Assessing User Fees Under the Prescription Drug User Fee Amendments of 2017

Guidance for Industry

DRAFT GUIDANCE

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

October 2017
User Fees

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Assessing User Fees Under the Prescription Drug User Fee Amendments of 2017 Guidance for Industry[1]

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic.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 responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance provides stakeholders information regarding FDA's implementation of the Prescription Drug User Fee Amendments of 2017 (PDUFA VI) under Title I of the FDA Reauthorization Act of 2017. Because PDUFA VI created changes to the user fee program, this guidance explains the new fee structure and the types of fees for which entities are responsible.

This guidance describes the types of user fees authorized by PDUFA VI, the process for submitting payments to FDA, the consequences for failing to pay application fees or prescription drug program fees, and the process for requesting a reconsideration of a user fee assessment. The guidance also describes how FDA determines which products are subject to a fee and discusses certain changes to the FDA's policies under the new law. FDA has separate guidance documents about PDUFA VI waivers, refunds, and reductions. This guidance does not address how FDA determines and adjusts fees each fiscal year (FY); nor does it address FDA's implementation of other user fee programs (e.g., Biosimilar User Fee Amendments, Generic Drug User Fee Amendments).[2] Throughout this guidance, references to *user fees* or the *user-fee program* are to prescription drug user fees collected under section 736 of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

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.

[1] This guidance has been prepared by the Division of User Fee Management and Budget Formulation, Office of Management, in the Center for Drug Evaluation and Research, in consultation with the Center for Biologics Evaluation and Research at the Food and Drug Administration.

[2] FDA will publish in the *Federal Register* the fee revenue and fee amounts for each fiscal year not later than 60 days before the start of each fiscal year. Section 736(c)(5) of the FD&C Act.

Changes to statutory provisions that are described in this draft guidance are effective with respect to fees assessed beginning on the first day of FY 2018.[3]

II. BACKGROUND

The Prescription Drug User Fee Act of 1992 (PDUFA I) added sections 735 and 736 to the FD&C Act, authorizing FDA to collect user fees for a 5-year period from persons that submit certain human drug applications for review or that are named in approved applications as the sponsor of certain prescription drug products. Since 1992, Congress has revised and extended PDUFA five times, each time for a 5-year period. Fees authorized by this legislation help fund the process for the review of human drug applications and have played an important role in expediting the drug review and approval process. The most recent reauthorization is Title I of the FDA Reauthorization Act of 2017, enacted on August 18, 2017.

PDUFA VI extends FDA's authority to collect user fees for FY 2018 through 2022 and revises the fees that the Agency collects and how it collects some fees. Discussions about the next reauthorization of PDUFA are expected to begin before or during FY 2022, the final fiscal year of PDUFA VI.

III. DEFINITIONS

For purposes of this guidance:

- The term ***affiliate*** means a business entity that has a relationship with a second business entity if, directly or indirectly, (1) one business entity controls, or has the power to control, the other business entity; or (2) a third party controls, or has the power to control, both of the business entities.[4]

- The term ***applicant*** means the owner, holder, or sponsor of a new drug application (NDA) or biologics license application (BLA).

- The term ***drug*** includes drug and biological products.[5]

- The term ***final dosage form*** means, with respect to a prescription drug product, a finished dosage form which is approved for administration to a patient without substantial further manufacturing (such as capsules, tablets, or lyophilized products before reconstitution).[6]

- The term ***human drug application*** means an application for (1) approval of a new drug submitted under section 505(b) of the FD&C Act or (2) licensure of a biological product under subsection (a) of section 351 of the Public Health Service Act (PHS Act).[7]

[3] FDA's fiscal year begins on October 1 and ends on September 30.
[4] Section 735(11) of the FD&C Act.
[5] For the purposes of this guidance, the terms *biologic* and *biological product* have the same meaning.
[6] Section 735(4) of the FD&C Act.

Such term does not include a supplement to such an application, does not include an application with respect to whole blood or a blood component for transfusion, does not include an application with respect to a bovine blood product for topical application licensed before September 1, 1992, an allergenic extract product, or an in vitro diagnostic biologic product licensed under section 351 of the PHS Act, does not include an application with respect to a large volume parenteral drug product approved before September 1, 1992, does not include an application for a licensure of a biological product for further manufacturing use only, and does not include an application or supplement submitted by a State or Federal Government entity for a drug that is not distributed commercially. Such term does include an application for licensure of a large volume biological product intended for single dose injection for intravenous use or infusion.

- The term ***person*** includes any affiliates of that person.[8] The term ***person*** includes an individual, partnership, corporation, or association.[9] This document will also use the term ***person*** when referring to an applicant.

- The term ***prescription drug product*** means a specific strength or potency of a drug in final dosage form:
  - for which a human drug application has been approved;
  - which may be dispensed only by prescription under section 503(b) of the FD&C Act; and
  - which is on the list of products described in section 505(j)(7)(A) of the FD&C Act (not including the discontinued section of such list) or is on a list created and maintained by the Secretary of Health and Human Services (Secretary) of products approved under human drug applications under section 351(a) of the PHS Act (not including the discontinued section of such list).

  Such term does not include:
  - whole blood or a blood component for transfusion;
  - a bovine blood product for topical application licensed before September 1, 1992, an allergenic extract product, or an in vitro diagnostic biologic product licensed under section 351 of the PHS Act;
  - a biological product that is licensed for further manufacturing use only; and
  - a drug that is not distributed commercially AND is the subject of an application or supplement submitted by a State or Federal Government entity.

  Such term does include a large volume biological product intended for single dose injection for intravenous use or infusion.[10]

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[7] Section 735(1) of the FD&C Act.
[8] Section 735(9) of the FD&C Act.
[9] Section 201(e) of the FD&C Act.
[10] Section 735(3) of the FD&C Act.

- The term ***supplement*** means a request to the Secretary to approve a change in a human drug application which has been approved.[11]

IV. CHANGES TO THE STRUCTURE OF THE PDUFA USER FEE PROGRAM

PDUFA VI authorizes the collection of two types of fees: (1) human drug application fees, which are collected at the time certain human drug applications are submitted; and (2) prescription drug program fees, which are collected annually for certain prescription drug products.[12] The statute directs FDA to set fee amounts for each fiscal year so that human drug application fees will account for 20 percent and prescription drug program fees will account for 80 percent of the total revenue amount for that fiscal year.[13]

Previously, section 736 of the FD&C Act authorized FDA to collect (1) human drug application and supplement fees, (2) prescription drug establishment fees, and (3) prescription drug product fees. PDUFA VI eliminates fees for supplements[14] as well as for establishments.[15] Applicants will be assessed annual prescription drug program fees for prescription drug products, rather than the prescription drug product fee assessed under PDUFA V.

In addition, PDUFA VI eliminates a provision under which applicants could apply for a waiver or refund of user fees on the basis that the fees to be paid by such person will exceed the anticipated present and future costs incurred by the Secretary in conducting the process for the review of human drug applications for such person, also known as the "the fees-exceed-costs waiver."

The Agency will continue to establish human drug application fees and prescription drug program fees for each fiscal year based on revenue amounts set forth in the statute, and will publish, in the *Federal Register*, the fees and fee revenue amounts for a fiscal year not later than 60 days before the start of that year.[16]

[11] Section 735(2) of the FD&C Act.
[12] The terms *prescription drug program fee* and *program fee* have the same meaning.
[13] Section 736(b)(2)(A) of the FD&C Act.
[14] The Agency considers it useful to provide guidance to applicants distinguishing between an original application, amendment, and supplement to accurately assess user fees. Information on what FDA believes should be submitted in marketing applications, amendments, or supplements to approved applications is provided in the guidance for industry *Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees*, available at: https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf.
[15] The establishment fee special rule that applied to establishments that manufacture positron emission tomography (PET) drugs was also eliminated.
[16] Section 736(c)(5) of the FD&C Act.

V. HUMAN DRUG APPLICATION FEES

Under PDUFA VI, FDA assesses a user fee for certain human drug applications. Each person that submits a human drug application beginning in FY 2018 is assessed an application fee under PDUFA VI as follows:

- A human drug application for which clinical data (other than bioavailability or bioequivalence studies) with respect to safety or effectiveness are required for approval is assessed a full application fee.
- A human drug application for which clinical data (other than bioavailability or bioequivalence studies) with respect to safety or effectiveness are not required for approval is assessed one-half of a full fee.[17]

Human drug application fees are due when the application is submitted.[18]

A. Exceptions to the Application Fee

There are two exceptions to the PDUFA application fee, described below:

(1) Previously Filed Applications. If an application

- was submitted by a person that paid the fee for the application,
- was accepted for filing, and
- was not approved or was withdrawn (without a waiver),

the submission of a human drug application for the same product by the same person (or the person's licensee, assignee, or successor) does not require an application fee.[19]

(2) Designated Orphan Drug. A human drug application for a prescription drug product that has been designated as a drug for a rare disease or condition pursuant to section 526 of the FD&C Act shall not be subject to an application fee unless the human drug application includes an indication for other than a rare disease or condition.[20] More information is provided in the guidance for industry *User Fee Waivers, Reductions, and Refunds for Drug and Biological Products* (Waivers Guidance).[21]

B. Applications Refused for Filing or Withdrawn

If an application is refused for filing or withdrawn without a waiver before filing, FDA will refund 75 percent of the application fee.[22] If an application is withdrawn after it is filed, FDA

[17] Section 736(a)(1)(A) of the FD&C Act.
[18] Section 736(a)(1)(B) of the FD&C Act.
[19] Section 736(a)(1)(C) of the FD&C Act.
[20] Section 736(a)(1)(F) of the FD&C Act.
[21] We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA Drugs guidance web page at https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.
[22] Section 736(a)(1)(D) of the FD&C Act.

may refund the fee or a portion of the fee if no substantial work was performed on the application after the application was filed. FDA has the sole discretion to refund a fee or a portion of the fee. The FDA's determination concerning a refund on this basis (no substantial work was performed on the application) is not reviewable.[23]

An application that was submitted but refused for filing or withdrawn before being accepted or refused for filing, shall be subject to the full fee when resubmitted or filed under protest, unless the fee is waived or reduced under one of the provisions identified in section VII of this guidance.[24]

VI. PRESCRIPTION DRUG PROGRAM FEES

In general, each person[25] named as the applicant in a human drug application and that, after September 1, 1992, had pending with the FDA a human drug application or supplement is required to pay the annual prescription drug program fee for each prescription drug product that is identified in such a human drug application approved as of October 1 of such fiscal year.[26, 27]

Applicants may not be assessed more than five prescription drug program fees for a fiscal year for prescription drug products identified in a single approved application.[28, 29]

A prescription drug product is **not** assessed a prescription drug program fee if:

- the product is on the list compiled under section 505(j)(7) with a potency described in terms of per 100 milliliters (large volume parenteral);[30] or
- the product is the same as another product approved under
  - an application filed under sections 505(b) or 505(j) of the FD&C Act and that other product is not in the list of discontinued products compiled under section 505(j)(7) of the FD&C Act,
  - an abbreviated application filed under section 507 of the FD&C Act (as in effect on the day before November 21, 1997), or

[23] Section 736(a)(1)(G) of the FD&C Act.
[24] Section 736(a)(1)(E) of the FD&C Act.
[25] "The term 'person' includes an affiliate thereof." Section 735(9) of the FD&C Act.
[26] Section 736(a)(2)(A) of the FD&C Act.
[27] For example, if an application is approved before or on October 1, 2017, then the product that is identified in the application may be assessed a program fee for FY 2018 and subsequent fiscal years. But, if an application is approved on or after October 2, 2017, then the product that is identified in the application may not be assessed a program fee for FY 2018; it would be eligible for assessment of program fees for subsequent fiscal years.
[28] Section 736(a)(2)(C) of the FD&C Act.
[29] For example, an applicant that has 10 drug products identified in an approved NDA for 10 different strengths of tablet dosage form products is eligible for an assessment for a maximum of 5 program fees. As another example, an applicant that has 6 biologic products identified in an approved BLA for 3 strengths of liquid injectable and 3 strengths of lyophilized products will be assessed 5 program fees.
[30] Section 736(a)(2)(B)(i) of the FD&C Act.

- an abbreviated new drug application (ANDA) prior to the implementation of the Drug Price Competition and Patent Term Restoration Act of 1984.

Prescription drug program fees are due on the later of the first business day on or after October 1 of each fiscal year, or the first business day after the enactment of an appropriations Act providing for the collection and obligation of fees for such fiscal year under this section.[31] Applicants may pay fees before the date on which they are due.[32]

A. When and Where Prescription Drug Products Are Listed

Prescription drug products eligible for a prescription drug program fee are on the list of products described in section 505(j)(7)(A) of the FD&C Act (not including the discontinued section of such list) or on a list created and maintained by the Secretary of products approved under human drug applications under section 351(a) of the PHS Act (not including the discontinued section of such list).[33]

1. In General

The list of products described in section 505(j)(7)(A) of the FD&C Act is the FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations*[34] (commonly known as the "Orange Book"), which includes products that are the subject of approved human drug applications submitted under section 505(b) and approved under section 505(c) of the FD&C Act. FDA publishes updates to the list each month.[35] Drugs are considered to be added to the Orange Book on the day they are approved rather than on the date FDA publishes its next Orange Book update.[36] For example, if a drug product submitted for approval under section 505(b) of the FD&C Act is approved on September 15, it is considered to be added to the Orange Book on September 15. Unless the drug product is moved from the "Prescription Drug Product List" in the Orange Book (the "active list") to the "Discontinued Drug Product List," it may be assessed a program fee for the next fiscal year even if FDA does not publish an update to the Orange Book before the day fees are due.

FDA also maintains a list of products approved under human drug applications under section 351(a) of the PHS Act and also considers such drugs to be added to the list on the date they are approved. FDA periodically provides the public with information about its list by publication to the Agency website in two locations. Biologics regulated by the Center for Drug Evaluation and Research (CDER) are listed on the *CDER Billable Biologic Product List*, and biologics regulated by the Center for Biologics Evaluation and Research (CBER) may be found on the list of *User*

[31] Section 736(a)(2)(A) of the FD&C Act.
[32] Section 736(g)(2)(C) of the FD&C Act authorizes FDA to accept payment of PDUFA fees for a fiscal year prior to the due date for such fees, in accordance with authority provided in advance in a prior year appropriations Act.
[33] Section 735(3)(C) of the FD&C Act.
[34] The Orange Book is available at https://www.accessdata.fda.gov/scripts/cder/ob/default.cfm.
[35] Section 505(j)(7)(A)(ii) of the FD&C Act.
[36] Section 505(j)(7)(B) of the FD&C Act.

Fee Billable Biologic Products and Potencies Approved Under Section 351 of the PHS Act (collectively, the Biologics Lists).[37]

Applicants may raise questions about product listings with the FDA as follows:

- For NDA products, an applicant should contact the Orange Book staff at OrangeBook@fda.hhs.gov.
- For CDER biological products, an applicant should contact CDER User Fee staff at CDERCollections@fda.hhs.gov.
- For CBER biological products, an applicant should contact CBER User Fee staff at CBERPDUFAstaff@fda.hhs.gov.

Sponsors should send the CDER User Fee staff (CDERCollections@fda.hhs.gov) a courtesy copy of information sent to the Orange Book staff or CBER User Fee staff to help ensure accurate billing.

2. Moving a Drug Product to the Discontinued Section of the Orange Book or Biologics List

A drug product is not assessed a prescription drug program fee for a fiscal year if it is in the discontinued section of the Orange Book or the discontinued section of the Biologics List on the date fees are assessed.[38] Applicants that have decided to stop marketing a prescription drug product, or that have decided to delay launch of a product until after its approval date, should request to have the product moved to the discontinued section at their earliest opportunity to give FDA sufficient time to process the request before fees are assessed. In most cases, we expect that an applicant intending to discontinue or delay marketing a drug product will notify FDA well in advance.[39] If a drug product remains on the "Prescription Drug Product List" of the Orange Book or the Biologics List as of October 1, the applicant may be assessed a program fee for the drug even if it is not being marketed.

Requests to move a product to the discontinued section should be submitted either (1) to the Orange Book staff, for products approved under section 505 of the FD&C Act, or (2) to the relevant User Fee staff (CDER or CBER) for products approved under section 351(a) of the PHS Act, at the relevant email address listed in section VI.A.1 of this guidance. All requests should clearly identify the product to be moved and the date that its not-marketed status begins and, if applicable, would end. Upon receiving such a request, FDA may ask the applicant for further information to confirm the product's not-marketed status. If the applicant submits a request as

[37] Available at https://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm151732.htm.
[38] Sections 735(3) and 736(a)(2)(A) of the FD&C Act.
[39] Under new section 506I of the FD&C Act, added by section 804 of FDA Reauthorization Act of 2017 (FDARA), the holder of an application approved under section 505(c) of the FD&C Act is required to notify FDA in writing 180 days prior to withdrawing the approved drug from sale or, if that is not practicable, as soon as practicable but not later than the date of withdrawal.

set forth in this paragraph and FDA does not deny the request, then for purposes of assessing user fees, FDA intends to consider the product to have been moved to the discontinued section on the date that the request was received or on the date the product is no longer marketed, whichever is later.

Please note that applicants seeking to move a prescription drug product to a discontinued list should clearly indicate the date on which their product is no longer marketed. Applicants should **not** rely on communications with a review division, the product listing staff, or FDA components other than the Orange Book Staff or the CDER or CBER User Fee staff, as appropriate. Communication with the wrong division of FDA, or in a manner that does not make clear when a product is no longer marketed, may mean that a prescription drug product is not moved to the discontinued section of the Orange Book or the Biologics List before the date program fees are assessed and may result in the applicant being required to pay a fee for the product.

B. "Same Product as Another Product"[40] Prescription Drug Program Fee Exception

Section 736(a)(2)(B)(ii) of the FD&C Act provides that a prescription drug product will not be assessed a prescription drug program fee if it is the same product as another product that was approved under an application filed under section 505(b) or 505(j) of the FD&C Act and is not in the list of discontinued products compiled under section 505(j)(7) of the FD&C Act.

For purposes of this section, we interpret the term *same product as another product* to mean a drug product that FDA has determined is therapeutically equivalent to another drug product. Therapeutically equivalent products are approved drug products that are pharmaceutical equivalents[41] for which bioequivalence[42] has been demonstrated and that can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling. Generally, products classified as therapeutically equivalent can be substituted with the full expectation that the substituted product will produce the same clinical effect and safety profile as the prescribed product. FDA publishes its conclusions regarding therapeutic equivalence in the Orange Book.

The "same product" provision in section 736(a)(2)(B)(ii) of the FD&C Act is intended to provide drugs with a user fee exception if they are subject to competition from generic drug products.[43]

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[40] Section 736(a)(2)(B)(ii) of the FD&C Act.

[41] Pharmaceutical equivalents are drug products in identical dosage forms and routes of administration that contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified-release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; do not necessarily contain the same inactive ingredients; and meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates. 21 CFR 314.3.

[42] Bioequivalence is the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study. 21 CFR 314.3.

[43] H.R. Rept. 102-895 (Sept. 22, 1992), at page 16.

The term *generic drug* is often used to refer to a drug named in an ANDA submitted under section 505(j) of the FD&C Act. For purposes of section 736(a)(2)(B)(ii) of the FD&C Act, we believe Congress also meant to provide the exception to products not named in an ANDA whose therapeutic equivalence to another product makes them generally substitutable for that other product, because such products could offer the same type of competition as products approved under an ANDA.[44]

Certain drug products identified in applications filed under section 505(b)(2) of the FD&C Act may not have a classification of therapeutic equivalence at the time they are approved, and FDA may undertake therapeutic equivalence evaluations with respect to such drug products. A person seeking a therapeutic equivalence rating for a drug product filed under section 505(b)(2) of the FD&C Act and approved under section 505(c) of the FD&C Act may petition the Agency through the citizen petition procedure (see 21 CFR 10.25(a) and 21 CFR 10.30).[45]

Please note that if an applicant has petitioned the Agency for a therapeutic equivalence rating for a 505(b)(2) drug product but has not yet received a determination regarding therapeutic equivalence, the applicant can only seek a refund of the prescription drug program fee for a fiscal year by submitting a written request for a refund not later than 180 calendar days after the prescription drug program fee is due.[46] Refund requests submitted after that date are not timely and will not be considered. See section IX below for information on refunds and appeals process.[47]

C. Liquid Parenteral Biological Products Approved under Section 351 of the PHS Act

1. Assessing the Strength or Potency of a Drug in Final Dosage Form

As described above, applicants of approved applications are assessed an annual program fee for each eligible prescription drug product, up to a maximum of five program fees for a fiscal year for each approved application.

When evaluating the specific strength or potency of a drug in final dosage form for purposes of assessing program fees for liquid parenteral biological products, FDA intends to take into consideration both the total amount of drug substance in mass or units of activity in a product and the concentration of drug substance (mass or units of activity per unit volume of product). Products considered to have a different strength or potency in a final dosage form will be given

[44] The Agency has long used the process for assigning therapeutic equivalence codes to determine whether a drug qualifies for this exception and, on some occasions, has awarded the same-product exception to a drug that FDA does not consider to be therapeutically equivalent to other pharmaceutically equivalent products. We are proposing to adopt the interpretation stated in this guidance, which we believe better reflects the purpose of the statute.

[45] Orange Book Preface to the 37th Edition at section 1.10, available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm079068.htm.

[46] The FD&C Act does not provide for deferral of user fees, and FDA does not grant deferrals of user fees, based on pending requests for therapeutic equivalence evaluations. FDA therefore expects that all fees assessed will be paid when due without regard to a pending request for a therapeutic equivalence evaluation.

[47] More information is provided in the Waivers Guidance.

separate entries in the Biologics List and subject to separate program fees. This constitutes a change in our evaluation of such products. FDA previously considered only the concentration of drug substance in liquid parenteral drug products approved under section 351 of the PHS Act, without taking into account the total amount of drug substance in the product, in determining the specific strength or potency of a drug in final dosage form for purposes of assessing product fees. The approach described in this guidance is intended to align our treatment of products approved under section 351 of the PHS Act with the way the Agency generally assesses fees for products approved under section 505 of the FD&C Act, providing consistency in our implementation of the program fee. FDA also notes that any effect of this approach on sponsors of products subject to the prescription drug program fee will be capped by the limit of five prescription drug program fees for a fiscal year for each approved application.

2. Auto-Injectors, Prefilled Syringes, and Vials

An auto-injector that has the same strength or potency as a prefilled syringe or vial will generally be assessed a separate prescription drug program fee. This is intended to align the Agency's assessment of fees for products approved under section 351 of the PHS Act with its assessment of fees for products approved under section 505 of the FD&C Act.[48]

D. Orphan Drug Exemption

A drug designated under section 526 of the FD&C Act for a rare disease or condition and approved under section 505 of the FD&C Act or under section 351 of the PHS Act shall be exempt from prescription drug program fees if the drug meets all of the following conditions:

- the drug meets the public health requirements that are applied to requests for waivers for prescription drug program fees, and

- the drug is owned or licensed and is marketed by a company, including its affiliates, that had less than $50 million in gross worldwide revenue during the previous year.[49]

This exemption applies with respect to a drug only if the applicant involved submits a certification that its gross worldwide revenues did not exceed $50 million for the preceding 12 months before the exemption was requested.[50, 51]

VII. WAIVERS OF PDUFA FEES

Section 736(d) of the FD&C Act provides that FDA will grant a waiver of or reduction in one or more user fees assessed under section 736(a) of the FD&C Act where it finds that one or more of the following is true:

[48] The distinction described in this guidance between (1) auto-injectors and (2) prefilled syringes or vials is for the purposes of assessing the prescription drug program fee only and not for any other purpose.
[49] Section 736(k)(1) of the FD&C Act.
[50] Section 736(k)(2) of the FD&C Act.
[51] More information is provided in the Waivers Guidance.

- A waiver or reduction is necessary to protect the public health.

- The assessment of the fee would present a significant barrier to innovation because of limited resources available to the person or other circumstances.[52]

- The applicant is a small business submitting its first human drug application to the Secretary for review.

For more information on these waiver and reduction provisions, sponsors may refer to the Waivers Guidance.

VIII. EFFECT OF FAILURE TO PAY FEES

A human drug application or supplement submitted by a person subject to fees under section 736(a) of the FD&C Act is considered incomplete and will not be accepted for filing until *all* such fees owed by the person have been paid.[53] For example, if a person submits an application without an application fee or if the person is in arrears for nonpayment of any prescription drug program fees, the application will be incomplete and FDA will not accept it for filing. Note that the term *person* as used here includes an affiliate of the person, which means that an affiliate's failure to pay all of the user fees that it owes will affect the applicant's ability to file an application.

IX. PAYMENT INFORMATION AND PROCEDURES

This section briefly describes the general process for assessing and issuing annual invoices for prescription drug program fees under PDUFA VI. More detailed instructions will be provided in FDA's direct notice to affected applicants.

A. Prescription Drug Program Fee Notifications

FDA will issue a notice to applicants regarding their prescription drug products in preparation for assessing prescription drug program fees. These notices will be sent before the due date for prescription drug program fees. Applicants will have the opportunity to review the notice and notify FDA of any changes in contact information, changes in prescription drug product marketing status, or any other information the Agency needs to issue an accurate annual invoice.

B. Prescription Drug Program Fee Assessments and Payments

[52] Two special circumstances that may affect eligibility for waivers or reductions under the barrier to innovation waiver provision are addressed in separate waiver guidances. Companies participating in the President's Emergency Plan for AIDS Relief should consult the guidance for industry *User Fee Waivers for FDC and Co-Packaged HIV Drugs for PEPFAR*. Companies submitting combination products under 21 CFR 3.2(e) should see the guidance for industry *Application User Fees for Combination Products*. We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA Drugs guidance web page at https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/def ault.htm.

[53] Section 736(e) of the FD&C Act.

FDA expects to issue invoices for prescription drug program fees around the end of September based on information available to the Agency at the time the invoices are prepared. Payments are due either on the first business day on or after October 1 of each fiscal year or the first business day after the enactment of an appropriations Act providing for the collection and obligation of fees for that fiscal year, whichever occurs later.[54]

FDA will issue additional invoices later, as needed, to capture program fees owed that were not previously invoiced. For example, fee-eligible prescription drugs that are approved between the date annual notices are prepared and October 1 may be the subject of a billing during the fiscal year. Invoices may also be issued after September for other reasons.

IX. FEE WAIVER, REDUCTION, OR REFUND REQUESTS AND APPEALS PROCESS

A. Waiver, Reduction, or Refund Request

An applicant may request a waiver or reduction of user fees, and may request a refund of fees it has paid, if it meets the statutory criteria.[55] Policies for such requests, and the permissible grounds for a waiver, reduction, or refund, are discussed in more detail in the Waivers Guidance. Note that any request for a waiver, reduction, or refund must be submitted no later than 180 days after such fee is due.[56]

B. Reconsideration Request

If FDA fully or partially denies a request for a waiver, refund, or reduction of user fees, the applicant may request reconsideration of that decision. A request for reconsideration should be made within 30 calendar days of the issuance of FDA's decision to fully or partially deny a request for a waiver, reduction, or refund of user fees.

FDA recommends that requests for reconsideration state the applicant's reasons for believing that FDA's decision is in error and include any additional information, including updated financial information that is relevant to the applicant's position. The Agency will issue a response upon reconsideration, setting forth the basis for the decision.

All requests for reconsideration (regardless of whether the product is regulated by CDER or CBER) should be submitted via email to CDERCollections@fda.hhs.gov and should be addressed to the following:

Division of User Fee Management and Budget Formulation

[54] Section 736(a)(2)(A) of the FD&C Act.

[55] The FD&C Act does not provide for deferral of user fees, and FDA does not grant deferrals of user fees, based on pending requests for a refund. FDA therefore expects that all fees assessed will be paid when due without regard to a pending request for a refund.

[56] Section 736(i) of the FD&C Act.

Attention: Division Director
Center for Drug Evaluation and Research

Alternatively, an applicant can mail the request to FDA via the carrier of its choice. For the most updated mailing address, visit the following FDA website: http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/default.htm.

C. Appeal Request

If a request is denied upon reconsideration, the applicant may choose to appeal the denial. A request for an appeal should be made within 30 calendar days of the issuance of FDA's decision to affirm its denial of a request for a waiver, refund, or reduction of user fees. The following information should be included in the appeal:

- The original request;
- The denial of the original request;
- The reconsideration request;
- The denial of the reconsideration request; and
- A statement of the applicant's reasons for believing that the prior conclusions were in error.

No new information or new analyses should be presented in the appeal request. If new information or analyses are presented in the appeal request, the appeal will not be accepted and the matter will be referred back to the original deciding authority to consider the new information or analyses.

All requests for appeals for either CDER or CBER products should be submitted to the Director of CDER's Office of Management via CDERCollections@fda.hhs.gov, and a copy should be submitted to the CDER Formal Dispute Resolution Project Manager. The contact information can be found on the CDER Formal Dispute Resolution web page.[57] Alternatively, an applicant can mail the request to FDA via the carrier of its choice. For the most updated mailing address, visit the following FDA website: http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/default.htm.

After FDA reviews the information submitted in the appeal request, for CDER regulated products, the Director of CDER's Office of Management will issue a written decision on the applicant's request; for CBER regulated products, the Director of CBER will issue a written decision on the applicant's request.

[57] Available at https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ContactCDER/ucm444092.htm.

CDER Products

If the applicant's appeal is denied at one management level, the applicant can appeal the same matter to the next higher management level in the CDER chain of command. A new request should be submitted for each appeal to the next management level and should follow the process provided in this guidance. If the applicant has exhausted the CDER management levels and remains unsatisfied with the decision, the applicant may request review of the matter by the Commissioner of Food and Drugs (Commissioner) under 21 CFR 10.75(c). Requests for review by the Commissioner should be submitted to the FDA's Ombudsman, with a copy provided to CDER. Review of such matters by the Commissioner is discretionary.[58]

CBER Products

If the applicant's appeal is denied by the Director of CBER, the applicant may request review of the matter by the Commissioner under 21 CFR 10.75(c). Requests for review by the Commissioner should be submitted to the FDA's Ombudsman, with a copy provided to CBER. Review of such matters by the Commissioner is discretionary.

X. OTHER RESOURCES

The following guidance documents may be helpful:

- Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees[59]
- User Fee Waivers, Reductions, and Refunds for Drug and Biological Products[60]
- User Fee Waivers for FDC and Co-Packaged HIV Drugs for PEPFAR[61]

The following manuals of policies and procedures (MAPPs) may be helpful:

- MAPP 6020.4 Classifying Resubmissions of Original NDAs, BLAs, and Efficacy Supplements in Response to Complete Response Letters[62]
- MAPP 6050.1 Refusal to Accept Applications for Filing From Applicants in Arrears[63]

[58] See 40 FR 40682, 40693 (September 3, 1975).
[59] Available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf.
[60] Available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm079298.pdf.
[61] Available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079324.pdf.
[62] Available at https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM082002.pdf.

Additional information is also available on the FDA User Fees web page. For any questions, please email the Prescription Drug User Fee staff at CDERCollections@fda.hhs.gov or call 301-796-7900.

[63] Available at https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM082029.pdf.