Prescription Drug User Fee Act Waivers, Reductions, and Refunds for Drug and Biological Products

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DRAFT GUIDANCE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)

June 2018
User Fees

Prescription Drug User Fee Act Waivers, Reductions, and Refunds for Drug and Biological Products

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Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353
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Food and Drug Administration
10903 New Hampshire Ave., Bldg. 71, Room 3128
Silver Spring, MD 20993-0002
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Prescription Drug User Fee Act Waivers, Reductions, and Refunds for Drug and Biological Products 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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic.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 recommendations to applicants regarding requests for waivers, refunds, and reductions of user fees assessed under sections 735 and 736 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) for drugs, including biological products.[2] This guidance is a revision of the guidance for industry entitled *User Fee Waivers, Reductions, and Refunds for Drug and Biological Products*, issued in September 2011.

This revised draft guidance describes (1) the types of waivers, refunds, and reductions available under the user fee provisions of the FD&C Act, (2) the procedures for requesting waivers, refunds, or reductions, and (3) the process for requesting a reconsideration or appeal of an FDA decision. The draft guidance also provides clarification on related issues such as user fee exemptions for orphan drugs.

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, Center for Drug Evaluation and Research, in consultation with the Center for Biologics Evaluation and Research.

[2] For the purposes of this document, unless otherwise specified, references to "drugs" or "drug products" include drugs submitted under section 505(b) of the FD&C Act and biological products licensed under section 351(a) of the PHS Act, other than biological products that also meet the definition of a device in section 201(h) of the FD&C Act (21 U.S.C. 321(h)).

II. BACKGROUND

The Prescription Drug User Fee Act of 1992 (PDUFA I) amended the FD&C Act, and authorized FDA to collect user fees for 5 years from companies that produce certain human drug and biological products. PDUFA must be reauthorized every 5 years, and has been reauthorized 5 times since PDUFA I, most recently in 2017 under Title I of the FDA Reauthorization Act of 2017 (PDUFA VI).

PDUFA VI authorizes FDA to assess application fees for certain human drug and biological product applications when those applications are submitted. In addition, PDUFA VI authorizes FDA to assess annual prescription drug program fees (program fees) for certain approved drug and biological products.[3]

Because of the way the user fee program is structured in the FD&C Act, the total amount FDA collects in user fees is independent of the number of waivers or reductions in fees that are granted. Target revenues are established in accordance with a statutory formula, and the amount of each type of fee (application and program) is determined based on historical data of how many applications and products were assessed fees in the previous fiscal years. Therefore, the number of waivers, refunds and reductions granted in a fiscal year is factored into the statutory formula and may result in an increase or decrease in application and program fees for the following year to meet the annual statutory revenue targets.

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, (A) one business entity controls, or has the power to control, the other business entity; or (B) 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), submitted under section 351(a) of the Public Health Service (PHS) Act.

- The term ***application*** includes both NDAs, submitted under section 505 of the FD&C Act, and BLAs, submitted under section 351(a) of the PHS Act.

- The term ***drug*** includes drug and biological products.

[3] Information on application and program fees, including fee rates, PDUFA goals, and other user fee related issues can be found on FDA's PDUFA website: http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/default.htm.

[4] Section 735(11) of the FD&C Act.

- 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 section 351(a) of the PHS Act.[5] For purposes of this guidance, the term ***human drug application*** does not include the following:

    - A supplement to such an application;
    - An application with respect to whole blood or a blood component for transfusion;
    - An application with respect to a bovine blood product for topical application licensed before September 1, 1992;
    - An application for an allergenic extract product;
    - An in vitro diagnostic biologic product licensed under section 351 of the PHS Act;
    - An application with respect to a large volume parenteral drug product approved before September 1, 1992;
    - An application for a licensure of a biological product for further manufacturing use only; and,
    - An application submitted by a State or Federal Government entity for a drug that is not distributed commercially.[6]

- The term ***person*** means the person subject to fees and includes any affiliates of that person.[7] The term ***person*** includes an individual, partnership, corporation, and association.[8] 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 FDA of products approved under human drug applications under section 351(a) of the PHS Act (not including the discontinued section of such list).[9]

    Such term does not include:

    - Whole blood or a blood component for transfusion;

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

- A bovine blood product for topical application licensed before September 1, 1992;
- An allergenic extract product;
- 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.[10]

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

- The term ***financial resources*** means the current financial assets, including cash and any other income available other than cash in the form of liquid securities and credit lines, of an applicant and its affiliates. See section IV.C. below for more information.

IV. TYPES OF WAIVERS AND REDUCTIONS

According to section 736(d) of the FD&C Act, FDA will grant to an applicant 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:

- 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.

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

Sections IV.A through IV.C below describe FDA's considerations for each type of waiver.[12]

[10] Section 735(3) of the FD&C Act.

[11] Section 735(2) of the FD&C Act.

[12] There are three additional special circumstances that may affect an applicant's eligibility for waivers or reductions under the public health and barrier to innovation waiver provision:

(1) for applicants participating in the President's Emergency Plan for AIDS Relief (PEPFAR), see guidance for industry, *User Fee Waivers for FDC and Co-Packaged HIV Drugs for PEPFAR*;

(2) for applicants submitting combination products under 21 Code of Federal Regulations 3.2(e), see guidance for industry, *Application User Fees for Combination Products*; and,

(3) for applicants submitting applications for certain types of positron emission tomography (PET) drugs (specifically, FDG F 18 injection, ammonia N 13 injection, and sodium fluoride F 18injection), see 21 FR 12999, 13004 (Mar. 10, 2000), and guidance for industry, *FDA Oversight of PET Drug Products: Questions and Answers*. Please note that the waivers for these PET drugs only apply to application fees; applicants who would like program fees waived may request a public health or barrier-to-innovation waiver, as is further described in this guidance. Any applicant submitting an application that may present these special circumstances should consult the relevant guidance and statutory provisions. FDA updates guidances periodically. To make sure you have the most recent version of a guidance, visit the FDA Drugs guidance website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

A. Public Health

Under section 736(d)(1)(A) of the FD&C Act, an applicant may qualify for a waiver or reduction in application or program fees if the waiver or reduction is necessary to protect the public health. Under this provision, FDA considers the following questions in determining whether to grant a public health waiver or reduction in user fees:

- Does the product protect the public health?

- Is the waiver or reduction ***necessary*** to continue an activity that protects the public health?

Applicants should address both of these questions when applying for a public health waiver or reduction in fees.

1. Does the product protect the public health?

For user fee purposes, a product that has been approved for marketing in the United States is not automatically deemed to be a product that protects the public health. In evaluating whether a product protects the public health, the Agency generally intends to ask the following questions:

- Is the drug product a significant improvement (or does it have the potential to be a significant improvement if the drug product is not yet approved) compared to other marketed products, including other dosage forms or routes of administration and non-drug products or therapies?

- Are there other treatment alternatives in the U.S. market? The existence of comparable treatment alternatives would weigh against a determination that a product is necessary to protect the public health.

- Has the drug product been designated as a priority drug, accepted into one of FDA's expedited programs for serious conditions,[13] granted fast track status,[14] or determined to be a new molecular entity? Affirmative answers to these questions usually indicate that a product protects the public health.

[13] Further information regarding priority drugs can be found in the guidance for industry, *Expedited Programs for Serious Conditions – Drugs and Biologics*, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm358301.pdf, and in CDER's Manual of Policies and Procedures (MAPP) 6020.3R, *Review Designation Policy: Priority (P) and Standard (S).* MAPP 6020.3R is available at https://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/manualofpoliciesprocedures/ucm082000.pdf.

[14] Further information regarding fast track status is available at https://www.fda.gov/forpatients/approvals/fast/ucm20041766.htm.

- Does the drug product demonstrate an increased effectiveness in the treatment, prevention, or diagnosis of disease?

- Does it eliminate or substantially reduce a treatment-limiting drug reaction?

- Does the drug product enhance patient adherence to treatment?

- Has the drug product shown potential evidence of safety and effectiveness for a new or underserved subpopulation (e.g., treatment for a drug resistant microbe or response to a homeland security concern)?

- Is the drug product intended for the diagnosis or treatment of a serious or life-threatening condition?

- Does the drug product address unmet medical needs or demonstrate the potential to do so?

- Is the product designated as a drug for a rare disease or condition under section 526 of the FD&C Act (i.e., does it have an orphan designation)?

- If the drug product is approved, is the product recognized as an effective treatment option that significantly impacts the public health?

- If the product is approved, is it available to the public? There is no benefit to the public health if a product is not made available to the public.[15]

2. Is the waiver or reduction necessary to continue an activity that protects the public health?

To determine whether a waiver or reduction in user fees is necessary to continue an activity that protects the public health, the Agency considers not only the benefit of the activity to the public health, but also whether the waiver or reduction is necessary. The legislative history of PDUFA I indicates that FDA may waive or reduce fees unless such a waiver or reduction is not necessary to protect the public health, or it is apparent that the fee will not be a disincentive to innovation.[16] It also indicates that FDA should consider the "limited resources" of the applicant when evaluating a request for a fee waiver or reduction under section 736(d).[17] Therefore, the Agency believes that a financial test is appropriate for the public health waiver provision. The Agency considers the relationship between current liabilities and the financial resources of the applicant, including affiliates, requesting the waiver or reduction. The financial considerations are discussed in section IV.C below.

[15] FDA would consider products stockpiled for homeland security concerns as available to the public for user fee waiver purposes.

[16] See House Report 102-895 (1992) at 17; 138 Cong. Rec. S. 17239 (Oct. 7, 1992).

[17] Id.

B. Barrier to Innovation

Under section 736(d)(1)(B) of the FD&C Act, an applicant may qualify for a waiver or reduction in application or program fees when the assessment of the fees would present a significant barrier to innovation because of limited resources available to the applicant or other circumstances. Under this provision, FDA considers the following questions in deciding whether to grant a barrier-to-innovation waiver:

- Is the product or other products or technologies under development by the applicant innovative?

- Would the fee(s) be a ***significant barrier*** to the applicant's ability to develop, manufacture, or market innovative products or to pursue innovative technology?

To qualify for a waiver or reduction in user fees under this provision, an applicant should address both questions.

1. *Is the product innovative or is the company pursuing other innovative drug products or technologies?*

A product that has been approved for marketing in the United States is not automatically deemed to be innovative for user fee purposes. In evaluating requests for barrier-to-innovation user fee waivers or reductions, the Agency generally intends to consider the following questions:

- Does the drug product or technology demonstrate advanced "breakthrough" research, new, progressive methods, and/or forward thinking in the treatment or diagnosis of disease, or does it have the potential to be at the forefront of new medical technology?

- Are there other treatment alternatives available? The existence of comparable alternatives would weigh against a determination that a product is innovative.

- Does the drug product or technology introduce a unique or superior method for diagnosing, curing, mitigating, treating, or preventing a disease, or for affecting a structure or function of the body?

- Has the drug product been designated as a priority drug, accepted into one of FDA's expedited programs for serious conditions,[18] granted fast track status,[19] or determined to be a new molecular entity?

- Does the applicant have an *active* investigational new drug application (IND) under which the applicant is evaluating a potentially unique or superior method for diagnosing, curing, mitigating, treating, or preventing a disease, or for affecting a structure or function of the body? To determine whether an applicant's IND would be considered *active*, the Agency may consider the following:

    - Is the applicant currently conducting a clinical trial for the investigational drug?[20]
    - Has the applicant recently participated in meetings and discussions with FDA about the IND progress?
    - Is the applicant actively developing the investigational drug? Does the applicant detail such development in its IND annual report?

- Has the applicant recently received a Federal grant for innovation? An example of a Federal grant program that may qualify as innovative is the National Institutes of Health's Small Business Innovative Research Program.

2. *Does the fee create a significant barrier to the applicant's ability to develop, manufacture, or market innovative products or to pursue innovative technology?*

To determine whether a fee would be a significant barrier to an applicant's ability to develop, manufacture, or market innovative products or to pursue innovative technology, the Agency considers the relationship between the current liabilities and financial resources of the applicant and its affiliates. The financial considerations are discussed below.

[18] Further information regarding priority drugs can be found in the guidance for industry, *Expedited Programs for Serious Conditions – Drugs and Biologics*, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm358301.pdf, and in CDER's MAPP 6020.3R, *Review Designation Policy: Priority (P) and Standard (S).* MAPP 6020.3R is available at https://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/manualofpoliciesprocedures/ucm082000.pdf.

[19] Further information regarding fast track status is available on the internet at https://www.fda.gov/forpatients/approvals/fast/ucm20041766.htm.

[20] FDA may use any available information, including but not limited to ClinicalTrials.gov, to determine whether the applicant is currently conducting a clinical trial.

C. Financial Considerations for Public Health and Barrier-to-Innovation Waivers and Reductions

1. Financial Resources of the Applicant and Affiliates

When evaluating requests for waivers or reductions in user fees under the public health or barrier-to-innovation provisions, the Agency considers the financial resources of the applicant and its affiliates.

Section 736(d)(2) of the FD&C Act states that, in determining whether to grant a waiver or reduction in a user fee, FDA shall consider only the circumstances and financial resources of the applicant and any affiliate of the applicant. Under the FD&C Act, the applicant is the person[21] who is responsible for payment of the fees and the person who must qualify for a waiver or reduction in user fees.[22] Accordingly, the statute does not allow persons other than those legally subject to user fees, such as a distributor that is not an affiliate, to qualify for or receive waivers or reductions of user fees.

2. Consideration of Limited Financial Resources

The limited financial resources of an applicant and its affiliates are an important indicator of whether user fees are a barrier to innovation or a waiver or reduction is necessary to protect the public health. Based on over 25 years of experience in implementing the user fee program, FDA has determined that most applicants that, including the resources of its affiliates, have financial resources of less than $20 million of working capital are those least able to pay the fees. Therefore, the Agency generally intends to use $20 million as its marker for evaluating whether an applicant and its affiliates have limited resources such that a waiver or reduction is *necessary* to protect the public health and whether the fees are a *significant barrier* to innovation. An applicant with $20 million or more in financial resources, including the financial resources of affiliates, generally will not be considered to have limited resources for user fee purposes.

FDA generally intends to consider the working capital of an applicant and its affiliates to determine whether the applicant has limited financial resources. Working capital is an objective measure of the resources available to the applicant and is defined by generally accepted accounting principles. To calculate working capital, FDA intends to review current assets and current liabilities of applicants and their affiliates to determine if an applicant has limited financial resources. Net proceeds that increase the cash flow of an applicant and affiliates are also an important factor in determining whether the applicant and its affiliates have limited financial resources. FDA recommends that applicants provide financial information according to the fiscal year, which begins October 1 and ends September 30. If an applicant's financial records are not organized by the U.S. government's fiscal year, an applicant may submit financial information from the 12 months preceding the date of the waiver request. Section VI.C. provides more information on the type of documentation applicants may submit to support its assertions of its limited resources.

[21] Under section 735(9) of the FD&C Act, *person* includes an affiliate thereof.

[22] See sections 736(a)(1), 736(a) (2), and 736(d) of the FD&C Act.

FDA does not intend to deduct marketing costs when calculating an applicant's working capital. Because even a very large applicant may have operating losses, FDA does not intend to consider lack of profitability as evidence of limited resources. The Agency also does not intend to consider product sales figures to be evidence of limited resources, because even a large and profitable company can have low sales figures for an individual product, but not need a waiver to continue an activity that is necessary to protect the public health or because the fees would present a significant barrier to innovation.

FDA considers the financial resources of applicants that are State or Federal government entities differently. The Agency generally intends to consider State or Federal government entities with less than $20 million in total annual revenues ***from the sale of drugs*** to have limited resources for user fee purposes. A government entity is able to devote only a small amount of money to drug development activities relative to the entity's budget and the total State or Federal budget. In addition, government entities generally receive only a small amount of revenue from commercial distribution of a drug, as compared with total revenues. FDA believes that Congress intended to minimize the burden on State and Federal government entities by focusing attention on their drug development revenues, not the overall revenues of the entity or the State or Federal government.[23] Section V.B. provides information on exemptions from application and program fees for State or Federal government entities that do not distribute commercially.

D. Small Business

Under section 736(d)(1)(C) of the FD&C Act, an applicant is eligible for a waiver of the ***application fee*** if the applicant is a small business submitting its first human drug application to the Agency for review and does not have another product approved under a human drug application and introduced or delivered for introduction into interstate commerce.[24]

To qualify for a small business waiver of the application fee, an applicant must:

- Employ fewer than 500 employees, including employees of affiliates;[25]
- Not have a drug product that has been approved under a human drug application and introduced or delivered for introduction into interstate commerce;[26] and
- Be submitting its first human drug application, including its affiliates. [27]

[23] For example, the FD&C Act exempts a State or Federal government entity from application and program fees for a drug product that is not distributed commercially. Sections 735(1) and (3) of the FD&C Act.

[24] There is no specific provision in the FD&C Act for a waiver or reduction of program fees for small businesses. However, small businesses may apply for a waiver or reduction of program fees through the public health or barrier-to-innovation waiver provisions. See discussions in sections IV.A-IV.C above.

[25] Section 736(d)(3)(A) of the FD&C Act.

[26] Id.

[27] Section 736(d)(1)(C) of the FD&C Act.

1. Small Business Waiver and Refund Requests

To qualify for a small business waiver of the application fee, an applicant should submit to FDA Form FDA 3971, attached as Appendix 1. If an applicant submitted an NDA or BLA with a payment and would like to request a small business waiver and refund, the applicant should submit Form FDA 3971 to request the refund within 180 calendar days of when the application fee is due. Section VI.C provides further information about Form FDA 3971 and the waiver request process.

FDA recognizes that some information provided by companies may be confidential. FDA will treat confidential commercial or financial information consistent with applicable federal laws and regulations (see section IX).

2. Expiration Date of the Small Business Waiver

If a small business waiver is granted, the applicant should submit its human drug application within 1 year after the date of the small business determination since circumstances supporting a small business waiver can change rapidly. For example, an applicant could merge with a larger company and therefore no longer be considered a small business. Similarly, an applicant could purchase an NDA from an unaffiliated company and, therefore, would have a drug product that has been approved under a human drug application and introduced into or delivered for introduction into interstate commerce.

If an applicant is granted a small business waiver and is unable to submit the application within 1 year of the determination, the applicant should request a new small business waiver by following the instructions provided in section VI.C. The Agency generally intends to examine the newly submitted information to confirm that the applicant is still eligible for a small business waiver.

3. Small Business Waivers of Application Fees for Future Human Drug Applications

After an applicant or its affiliate is granted a small business waiver and submits its first human drug application, the applicant cannot receive another small business waiver. That means that the applicant or its affiliate is not eligible to receive a small business waiver for any subsequent human drug application, even if the first application is withdrawn or refused for filing.[28] An applicant that received a small business waiver for an application that was later refused for filing or withdrawn, however, may renew its request for a small business waiver if the applicant resubmits the same application.

If an applicant does not submit the application for which it was granted a small business waiver, the applicant may qualify again for a small business waiver.

[28] Section 736(d)(3)(B) of the FD&C Act.

V. EXEMPTIONS AND REFUNDS

A. Orphan Designated Products

1. Application Fees

Under section 736(a)(1)(F) of the FD&C Act, a human drug application for a product that has been designated as a drug for a rare disease or condition (referred to as an orphan drug) under section 526 of the FD&C Act is not subject to an application fee unless the human drug application includes an indication for other than a rare disease or condition.

If an application qualifies for an orphan exemption, the applicant does not need to send FDA a written request. The applicant should simply notify FDA that it is claiming the orphan exemption when it completes and submits the User Fee Cover Sheet, Form FDA 3397.[29] The User Fee Cover Sheet should be included with the application, and a brief statement claiming the orphan exception should be included in the cover letter. ***If the applicant paid the application fee in advance of receiving the orphan drug designation, the applicant must submit a written request for a refund no later than 180 calendar days after such fee is due.***[30] For an applicant who paid the application fee in advance and has not yet received an orphan drug designation, FDA recommends that the applicant request a refund in the cover letter at the time the applicant submits the application, in anticipation of receiving orphan drug designation. If orphan designation is granted more than 180 calendar days after the application is submitted, the applicant will not be eligible for a refund at that time *unless* it submitted a refund request within 180 calendar days of submitting the application. Section VI provides further information about refund requests.

2. Program Fees

Under section 736(k) of the FD&C Act, a drug product 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 section 351 of the PHS Act is exempt from the program fee if it meets the public health requirements contained in the FD&C Act as such requirements are applied to requests for waivers of the program fee. In addition, the applicant must have less than $50 million in gross worldwide revenue during the year preceding the request for exemption.[31]

An applicant seeking to avail itself of this exemption should submit a certification that its gross worldwide revenues, including affiliates, did not exceed $50 million for the 12 months before the request.[32] The applicant should also submit financial documentation that supports the certification, such as financial statements that show intangible assets, other income, net gain on financial assets, foreign exchange gains, and interest income.

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[29] For more information about completion and submission of the User Fee Cover Sheets, see http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm119184.htm.

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

[31] Section 736(k)(1)(B) of the FD&C Act.

[32] Section 736(k)(2) of the FD&C Act.

Upon review of an applicant's certification and accompanying information, FDA may contact the applicant to request further information, if needed, and for clarification of the information asserted in the applicant's certification. FDA may request information about the applicant and its affiliates, such as financial statements, annual reports, and documents identifying affiliate relationships. If such information is not provided, FDA may not be able to verify an applicant's certification and therefore may deny the orphan drug exemption request. Section VI provides information about how to submit a request for an exemption or refund of the program fee.

B. State or Federal Government Entity

An application submitted by a State or Federal government entity for a drug that is ***not distributed commercially*** is not considered a "human drug application" under section 735(1) of the FD&C Act. If the application is not considered a human drug application, then application fees are not assessed and the program fee does not apply.

For the purposes of the State and Federal exemption from user fees under the FD&C Act, FDA interprets ***distributed commercially*** means any distribution in exchange for financial reimbursement, goods, or services, whether or not the amount of the charge covers the full costs associated with the product. Under FDA's interpretations, any recovery by the applicant of all or part of the costs of manufacture or distribution of a product would make the distribution commercial.

C. No Substantial Work

Under section 736(a)(1)(G) of the FD&C Act, if an application is withdrawn after the application is filed, FDA 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 sole discretion in determining whether any portion of the fee may be refunded. A determination concerning a refund under this section is not reviewable.[33]

VI. SUBMITTING REQUESTS FOR WAIVERS, REDUCTIONS, AND REFUNDS

A. Timing of Requests

1. Deadline to Request a Waiver, Reduction, or Refund

Under section 736(i) of the FD&C Act, to qualify for a waiver or reduction in user fees as well as a refund for a fee paid, an applicant must submit to FDA a written request for a user fee waiver, reduction or refund no later than 180 calendar days after the fee is due.

[33] Section 736(a)(1)(G) of the FD&C Act.

For example, if an applicant receives a program fee invoice from FDA, FDA expects the invoice to be paid by the due date. The applicant can then submit a written request for a waiver, reduction, or refund of the fee(s) within 180 calendar days from the date when the invoice is due. If the request is submitted within 180 calendar days of the due date (i.e., if the request is timely), FDA will evaluate the applicant's request. If FDA determines that the applicant qualifies for a waiver, reduction, or refund, the Agency will grant the applicant's request.

To avoid having to pay a fee, an applicant can submit a request for a waiver or reduction in advance of when the program fee invoice is due to be paid, or in advance of submitting an application (see sections VI.A.3 and 4 below).

If the applicant submits a waiver or exemption request and pays the relevant fee before receiving a determination from FDA on the waiver or exemption, the applicant should submit a refund request not later than 180 calendar days after such fee is due in order to qualify for a refund.

2. Consequences for Failure to Pay User Fees Due to Waiver or Reduction Delays

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. 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.

3. Recommended Time Frame to Submit a Request for a Waiver or Reduction of the Application Fee

FDA encourages applicants to submit a request for a waiver or reduction in an application fee approximately 3-4 months before submission of the application. Under normal circumstances and depending on available resources, FDA will try to make its determination on the waiver request before the application is submitted upon which the fee is due.

FDA discourages applicants from submitting application fee waiver or reduction requests more than 4 months before the submission of an application because the circumstances that support an applicant's request are subject to change. FDA considers it unreasonable to assume that those circumstances will continue to exist for longer than 4 months before the submission of an application.

4. Recommended Time Frame to Submit a Request for a Waiver or Reduction of the Program Fee

The time frame to submit a request for a waiver or reduction of the program fee is the same as for an advance request for an application fee waiver or reduction: an applicant seeking a waiver

or reduction of the program fee should generally submit a request for a waiver or reduction 3 to 4 months before the fee is due. Annual program fees are due on October 1, or the first business day after the enactment of the appropriations act providing for the collection and obligation of PDUFA fees for that fiscal year, whichever occurs later.[34] Thus, an applicant that wishes to obtain a waiver or reduction in advance should submit its request between June 1 and July 1. Under normal circumstances and depending on available resources, FDA will try to complete its evaluation of the request before the due date of the program fee.

The FD&C Act does not provide for deferral of user fees, and FDA does not grant deferrals of user fees based on pending waiver or reduction requests. FDA therefore expects that all program fees will be paid without regard to a pending request for a fee waiver or reduction. This approach ensures that the steady funding stream Congress intended will be achieved, and should deter the filing of frivolous waiver or reduction requests.

Ordinarily, FDA expects to grant a reduction or waiver of a program fee only for the current year. If an applicant wishes to have a program fee waived or reduced for assessments in future years, it should make a new request for a waiver or reduction each year.

B. Content and Format of Requests, Excluding Small Business Waiver Requests

1. General Information

Requests for CDER and CBER user fee waivers, reductions, and refunds will be reviewed and granted or denied by the Division of User Fee Management and Budget Formulation within CDER. However, reduction and refund requests for biological products regulated by CBER will be reviewed and granted or denied by CBER's Center Director.

FDA recommends that each waiver or reduction request be submitted in writing and that it contain the following information:

- Name of applicant requesting the waiver, including company name, address, contact, telephone number, and e-mail address
- If an agent is submitting the request on behalf of an applicant, authorization from the applicant for the agent to act on the applicant's behalf
- Application number, i.e. NDA, BLA, or IND
- Trade and established names of product(s) covered by the waiver request
- Identification of the specific fee(s) for which the waiver, refund, or reduction is requested

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

- Date on which the user fee payment was made or will be made for which a waiver or reduction is requested

- Statutory provision under which a waiver or reduction is requested

- Information and analyses demonstrating eligibility for the waiver or reduction

- Rationale for why the waiver, reduction or refund request should be granted

- A list of the applicant's affiliates[35]

- For public health and barrier to innovation waivers, a current annual financial report for the applicant and the applicant's affiliates. If a current annual financial report is not available, a report that includes total cash and cash equivalents, accounts receivables, inventories, short and long-term investment marketable securities, deferred revenue, prepaid expenses and any other net proceeds received during the fiscal year that will increase the applicant's and its affiliates' cash flow even if not recorded under current assets

- For requests for an orphan drug exemption to the program fee, a certification that its gross worldwide revenues, including affiliates, did not exceed $50 million for the 12 months before the request and financial documentation that supports the certification, such as financial statements that show intangible assets, other income, net gain on financial assets, foreign exchange gains, interest income, and net proceeds

2. Additional Specific Information for Application Fee Waiver or Reduction Requests

In addition to the general information specified above, requests for waivers or reductions in **application fees** should include the following:

- Date the application was or is intended to be submitted

- Whether clinical data are expected to be required for approval

3. Additional Specific Information Requested for Program Fee Waiver or Reduction Requests

In addition to the general information specified above, requests for waivers or reductions in the **program fee** should include the following:

[35] When determining whether parties are affiliated, the critical factor is whether one party controls or has the power to control another entity, or if a third party has the power to control both entities. In such cases, FDA recommends that the applicant submit any agreements between an applicant and the other entities that demonstrate the nature of the relationship the applicant has with the entity.

- Name of the application holder, if different from the name of the applicant requesting the waiver

- Specific strength, dosage form, and route of administration

- Invoice date and number (or copy of the invoice)

C. Content and Format of Request for a Small Business Waiver

To qualify for a small business waiver of the application fee, an entity must submit to FDA a written request for such a waiver and a certification that the entity meets the requirements for the waiver. Applicants should submit requests for a small business waiver of the application fee and refund due to the small business waiver via Form FDA 3971, attached as Appendix 1. The completed form should be submitted via email to CDERCollections@fda.hhs.gov with the subject line, Small Business Waiver Request – [Applicant Name].

Upon receipt of Form FDA 3971, FDA may contact the applicant to request additional information and clarification of the information supporting the assertions in Form FDA 3971. Examples of information that may be requested include, but are not limited to the following:

- A copy of the applicant's Articles of Incorporation and Bylaws;

- The applicant's last annual statement to shareholders; and

- A breakdown of the number of persons employed full time, part time, temporarily, or otherwise by the applicant and affiliates during each of the pay periods for the 12 months preceding the company's certification.

Occasionally, FDA finds entities to be affiliated with the applicant that the applicant did not identify as one of its affiliates in its initial waiver or exemption submission. When determining whether parties are affiliated for purposes of user fee assessment under PDUFA, the critical factor is whether one party controls or has the power to control another entity, or if a third party has the power to control both entities.[36] In such cases, FDA recommends that the applicant submit copies of any agreements between an applicant and the other entities that demonstrate the nature of the relationship the applicant has with the entity. If the requested supporting documentation is not submitted, FDA may deny the small business waiver request because there is insufficient evidence that the applicant meets the requirements in section 736(d)(1)(C) of the FD&C Act.

Once FDA has identified and confirmed which entities are properly considered affiliates of the applicant and determined whether the applicant qualifies as a small business, it will evaluate whether the applicant is eligible for the small business waiver. Specifically, FDA determines whether the applicant or any of its affiliates has previously submitted a human drug application,

[36] See section 735(11) of the FD&C Act.

and whether the applicant has a drug product that has been approved under a human drug application and introduced or delivered for introduction into interstate commerce. After FDA assesses the applicant's eligibility for a small business waiver FDA will notify the applicant whether the waiver is granted.

D. Refund Requests

To qualify for an application or program fee refund, an applicant must submit to FDA a written request for a refund not later than 180 calendar days from the date the fee is due.[37] Applicants may submit their written request for an application fee refund in the submission cover letter of their application. A copy of the cover letter or program fee refund request (for both CBER and CDER products) should be submitted via email to CDERCollections@fda.hhs.gov.

Alternatively, an applicant may 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.

VII. FDA RESPONSES TO REQUESTS FOR WAIVERS, REDUCTIONS, AND REFUNDS

FDA will review waiver, refund and reduction requests, consulting with relevant Agency officials as appropriate. If needed to support applicants' assertions that the applicant qualifies, FDA may request additional information and documentation from the applicant during its review of a waiver, reduction, or refund request. Failure to provide the requested information or documentation may result in a denial of a waiver, reduction, or refund. The Agency will respond to all such requests in a timely fashion based on available resources and collection time for additional information.

VIII. APPEALS PROCESS

A. 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, refund, or reduction of user fees.

FDA recommends that requests for reconsideration state the applicant's reasons for believing that the 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.

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

All requests for reconsideration (for both CBER and CDER regulated products) should be submitted via email to CDERCollections@fda.hhs.gov and should be addressed to the Division of User Fee Management and Budget Formulation, Attention: Division Director, Center for Drug Evaluation and Research.

Alternatively, an applicant may 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.

B. 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 waiver request
- The denial of the original waiver request
- The reconsideration request
- The denial of the reconsideration request
- A statement of the applicant's belief that the prior conclusions were in error.

No new information or new analyses should be presented in the appeal request. If new information and/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 official to consider the new information or analyses.

All requests for appeals (for both CBER and CDER 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.[38] 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

[38] See https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ContactCDER/ucm444092.htm.

applicant's request; for CBER regulated products, the Director of CBER will issue a written decision on the applicant's request.

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 Center 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 Center's management levels and remains unsatisfied with the decision, 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 FDA's Ombudsman, with copies provided to the Center that denied the appeal. Review of such matters by the Commissioner is discretionary.[39]

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 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 copies provided to the Center that denied the appeal. Review of such matters by the Commissioner is discretionary.

IX. DISCLOSURE OF PUBLIC INFORMATION

FDA may disclose information publicly about its actions granting or denying waivers, refunds and reductions. This disclosure will be consistent with the laws and regulations governing the disclosure of confidential commercial or financial information.

X. PAPERWORK REDUCTION ACT OF 1995

This guidance contains information collection provisions that are subject to review and approval by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). "Collection of information" is defined in 44 U.S.C. 3502(3) and 5 C.F.R. 1320.3(c) and includes Agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. The guidance refers to the following forms: (1) Form FDA 3397 and (2) Form FDA 3971.

The information collections of this draft guidance have been submitted for OMB renewal of approval under OMB control number 0910-0693.

[39] See 40 FR 40682, 40693 (Sep. 3, 1975).

Collection of information for completing and submitting Form FDA 3397 (Prescription Drug User Fee Cover Sheet) is previously approved under OMB control number 0910-0297. Collections of information associated with the submission of a new drug application or biologics license application are approved under OMB control numbers 0910-0001 and 0910-0338, respectively.

The time required to complete the information collections included in this guidance are estimated to average 16 hours for a request for a waiver, reduction, refund, or exemption of certain user fees; 24 hours per response for a reconsideration of a request; and 12 hours for an appeal of a waiver, reduction, or refund decision. These estimates include the time to review instructions, gather the data needed, and complete and review the information collection.

Form FDA 3971 is the collection of information submitted when requesting the small business waiver. Use of form FDA 3971 does not change the burden previously approved under OMB control number 0910-0693 for submitting or evaluating small business waivers. It facilitates the presentation of the information required for evaluation of the small business waiver with the use of a standardized form and an electronic fillable format.

Send any comments regarding the burden estimate or suggestions for reducing this burden to the following:

Department of Health and Human Services
Food and Drug Administration
Office of Operations
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Prescription Drug and Biosimilar User Fee Acts

Small Business Waiver and Refund Request

Form Approved: OMB No. 0910-0693
Expiration Date: October 31, 2020
See PRA Statement on last page.

Section I: Applicant Information

1. Applicant Name

Former Names *(if applicable)*

2. Telephone Number *(Including area and country codes)*

3. Fax Number *(Including area and country codes)*

4. Address *(No P.O. boxes allowed)*

Address 1 *(Street address)*

Address 2 *(Apartment, suite, unit, building, floor, etc.)*

City

State/Province/Region

Country

ZIP or Postal Code

5. Federal Tax ID Number *(Required for all U.S. applicants)*

6. DUNS Number

7. Number of Employees

8. User Fee Program for which the action is requested *(Select one)*

☐ PDUFA ☐ BsUFA

9. Human Drug/Biosimilar Biological Product Applications (Applicant)

Product Name

Application Number

Submission Date

Application Status *(Select from drop-down list)*

Is this the first application the Applicant has submitted to the FDA for review? ☐ Yes ☐ No

10. Human Drug/Biosimilar Biological Products (Applicant)

Does the Applicant have drug products approved under a human drug or biosimilar biological product application by the FDA that have been introduced or delivered for introduction into interstate commerce? ☐ Yes ☐ No

11. Small Business Waiver (Applicant)

Has the Applicant previously received a Small Business Waiver for a human drug or biosimilar biological product? *(See instructions for details.)* ☐ Yes ☐ No

Section II: Affiliate Information *(Enter information for each entity affiliated with the Applicant)*

Provide information for each of the Applicant's domestic and foreign affiliates. For multiple affiliates, click the "Add Affiliate" button for each additional entry. Refer to Instructions, Section II for additional information.

The Applicant does NOT have any Affiliates *(Check if applicable)***:** ☐

12. Affiliate Name

13. Affiliate Address *(No P.O. boxes allowed)*			14. DUNS Number
Address 1 *(Street address)*			15. Number of Employees
Address 2 *(Apartment, suite, unit, building, floor, etc.)*			
City	State/Province/Region		
Country		ZIP or Postal Code	

16. Name of Affiliate's Point of Contact	17. E-mail Address	18. Telephone Number

19. Small Business Waiver (Affiliate)

Has the Affiliate previously received a Small Business Waiver for a human drug or biosimilar biological product application? *(See instructions for details.)* ☐ Yes ☐ No

20. Human Drug/Biosimilar Biological Product Applications (Affiliate)

Has the Affiliate ever submitted a human drug or biosimilar biological product application? ☐ Yes ☐ No

Click for an additional set of Section II affiliate entries (includes items 12 through 20). May be repeated. Add Affiliate

Section III: Refund

21. Did the Applicant pay a fee for this application for _____ prior to requesting this Small Business Waiver?
Product Name

☐ Yes ☐ No

NDA or BLA Number	Payment Amount	PIN/Invoice Number	Payment Reference Number	Refund Amount Requested

Section IV: Certification

Review, sign, and date the following certification statement:

I CERTIFY THAT _____
Applicant Name (must be identical to item 1)

BSUFA:

i Has fewer than 500 employees, including employees of Affiliates;

ii. Does not have a drug product that has been approved under a human drug application or biosimilar biological product application by the FDA and introduced or delivered for introduction into interstate commerce;

iii. Requests a Small Business Waiver for the first biosimilar biological product application that the Applicant or its Affiliate has submitted.

PDUFA:

i Has fewer than 500 employees, including employees of Affiliates;

ii. Does not have a drug product that has been approved under a human drug application by the FDA and introduced or delivered for introduction into interstate commerce;

iii. Requests a Small Business Waiver for the first human drug application that the Applicant or its Affiliate has submitted.

I further certify that, to the best of my knowledge, the information I have provided in this form is complete, accurate and has been verified. I understand that submission of a false certification may subject me to criminal penalties under 18 U.S.C. § 1001 and other applicable federal statutes.

22. Name of Applicant's Responsible Official	23. Title
24. Telephone Number	25. Email Address

26. Responsible Official's Address		
Address 1 *(Street address)*		
Address 2 *(Apartment, suite, unit, building, floor, etc.)*		
City	State/Province/Region	
Country	ZIP or Postal Code	

27. Signature	28. Date *(mm/dd/yyyy)*
To enable the signature field, please fill out all prior required fields. For a list of required fields which have not yet been filled out, please click here.	

Send Completed Form FDA 3971 to FDA via

Email (preferred): *CDERCollections@FDA.HHS.GOV* **or** **Physical Mail:** Division of User Fee Management and Budget Formulation
Food and Drug
Administration 10001 New
Hampshire Ave. Silver
Spring, MD 20993-0002

FDA Use Only

Date Received: _____ ☐ **Approved** ☐ **Denied**

Privacy Act Notice: This notice is provided pursuant to the Privacy Act of 1974, 5 U.S.C. § 552a. The collection of this information is authorized by 21 U.S.C. § 379h and 21 U.S.C. § 379j-52. FDA will use the information to assess, collect and process user fee payments, and, facilitate debt collection under the Debt Collection Improvement Act. FDA may disclose information to courts and the Department of Justice in the context of litigation and requests for legal advice; to other Federal agencies in response to subpoenas issued by such agencies; to HHS and FDA employees and contractors to perform user fee services; to the National Archives and Records Administration and General Services Administration for records management inspections; to the Department of Homeland Security and other Federal agencies and contractors in order to respond to system breaches; to banks in order to process payment made by credit card; to Dun and Bradstreet to validate submitter contact information, and to other entities as permitted under the Debt Collection Improvement Act.

Furnishing the requested information is mandatory unless otherwise indicated. Failure to supply the information could prevent FDA from processing user fee payments and waivers. Additional detail regarding FDA's use of information is available online: Privacy Act and Website Policies.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 40 minutes per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Operations
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."