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User Fees and Refunds for Premarket Approval Applications and Device Biologics License Applications

Guidance for Industry and Food and Drug Administration Staff

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For questions regarding submissions to the Center for Devices and Radiological Health (CDRH), contact the Office of Regulatory Programs / Division of Submission Support / PMA, HDE, Q-Submission, and Device Tracking Lifecycle Team at 301-796-5640, or by email at OPEQSubmissionSupport@fda.hhs.gov.

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
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Preface

Public Comment

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Guidance for Industry and Food and Drug Administration Staff

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 or Office responsible for this guidance as listed on the title page.

I. Introduction

The Medical Device User Fee Amendments of 2022[1] (MDUFA V), amended the Federal Food, Drug, and Cosmetic Act (FD&C Act) to authorize FDA to collect user fees for the review of certain premarket submissions received on or after October 1, 2022, including premarket approval applications (PMAs) and certain biologics license applications (BLAs).[2] The additional funds obtained from user fees will enable FDA, with the cooperation of industry, to improve the medical device review process to meet certain performance goals and implement improvements for the medical device review process as outlined in the letter from the Secretary of Health and Human Services to Congress.[3] For more information on performance goals for PMAs, see the guidance "FDA and Industry Actions on Premarket Approval Applications (PMAs): Effect on FDA Review Clock and Goals Performance."[4]

The purpose of this guidance document is to identify: (1) the types of PMAs and BLAs subject to device user fees; (2) exceptions to user fees; and (3) the actions that may result in refunds of user fees that have been paid.

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[1] See Title II of the FDA User Fee Reauthorization Act of 2022 (Public Law 117-180).
[2] For additional information on medical device user fees, including the user fees for the current fiscal year, please see https://www.fda.gov/industry/fda-user-fee-programs/medical-device-user-fee-amendments-mdufa
[3] See 168 CONG. REC. S5194-S5203 (daily ed. September 28, 2022) (Food and Drug Administration User Fee Reauthorization). The MDUFA V Commitment Letter is also available at https://www.fda.gov/media/158308/download. Performance goals established for BLAs are also outlined in this commitment letter.
[4] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-and-industry-actions-premarket-approval-applications-pmas-effect-fda-review-clock-and-goals

For information regarding bundling of multiple submissions, see "Bundling Multiple Devices or Multiple Indications in a Single Submission."[5]

In general, FDA's guidance documents 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. Types of PMAs Subject to User Fees[6]

In accordance with the FD&C Act, as amended by MDUFA V, the following types of PMAs[7] are subject to user fees:

- Original PMAs;
- Modular PMAs;
- Premarket Reports;
- Licensing Agreement PMAs;
- Panel-Track Supplements;
- 180-Day Supplements;
- Real-Time Supplements;
- 30-day Notices; and
- Periodic Reports.

A. Original PMAs

An original PMA is one in which all elements required under 21 CFR 814.20 are submitted at the same time in a single application. For original PMAs submitted on or after October 1, 2022, FDA will assess the user fee in effect at the time of the submission.[8]

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. For modular PMAs submitted on or after October 1, 2002, FDA will assess the user fee in effect for an original PMA at the time of submission of

[5] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/bundling-multiple-devices-or-multiple-indications-single-submission
[6] See section 738(a)(2)(A) of the FD&C Act.
[7] Section 737(1) of the FD&C Act includes product development protocols within the definition of premarket applications subject to user fees.
[8] See section 738(b)(2) of the FD&C Act.

the first module.[9] For more information on the modular PMA process, see the guidance document, "Premarket Approval Application Modular Review."[10]

C. Premarket Reports

A premarket report (PMR) is a marketing application for class III reprocessed single use devices (SUDs) that otherwise would have required a PMA.[11] Among other information, a PMR must include validation data regarding cleaning, sterilization, and functional performance of the reprocessed device to ensure it is substantially equivalent to a legally marketed device. For PMRs submitted on or after October 1, 2022, FDA will assess the user fee in effect for an original PMA at the time of the submission.

D. Licensing Agreement PMAs

A licensing agreement PMA involves a PMA applicant (hereafter referred to as a licensor) entering 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 agreement PMA, 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 FD&C 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.[12] Therefore, original 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.

E. Panel-Track Supplements

Section 737(4)(B) of the FD&C 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." For more information on panel-track supplements, see the guidance document,

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[9] See section 738(a)(2)(C) of the FD&C Act.
[10] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/premarket-approval-application-modular-review
[11] See section 515(c)(2)(A) of the FD&C Act.
[12] See section 738(a)(2)(A) of the FD&C Act.

"Modifications to Devices Subject to Premarket Approval (PMA) – The PMA Supplement Decision-Making Process."[13]

For panel-track supplements submitted on or after October 1, 2022, FDA will assess the user fee in effect at the time of submission.[14]

F. 180-Day Supplements

Section 737(4)(C) of the FD&C 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." For more information on 180-day supplements, see the guidance document, "Modifications to Devices Subject to Premarket Approval (PMA) – The PMA Supplement Decision-Making Process."[15]

For 180-day supplements submitted on or after October 1, 2022, FDA will assess the user fee in effect at the time of the submission.[16]

G. Real-Time Supplements

Section 737(4)(D) of the FD&C 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, 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." For more information on real-time supplements, see the guidance documents, "Real-Time Premarket Approval Application (PMA) Supplements"[17] and "Modifications to Devices Subject to Premarket Approval (PMA) – The PMA Supplement Decision-Making Process."[18]

For real-time supplements submitted on or after October 1, 2022, FDA will assess the user fee in effect at the time of the submission.[19]

H. 30-Day Notices

Section 737(5) of the FD&C Act defines "30-day notice" as "a notice under section 515(d)(5) that is limited to a request to make modifications to manufacturing procedures or methods of

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[13] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/modifications-devices-subject-premarket-approval-pma-pma-supplement-decision-making-process
[14] See section 738(a)(2)(A)(iii) of the FD&C Act.
[15] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/modifications-devices-subject-premarket-approval-pma-pma-supplement-decision-making-process
[16] See section 738(a)(2)(A)(iv) of the FD&C Act.
[17] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/real-time-premarket-approval-application-pma-supplements
[18] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/modifications-devices-subject-premarket-approval-pma-pma-supplement-decision-making-process
[19] See section 738(a)(2)(A)(v) of the FD&C Act.

manufacture affecting the safety and effectiveness of the device." Additionally, per 21 CFR 814.39(f) "If the [30-day] notice is not adequate, FDA shall inform the applicant in writing that a 135-day PMA supplement is needed and shall describe what further information or action is required for acceptance of such change." For more information on 30-day notices and 135-day supplements, see the guidance documents, "30-Day Notices, 135-Day Premarket Approval (PMA) Supplements and 75-Day Humanitarian Device Exemption (HDE) Supplements for Manufacturing Method or Process Changes"[20] and "Modifications to Devices Subject to Premarket Approval (PMA) – The PMA Supplement Decision-Making Process."[21]

For 30-day notices received on or after October 1, 2022, FDA will assess the user fee in effect at the time of the submission.[22] 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.

I. Periodic Reports

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 timeframe 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 post-approval study reports, which are discussed in the guidance document, "Procedures for Handling Post-Approval Studies Imposed by Premarket Approval Application Order."[23] Under section 738(a)(2)(A)(x) of the FD&C Act, 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.[24] Note that PMAs are not subject to the periodic reporting user fee until the first fiscal year following approval of the original PMA. Typically, this corresponds to when the first periodic report would be due. Also, devices with approved PMAs that have been subsequently reclassified into class II or withdrawn 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 approved PMA identified in the periodic report.

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[20] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/30-day-notices-135-day-premarket-approval-pma-supplements-and-75-day-humanitarian-device-exemption

[21] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/modifications-devices-subject-premarket-approval-pma-pma-supplement-decision-making-process

[22] See section 738(a)(2)(A)(vi) of the FD&C Act.

[23] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/procedures-handling-post-approval-studies-imposed-pma-order

[24] See section 738(a)(2)(A)(x) of the FD&C Act.

III. Types of Biologics License Applications Subject to Device User Fees

In accordance with the FD&C Act, as amended by MDUFA V, the following applications for devices subject to licensure under section 351 of the Public Health Service Act, are subject to user fees:

- Original biologics license applications (BLAs), which are included in the user fee definition of "premarket application" in section 737(1) of the FD&C Act; and
- BLA Efficacy Supplements (BLSs), which are defined for user fee purposes in section 737(4)(E) of the FD&C Act.

Under sections 738(a)(2)(A)(i) and (vii) of the FD&C Act, both applications are assessed the user fee applicable to a premarket application that is in effect at the time of the submission.

A. Original BLAs

An original BLA is one in which all elements required under 21 CFR 601.2 are submitted at the same time in a single application. User fees will be assessed for original applications.

B. BLA Efficacy Supplements

According to section 737(4)(E) of the FD&C Act, "efficacy supplement" is defined as "a supplement to an approved premarket application under section 351 of the Public Health Service Act that requires substantive clinical data."

User fees will be assessed for efficacy supplements containing the types of clinical data that are required to form the primary basis for approval, e.g., study reports or literature reports that are explicitly or implicitly represented by the applicant to be adequate and well-controlled trials.

For purposes of assessing user fees, "clinical data" do not include data used solely to modify the labeling to add a restriction that would improve the safe use of the product (e.g., to add a limitation or warning to the labeling). In addition, supplements to BLAs based solely on equivalence studies (in-house testing with limited external testing) are not considered to contain clinical data for purposes of assessing user fees.

For the types of changes listed below, substantive clinical data are generally necessary to demonstrate the equivalence of the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product. Therefore, applicants should submit an efficacy supplement and pay the associated fee for:

- a new indication for use (e.g., new platform, new patient population/disease state);
- a significant change in design; or
- a significant change in performance.

For example, a change in an HIV test kit for blood donor screening to include an additional strain or a change in a Blood Grouping Reagent to include a different source of raw material (e.g., changing from one monoclonal antibody cell line to another) both require substantive clinical data to support the change. Therefore, these would be classified as efficacy supplements and would require payment of the associated user fee.

IV. Exceptions to User Fees

Under the FD&C Act's user fee provisions, any PMA or BLA that is intended solely for a pediatric population is exempt from user fees.[25] There may be situations where, upon review of the device and its intended population, FDA determines that the application qualified for the pediatric exception although the applicant did not request a waiver. In such a case, FDA would refund the user fee upon request. However, if after approval of an original or modular PMA or a BLA for pediatric use, the applicant proposes conditions of use for an adult population, the supplement is subject to the full user fee of a traditional PMA or BLA in effect at the time of submission.[26]

A first ever original PMA or BLA submitted by a qualifying small business is also granted a one-time waiver of the user fee. To quality for this exception, a business, together with its affiliates, must have gross receipts or sales of no more than $30 million for the most recent tax year.[27]

Additionally, a BLA submitted under section 351 of the Public Health Service Act for a product licensed for further manufacturing use only is exempt from user fees.[28]

The FD&C Act also allows an exception from user fees for a PMA or BLA submitted by a state or federal government entity "unless the device involved is to be distributed commercially."[29] While permitted by statute, FDA does not commonly receive PMAs or BLAs submitted under these circumstances.

The following PMA supplements are not subject to user fees and do not require submission of user fee cover sheets:

- Special PMA supplement – Changes Being Effected (CBE);
- PMA supplement for manufacturing/sterilization site change without associated design changes;
- PMA supplement for trade name change;
- PMA supplement for post approval study protocol; and
- PMA post approval study labeling update.

[25] See section 738(a)(2)(B)(v)(I) of the FD&C Act.
[26] See section 738(a)(2)(B)(v)(II) of the FD&C Act.
[27] See section 738(d)(1) of the FD&C Act.
[28] See section 738(a)(2)(B)(ii) of the FD&C Act.
[29] See section 738(a)(2)(B)(iii) of the FD&C Act.

The following BLA supplements submitted in accordance with 21 CFR 601.12 are not subject to user fees:

- Prior Approval Supplements (PASs) that do not meet the definition of an efficacy supplement
- Changes Being Effected in 30 days (CBE-30s)
- Changes Being Effected (CBEs)
- Annual reports (ARs)

V. User Fee Payments

As outlined below, there are three ways you may submit your user fee.[30] Be sure to include the Payment Identification Number (PIN, beginning with MD)[31] and the FDA P.O. Box on your check, bank draft, or U.S. Postal Money Order. Also, you should include a printed copy of your User Fee Cover Sheet (Form FDA-3601, accessible through FDA's User Fee System at https://userfees.fda.gov/OA_HTML/fdaCAcdLogin.jsp) with your payment.

1) Preferred method – Credit Card or Electronic Check (ACH): FDA has partnered with the U.S. Department of the Treasury to utilize https://www.pay.gov, a Web-based payment system, for online electronic payment. You may make a payment via electronic check or credit card after submitting your cover sheet. To pay online, select the "Pay Now" button. Credit card transactions for cover sheets are limited to $24,499.99.

2) Check: All paper checks must be in U.S. currency from a U.S. bank and made payable to the Food and Drug Administration. Please write your unique PIN, from the upper right-hand corner of your completed Medical Device User Fee cover sheet, on the check and mail the check to the appropriate address listed below. FDA will not be able to process your payment correctly without your cover sheet PIN.

   Check payments by mail:
   Food and Drug Administration
   P.O. Box 979033
   St. Louis, MO 63197-9000
   Note: In no case should payment be submitted with the application.

   Check payments delivered by a courier service:
   U.S. Bank
   ATTN: Government Lockbox 979033
   1005 Convention Plaza
   St. Louis, MO 63101
   Note: This address is for courier delivery only. If you have any questions concerning courier delivery, contact US Bank at (314) 418-4013.

[30] Additional information regarding payment of user fees is available at https://userfees.fda.gov/OA_HTML/mdufmaFAQ.html.
[31] A PIN is obtained after creating a User Fee Cover Sheet and selecting "Submit Cover Sheet to FDA."

3) Wire Transfer: Please include your application's unique PIN, from the upper right-hand corner of your completed Medical Device User Fee cover sheet, in your wire transfer. Without the PIN your payment may not be applied to your cover sheet and review of your application will be delayed.

   The originating financial institution may charge a wire transfer fee. Please ask your financial institution about the fee and include it with your payment to ensure that your cover sheet is fully paid.

   Wire transfer information:
   US Department of Treasury
   TREAS NYC
   33 Liberty Street
   New York, NY 10045

   FDA Deposit Account Number: 75060099
   US Department of Treasury routing/transit number: 021030004
   SWIFT Number: FRNYUS33

VI. User Fee Refunds

User fee refunds are handled as described below.

A. eCopy criteria not met for a PMA

FDA has issued the guidance, "eCopy Program for Medical Device Submissions,"[32] to implement section 1136 of Food and Drug Administration Safety and Innovation Act (FDASIA), which added section 745A(b) of the FD&C Act, and provides statutory authority to require eCopy. If FDA does not receive an eCopy, or receives an eCopy that cannot be accepted because it does not meet our technical standards, the omission or reasons for that failure will be communicated to the applicant in writing to aid in their creation of a valid replacement eCopy. If a valid eCopy is not received within 180 calendar days of this notification, the submission will be deleted from our system and FDA will refund the fee paid upon request. If you decide not to submit a valid replacement eCopy of your original submission in response to the eCopy hold notification, you may also send a written request to withdraw your submission before receiving a deletion letter and request a refund of the fee paid. Note that your fee will not be refunded if you fail to provide a valid eCopy of a response to an additional information request after first action on the PMA.

[32] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/ecopy-program-medical-device-submissions

B. Acceptance criteria not met for a PMA

If after an administrative review, FDA refuses to accept the PMA, the applicant will be notified within 15 calendar days of receipt that the submission has not been accepted. The applicant may submit additional information to the PMA to address the reasons for the refusal without submitting a new user fee. Alternatively, the applicant may send a written request to withdraw the submission and request a refund of the fee paid if the applicant decides not to provide additional information.

C. Applicant requests withdrawal of an Original PMA or Panel-Track Supplement before filing

If an applicant requests withdrawal of an original PMA or panel-track supplement after the acceptance decision but before FDA makes the filing decision, we will refund 75% of the user fee.[33]

D. Filing criteria not met for an Original PMA or Panel-Track Supplement

If FDA issues a not-filed letter for an original PMA or panel-track supplement, the applicant can request a refund of 75% of the fee paid.[34] When an applicant amends a PMA to respond to a not-filed letter, FDA will require the full user fee in effect at the time of submission. If FDA does not receive a response to a not-filed letter within 360 days, the PMA will be deleted from our system.[35] For additional information, please refer to the guidance, "Acceptance and Filing Reviews for Premarket Approval Applications (PMAs)."[36]

E. Applicant requests withdrawal of a filed Original 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.[37] 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. See the guidance document, "FDA and Industry Actions

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[33] See section 738(a)(2)(D)(ii) of the FD&C Act.
[34] See section 738(a)(2)(D)(i) of the FD&C Act.
[35] Under FDA regulations for review of PMAs, FDA also considers an original PMA or PMA supplement to have been voluntarily withdrawn if an applicant fails to respond in writing to a written request for an amendment within 180 days after the date FDA issues such request. See 21 CFR 814.44(g).
[36] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/acceptance-and-filing-reviews-premarket-approval-applications-pmas
[37] See section 738(a)(2)(D)(iii) of the FD&C Act.

on Premarket Approval Applications (PMAs): Effect on FDA Review Clock and Goals,"[38] for more information regarding PMA actions.

FDA will base any refund it issues when the application is withdrawn *after* a filing but *before* a first action is taken on the "level of effort already expended on the review," as required by the FD&C Act.[39] FDA believes that, in most instances, our level of effort can be appropriately assessed by the number of calendar 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 original 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 calendar 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 calendar days under review into consideration.

Although you may request that FDA reconsider its decision about a user fee refund, the Secretary has "sole discretion to refund a fee or portion of the fee" for an application withdrawn after filing but before a first action.[40] A determination by the Secretary concerning a refund is not reviewable.[41]

F. FDA has taken a first action on an Original PMA or Panel-Track Supplement

In accordance with the FD&C Act, if an applicant requests withdrawal of an original 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.[42]

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[38] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-and-industry-actions-premarket-notification-510k-submissions-effect-fda-review-clock-and-goals

[39] See section 738(a)(2)(D)(iii) of the FD&C Act.

[40] See section 738(a)(2)(D)(vi) of the FD&C Act.

[41] Id.

[42] See section 738(a)(2)(D)(iii).

G. Modular PMAs

For a modular PMA, the applicant is required by statute to pay a full fee for an original PMA when the first module is submitted.[43] 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 an original PMA review track. At that point, the filing review for that PMA is initiated. See the guidance document, "Premarket Approval Application Modular Review,"[44] for a complete discussion of the modular PMA review program.

User fee refunds for modular PMAs 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;[45] or
- when withdrawn after a second or subsequent module is submitted but before any first action *on that module*, the refund, if any, will be based on the "level of effort already expended on the review on the modules submitted."[46] For this situation, FDA intends to make refunds by referring to the following guidelines:
    - after a second module but before any first action *on that module*, 50% refund of the user fee;
    - after a third module but before any first action *on that module*, 25% refund of the user fee; or
    - after a fourth or subsequent module, no user fee refund.

H. Premarket Reports

For premarket reports, FDA will follow the same user fee refund provisions as described above for original PMAs in section VI, parts C through F.

I. Licensing Agreement PMAs

Licensing agreement PMAs are considered filed upon receipt. As stated previously, 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 FD&C Act.[47] 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 action, we intend to apply the refund policy discussed above for original PMAs (see section VI, part E above). If,

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[43] See section 738(a)(2)(C) of the FD&C Act.
[44] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/premarket-approval-application-modular-review
[45] See section 738(a)(2)(D)(iv) of the FD&C Act.
[46] See section 738(a)(2)(D)(v) of the FD&C Act.
[47] See section 738(a)(2)(D)(iii)

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 a first action (generally an approval order), FDA plans to refund the full user fee based on the level of effort.

J. 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 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)(2)(D)(iii) of the FD&C 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.

K. Real-Time Supplements

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

L. 30-Day Notices

For 30-day notices, or for 30-day notices that are converted to 135-day PMA supplements, FDA will follow the same user fee refund provisions as described above for 180-day supplements.

M. Periodic Reports

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

N. eCopy criteria not met for a BLA

If FDA does not receive an eCopy,[48] or receives an eCopy that cannot be accepted because it does not meet our technical requirements, the omission or reasons for that failure will be communicated to the applicant in writing to aid in their creation of a valid replacement eCopy. If a valid eCopy is not received within 180 calendar days of this notification, the submission will be closed in our system and FDA will refund the fee paid upon request. If you decide not to submit a valid replacement eCopy of your original submission in response to the eCopy hold notification, you may also send a written request to withdraw your submission before receiving a deletion letter and request a refund of the fee paid. Note that your fee will not be refunded if you fail to provide a valid eCopy of a response to an additional information request after first action on the BLA.

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[48] See the guidance document, "eCopy Program for Medical Device Submissions," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/ecopy-program-medical-device-submissions.

O. Applicant requests withdrawal of an Original BLA or Efficacy Supplement before filing

If an applicant requests withdrawal of an original BLA or efficacy supplement before FDA makes the filing decision, we will refund 75% of the user fee.[49]

P. Filing criteria not met for an Original BLA or Efficacy Supplement

If FDA issues a refusal to file letter for an original BLA or efficacy supplement, the applicant can request a refund of 75% of the fee paid.[50] When an applicant resubmits a BLA in response to a refusal to file letter, FDA will require the full user fee in effect at the time of resubmission.

Q. Applicant requests withdrawal of a filed Original BLA or Efficacy Supplement, but FDA has not taken a first action

FDA has the discretion to refund fees if an applicant withdraws its BLA or efficacy supplement after FDA has filed it but before we have taken a first action.[51] First action means the issuance of a complete response letter, an approval letter, or a withdrawal letter after the complete review of a filed complete application.

FDA will base any refund it issues when the application is withdrawn *after* a filing but *before* a first action is taken on the "level of effort already expended on the review," as required by the FD&C Act.[52] FDA believes that, in most instances, our level of effort can be appropriately assessed by the number of calendar 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 original BLAs and efficacy supplements:

- when withdrawn between the date of the filing decision and day 152, a 50% refund of the user fee;
- when withdrawn between day 152 and day 228, a 25% refund of the user fee; or
- when withdrawn after day 228, no user fee refund.

FDA recognizes, however, that when there are unusual circumstances, the number of calendar days that an application was under review may not provide a complete picture. Under such

[49] See section 738(a)(2)(D)(ii) of the FD&C Act.
[50] See section 738(a)(2)(D)(i) of the FD&C Act.
[51] See section 738(a)(2)(D)(iii) of the FD&C Act.
[52] Ibid.

unusual circumstances, FDA may take additional factors other than the number of calendar 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 a first action.[53] A determination by the Secretary concerning a refund is not reviewable.[54]

R. FDA has taken a first action on an Original BLA or Efficacy Supplement

In accordance with the FD&C Act, if an applicant requests withdrawal of an original BLA or efficacy 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.[55]

VII. How to Request a User Fee Refund

To facilitate the Agency's orderly issuance of refunds, you should submit a written request[56] for a refund to the appropriate Center in FDA within 180 calendar days after the fee was due.[57]

For devices regulated by CDRH, requests for refunds should be submitted to the current mailing address displayed on the website https://www.fda.gov/cdrhsubmissionaddress.

For devices regulated by CBER, requests for refunds should be submitted to the current mailing address displayed on the website https://www.fda.gov/about-fda/center-biologics-evaluation-and-research-cber/regulatory-submissions-electronic-and-paper.

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[53] See section 738(a)(2)(D)(vi) of the FD&C Act.
[54] Ibid.
[55] Section 738(a)(2)(D)(iii) of the FD&C Act does not provide FDA with authority to refund any portion of fees after the Agency has taken a first action on an application.
[56] The user fee payment refund request form is available at https://www.fda.gov/media/96650/download.
[57] See Section 738(j) of the FD&C Act.