to receive a hard copy. Please use the document number (**1681**) to identify the guidance you are requesting.

Additional copies of this guidance document are also available from the Center for Biologics Evaluation and Research (CBER), Office of Communication, Training and Manufacturers Assistance (HFM-40), 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448, or by calling 1-800-835-4709 or 301-827-1800, or from the Internet at http://www.fda.gov/cber/guidelines.htm.

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User Fees and Refunds for Premarket Approval Applications

This draft guidance document represents the Food and Drug Administration's (FDA's) current thinking on this topic.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 document. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance document.

I. Introduction

The Medical Device User Fee and Modernization Act of 2002 (MDUFMA) (Pub. 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 approval applications (PMAs) received on or after October 1, 2002. MDUFMA established user fee rates that vary depending on the type of PMA submitted. The Food and Drug Administration Amendments Act of 2007 (FDAAA) (Pub. L. 110-85) now requires user fees for 30-day notices and periodic reports. FDAAA also modifies the refund provision for modular PMAs.

The purpose of this draft guidance document is to identify: (1) the types of PMAs subject to user fees; (2) the types of PMAs that are not subject to user fees because they are expressly excluded from fees under the act; and (3) the actions that may result in refunds of user fees that have been paid. The primary difference between this version and the 2003 version is the addition of user fee and user fee refund information for 30-day notices and periodic reports, as well as the modified user fee refund provisions for modular PMAs. Once final, this document will supersede the 2003 guidance document of the same title.

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

[1] All references to sections 737 and 738 in this guidance document refer to sections 737 and 738 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 379i and 21 U.S.C. 379j, respectively).

II. Types of PMA Applications Subject to User Fees

In accordance with the act, as modified by FDAAA, the following types of PMA applications[2] are subject to user fees:

- Traditional PMAs;
- Modular PMAs;
- Licensing Agreement PMAs;
- Panel-Track Supplements;
- 180-day Supplements;
- Real-time Supplements;
- 30-day Notices; and
- Periodic Reports.

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. For traditional PMAs submitted on or after October 1, 2002, FDA will assess the user fee in effect at the time of the submission (e.g., $185,000 in fiscal year 2008 (FY 08)).[3]

B. Modular PMAs

A modular PMA is a compilation of sections or "modules" that are submitted at different times that together become a complete application.[4] For modular PMAs submitted on or after October 1, 2002, FDA will assess the user fee in effect for a traditional PMA at the time of submission of the first module.[5]

C. Licensing Agreement PMAs

A licensing agreement PMA involves a PMA applicant (hereafter referred to as a licensor) entering 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, after submitting the licensing agreement PMA to FDA, may request FDA to approve its own device, by referencing all 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 applicant, including the manufacture and distribution of a device that is identical to the licensor's. In addition, following approval of the licensing

[2] Section 737(1) of the act includes product development protocols within the definition of premarket applications subject to user fees.
[3] See 72 FR 58099, October 12, 2007; section 738(a)(2)(A)(i) of the act.
[4] For more information on the modular PMA process, see the guidance document entitled, "Premarket Approval Application Modular Review" at http://www.fda.gov/cdrh/mdufma/guidance/835.pdf.
[5] See section 738(a)(2)(C) of the act.

agreement, licensees may choose to make changes to their product. As for all PMA applicants, such changes may require the submission of a PMA supplement.

Under the act's 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, traditional PMAs and PMA supplements 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 user fees.

D. Panel-Track Supplements

Section 737(4)(B) of the act defines "panel-track supplement" as "supplement to an approved premarket application or premarket report under section 515 that requests a significant change in design or performance of the device, or a new indication for use of the device, and for which substantial clinical data are necessary to provide a reasonable assurance of safety and effectiveness."[7]

For panel-track supplements submitted on or after October 1, 2002, FDA will assess the user fee in effect at the time of submission (e.g., $138,750 for FY 08).[8]

E. 180-Day Supplements

Section 737(4)(C) of the act defines "180-day supplement" as "a supplement to an approved premarket application or premarket report under section 515 that is not a panel-track supplement and requests a significant change in components, materials, design, specification, software, color additives, or labeling."[9]

For 180-day supplements submitted on or after October 1, 2002, FDA will assess the user fee in effect at the time of the submission (e.g., $27,750 for FY 08).[10]

F. Real-Time Supplements

Section 737(4)(D) of the act defines "real time supplement" as "a supplement to an approved premarket application or premarket report under section 515 that requests a minor change to the device, such as a minor change to the design of the device, software,

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[6] See section 738(a)(2)(A) of the act.

[7] For more information on panel-track supplements, see the guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" at http://www.fda.gov/cdrh/ode/guidance/1584.pdf.

[8] See sections 738(a)(2)(A)(iii) and 72 FR 58099, October 12, 2007. From October 1, 2002 through September 30, 2007, the user fee for panel-track supplements was the same as for a traditional fee. FDAAA has reduced the user fee for panel-track supplements.

[9] For more information on 180-day supplements, see the guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" at http://www.fda.gov/cdrh/ode/guidance/1584.pdf.

[10] See section 738(a)(2)(A)(iv) of the act.

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."[11]

For real-time supplements submitted on or after October 1, 2002, FDA will assess the user fee in effect at the time of the submission (e.g., $12,950 for FY 08).[12]

G. 30-Day Notices

Section 737(5) of the act defines "30-day notice" as "a notice under section 515(d)(6) that is limited to a request to make modifications to manufacturing procedures or methods of manufacture affecting the safety and effectiveness of the device."[13]

For 30-day notices received on or after October 1, 2007, FDA will assess the user fee in effect at the time of the submission (e.g., $2,960 for FY 08).[14] If a 30-day notice is converted to a 135-day supplement, the user fee paid for the 30-day notice will not be refunded.

H. Periodic Reports[15]

Under section 212 of FDAAA, PMA applicants are subject to an "annual fee for periodic reporting concerning a class III device." FDA will assess the user fee in effect at the time of the submission of the periodic report (e.g., $6,475 for FY 08).[16] [17] Devices with approved PMAs that have been subsequently reclassified into class II are not subject to PMA regulations and, therefore, will not be assessed a periodic reporting user fee. Although FDA has allowed some applicants to submit bundled periodic reports, the annual fee is required for each PMA identified in the periodic report.

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[11] For more information on real-time supplements, see the guidance document entitled, "Real-Time Premarket Approval Application (PMA) Supplements" at http://www.fda.gov/cdrh/ode/guidance/673.pdf. In addition, see the guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" at http://www.fda.gov/cdrh/ode/guidance/1584.pdf.

[12] See section 738(a)(2)(A)(v) of the act.

[13] For more information on 30-day notices, see the guidance document entitled, "30-Day Notices and 135-Day PMA Supplements for Manufacturing Method or Process Changes" at http://www.fda.gov/cdrh/modact/daypmasp.pdf. In addition, see the guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" at http://www.fda.gov/cdrh/ode/guidance/1584.pdf.

[14] See section 738(a)(2)(A)(vi) of the act.

[15] In accordance with 21 CFR 814.82(a)(7), FDA may require, as a condition of approval, submission to FDA at intervals specified in the approval order of periodic reports containing the information required by 21 CFR 814.84(b). In most cases, after the PMA is approved, the PMA applicant is required to submit reports to FDA annually unless a different time frame is specified in the approval order. Accordingly, periodic reports are typically referred to by FDA and industry as "annual reports." Periodic reports are separate from the postapproval study reports, which are discussed in the guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" at http://www.fda.gov/cdrh/osb/guidance/1561.pdf.

[16] See section 738(a)(2)(A)(x) of the act.

[17] PMAs are not subject to the periodic reporting user fee until the first fiscal year following approval of the original PMA. This corresponds to when the first periodic report would be due.

III. Exception to User Fees

Under the act's user fee provisions, any PMA that is intended solely for a pediatric population is exempt from user fees.[18] There may be situations where, 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 would refund the user fee. However, if after approval of a traditional or modular PMA for pediatric use, the PMA applicant proposes conditions of use for an adult population, the supplement is subject to the full user fee in effect at the time of submission.[19]

The act also allows an exemption from user fees for a PMA submitted by a state or federal government entity "unless the device involved is to be distributed commercially."[20] While permitted by statute, FDA does not anticipate that many PMAs will be submitted under these circumstances.

IV. User Fee Refunds

User fee refunds are handled as described below. [21]

A. FDA refuses to file a Traditional PMA or Panel-Track Supplement

If FDA issues a non-filing letter for a traditional PMA or panel-track supplement, FDA will refund 75% of the fee paid.[22] When an applicant amends a PMA to respond to a non-filing letter, FDA will require the full user fee in effect at the time of submission.

B. 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 user fee.[23]

C. Applicant requests withdrawal of a filed Traditional PMA or Panel-Track Supplement, but FDA has not taken 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.[24] First actions

[18] See section 738(a)(2)(B)(v)(I) of the act.
[19] See section 738(a)(2)(B)(v)(II) of the act.
[20] See section 738(a)(2)(B)(iii) of the act.
[21] See section 738(a)(2)(D)(iii) of the act.
[22] See section 738(a)(2)(D)(i) of the act.
[23] See section 738(a)(2)(D)(ii) of the act.
[24] See section 738(a)(2)(D)(iii) of the act.

may be the issuance of a major deficiency letter, a not approvable letter, an approvable letter, an approval order, or a withdrawal letter.[25]

FDA will base any refund it issues *after* a filing, but *before* a first action is taken, on the "level of effort already expended on the review," as required by the act.[26] 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 intends to make refunds by referring to the following guidelines for traditional PMAs and panel-track supplements:

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

Although you may request that FDA reconsider its decision about a user fee refund, "[t]he Secretary has sole discretion to refund a fee or portion of the fee" for an application withdrawn after filing but before first action.[27] A determination by the Secretary concerning a refund is not reviewable.[28]

D. FDA has taken a first action on a Traditional PMA or Panel-Track Supplement

In accordance with the act, 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 user fee.[29]

[25] See the guidance document entitled, "FDA and Industry Actions of Premarket Approval Applications (PMAs): Effect on FDA Review Clock and Performance Assessment" at http://www.fda.gov/cdrh/mdufma/guidance/1218.pdf.
[26] See section 738(a)(2)(D)(iii) of the act.
[27] Section 738(a)(2)(D)(vi) of the act.
[28] Id. See the guidance document entitled, "Resolution of Disputes Concerning Payment or Refund of Medical Device User Fees Under MDUFMA" at http://www.fda.gov/cdrh/mdufma/guidance/1303.pdf.
[29] Section 738(a)(2)(D)(iii) of the act does not provide FDA with authority to refund any portion of fees after the agency has taken a first action on an application.

E. Modular PMAs

For a modular PMA, the applicant is required by statute to pay a full fee for a traditional PMA when the first module is submitted.[30] Although there is no filing review completed on the individual modules, actions can be taken. Module actions include an acceptance letter or a deficiency letter.

Upon receipt of the last module, the modular PMA is converted to a traditional PMA review track. At that point, the filing review for that PMA is initiated.[31]

User fee refunds for modular PMAs for which the first module was received between October 1, 2002 and September 30, 2007 will be handled in the following manner:

- when withdrawn prior to FDA's filing decision, a 75% refund of the user fee;[32]
- when withdrawn after the filing decision but before a first action, FDA will follow the guidelines presented in Section IV, Part D, above; or
- when withdrawn after the filing decision and a first action, no user fee refund.[33]

User fee refunds for modular PMAs for which the first module was received on or after October 1, 2007 will be handled in the following manner:

- when withdrawn *prior* to submission of a second module and *before* a first action on the first module, a 75% refund of the user fee;[34] or
- when withdrawn *after* a second or subsequent module is submitted but *before* any first action, the refund, if any, will be based on the "level of effort already expended on the review on the modules submitted." For this situation, FDA intends to make refunds by referring to the following guidelines:
    - after a second module but before any first action, 50% refund of the user fee;
    - after a third module but before any first action, 25% refund of the user fee; or
    - after a fourth or subsequent module, no user fee refund.

F. Licensing Agreement PMAs

Licensing Agreement PMAs are considered filed upon receipt. In cases where an applicant submits a licensing agreement PMA that includes new manufacturing procedures and/or a new manufacturing facility and requests withdrawal before FDA takes its first

[30] See section 738(a)(2)(C) of the act.
[31] See the guidance document entitled, "Premarket Approval Application Modular Review" for a complete discussion of the modular PMA review program at http://www.fda.gov/cdrh/mdufma/guidance/835.pdf. As detailed in this guidance document, the last module generally is the clinical module, and FDA bases its filing decision on this last module.
[32] See section 738(a)(2)(D)(ii) of the act.
[33] See section 738(a)(2)(D)(iii) of the act.
[34] See section 738(a)(2)(D)(ii) of the act.

action, we intend to apply the refund policy discussed above (see Section IV., part D. above) 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 user fee.

G. 180-Day Supplements

For 180-day supplements, FDA considers the application filed upon receipt. The fees for these types of supplements are significantly less than those required for traditional PMAs, and, generally, the reviews are conducted over a shorter period of time. Therefore, in accordance with FDA's authority under section 738(a)(2)(D)(iii) of the act, which bases the refund on the amount of effort expended, FDA does not intend to refund any amount of the user fee for this type of supplement after it has been filed.

H. Real-Time Supplements

For real-time supplements, FDA will follow the same user fee refund provisions as described above for 180-day supplements.

I. 30-Day Notices

For 30-day notices, FDA will follow the same user fee refund provisions as described above for 180-day supplements.

J. Periodic Reports

FDA does not intend to refund any amount of the annual fee for periodic reports.

V. How to Request a User Fee Refund

To request a refund, an applicant must submit a written request to the appropriate Center in FDA at the address below no later than 180 days after the fee was due.[35]

For products regulated by CDRH:

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

For products regulated by CBER:

Document Control Center, HFM-99
Center for Biologics Evaluation and Research

[35] See section 738(j) of the act.

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