Guidance for Industry

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

DRAFT GUIDANCE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)

March 2011
User Fees
Revision 1

Guidance for Industry

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Contains Nonbinding Recommendations

Draft – Not for Implementation

Guidance for Industry[1]
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This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. 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 Act) for drugs, including biological drug products. This guidance is a revision of the draft guidance entitled *Draft Interim Guidance Document for Waivers of and Reductions in User Fees* (1993 interim guidance), issued July 16, 1993.

This revised guidance describes (1) the types of waivers, refunds, and reductions available under the user fee provisions of the Act and (2) the procedures for requesting waivers, refunds, or reductions, and reconsiderations and appeals of FDA decisions on such requests. The revised guidance also provides clarification on related issues such as user fee exemptions for orphan drugs.

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

II. BACKGROUND

The Prescription Drug User Fee Act of 1992 (PDUFA I) authorized FDA to assess user fees for 5 years in conjunction with the review of human drug applications. This authorization to assess user fees was for fiscal years (FY) 1993 through FY 1997. PDUFA has been reauthorized three times. The Food and Drug Administration Modernization Act of 1997 reauthorized the user fee provisions for 5 years, beginning in FY 1998 (PDUFA II). The Prescription Drug User Fee

[1] This guidance has been prepared by the Office of Regulatory Policy (ORP), Center for Drug Evaluation and Research (CDER), in consultation with the Center for Biologics Evaluation and Research.

Amendments of 2002 reauthorized the user fee program for another 5 years, beginning in FY 2003 (PDUFA III), and the Food and Drug Administration Amendments Act of 2007 reauthorized the user fee program for another 5 years beginning in FY 2008 (PDUFA IV). The statute is up for reauthorization again in FY 2012.

The Act authorizes FDA to assess application fees for certain human drug and biological product applications or supplements when those applications or supplements are submitted. In addition, FDA can assess annual product fees for certain approved drug and biological products, and annual establishment fees for the facilities in which those products are made in final dosage form.[2]

Because of the way the program is structured in the 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, product, and establishment) is determined based on historical data of how many applications, products, and establishments were assessed fees in the previous fiscal year. Therefore, the more waivers or reductions are granted, the more fees must be increased the following year for applications, products, and establishments subject to fees to meet the annual statutory revenue targets. [3]

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).

- The term ***application*** includes both NDAs and BLAs.

[2] Information on product, establishment, and application fees, including fee rates, PDUFA goals, and other various user fee related issues can be found on FDA's PDUFA Internet site: http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/default.htm.

[3] Under the Act, FDA sets user fee target revenue each year. For example, if the FDA is to collect $600 million in a fiscal year, the $600 million is divided by 3 and each category, applications, products, and establishments would be expected to provide $200 million. FDA divides the target revenue in each category by the number of applications, products, or establishments it expects to assess fees to determine the fee for each individual application, product, or establishment. The more product fees FDA waives, the higher the product fee is in the subsequent fiscal year. For example, using the target revenue of $200 million, if we assessed fees for 2500 products for fiscal year A, the fee would be $80,000 per product. If FDA waived fees for 100 products, we would expect 2400 products to be assessed fees in the subsequent fiscal year, and the fee amount per product would increase ($200 million divided by 2400 = $83,333 per product). As a result, more companies might request waivers because of higher fee assessments.

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

181
182 • The term ***drug*** includes drug and biologic products.
183
184 • The term ***final dosage form*** means, with respect to a prescription drug product, a
185 finished dosage form which is approved for administration to a patient without substantial
186 further manufacturing.[5] Substantial further manufacturing does not include packaging.[6]
187 FDA generally considers a product to be in final dosage form unless one or more of the
188 following operations is required but has yet to be performed: mixing, granulating,
189 milling, molding, lyophilizing, tableting, encapsulating, coating, sterilizing, and filling
190 sterile, aerosol, or gaseous drugs into dispensing containers.
191
192 • The term ***human drug application*** means an application for (1) approval of a new
193 drug submitted under section 505(b) of the Act or (2) licensure of a biological drug
194 product under section 351 of the Public Health Service Act (PHS Act).[7] For purposes of
195 this guidance, the term ***human drug application*** does not include the following:
196
197 - A supplement to such an application
198 - An application with respect to whole blood or a blood component for transfusion
199 - An application with respect to a bovine blood product for topical application licensed
200 before September 1, 1992
201 - An application for an allergenic extract product
202 - An application for a device licensed under section 351 of the Public Health Service
203 Act
204 - An application with respect to a large volume parenteral drug product approved
205 before September 1, 1992
206 - An application for a licensure of a biological product for further manufacturing use
207 only
208 - An application submitted by a State or Federal Government entity for a drug that is
209 not distributed commercially.[8]
210
211 • The term ***person*** means the person subject to fees and includes any affiliates of that
212 person.[9] The term ***person*** includes an individual, partnership, corporation, and
213 association.[10] This document will also use the term ***person*** when referring to an
214 applicant.
215
216 • The term ***supplement*** means a request to the Secretary to approve a change in a
217 human drug application which has been approved.[11]
218

36[5] Section 735(4) of the Act.
37[6] *See* section 735(5) of the Act.
38[7] Section 735(1) of the Act.
39[8] Id.
40[9] Section 735(9) of the Act.
41[10] Section 201(e) of the Act.
42[11] Section 735(2) of the Act.

- The term ***financial resources*** means the total gross annual worldwide revenues and other available financial assets of an applicant and its affiliates.

IV. TYPES OF WAIVERS AND REDUCTIONS

According to section 736(d) of the Act, FDA will grant a waiver of or reduction in one or more user fees assessed under section 736(a) of the Act where it finds that an applicant meets the eligibility criteria under one of the following provisions:

- 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.[12]
- The applicant is a small business submitting its first human drug application to the Secretary for review.

The Act also provides for waiver or reduction of user fees if the fees would exceed the anticipated present and future costs incurred by the Secretary in conducting the process for the review of human drug applications for the person. Fees-exceed-the-costs waivers and reductions are not addressed in this guidance document.[13]

A. Public Health

Under section 736(d)(1)(A) of the Act, an applicant may qualify for a waiver of or reduction in application, product, and/or establishment fees if the waiver or reduction is necessary to protect the public health. Under this provision, FDA may grant a public health waiver of or reduction in user fees if the Agency finds that the following two criteria are met:

- The product protects the public health; and
- The applicant shows that a waiver or reduction is ***necessary*** to continue an activity that protects the public health.

[12] There are two additional special circumstances that may affect eligibility for waivers or reductions under the barrier to innovation waiver provision. Each is addressed in a separate waiver guidance. Specifically, for companies participating in the President's Emergency Plan for AIDS Relief, see the guidance document, *User Fee Waivers for FDC and Co-Packaged HIV Drugs for PEPFAR.* For companies submitting combination products under 21 Code of Federal Regulations 3.2(e), see the guidance for industry and FDA staff on *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 http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

[13] There is a separate guidance document that discusses the Agency's current thinking on the fees-exceed-the-costs waiver provision. For more information, see the guidance document, *Fees-Exceed-the-Costs Waivers Under the Prescription Drug User Fee Act*, and its addendum at the guidance web page.

To qualify for a waiver or reduction in user fees under this provision, an applicant must meet both criteria.

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 asks 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 treatment alternatives? The existence of alternatives would weigh against a determination that a product is necessary to protect the public health.

- Is the drug product designated as a priority drug,[14] has it been granted fast track status,[15] or has it been determined to be a new molecular entity? Affirmative answers to these questions usually indicate that a product protects the public health. Other questions the Agency may consider include:

    - 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 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 Act (i.e., does it have an orphan designation)?

[14] Further information regarding priority drugs can be found in the Center for Drug Evaluation and Research's (CDER's) Manual of Policies and Procedures (MAPP) 6020.3R, *Review Classification Policy: Priority (P) and Standard (S)*. MAPP 6020.3R is available on the Internet at http://www.fda.gov, search by MAPP number.

[15] Further information regarding fast track status can be found in CDER's guidance for industry on *Fast Track Development Programs — Designation, Development, and Application Review*.

- 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.[16]

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

To determine whether a waiver of or reduction in user fees is necessary to continue an activity that protects the public health, the Agency considers not only the benefit to the public health, but also whether the waiver or reduction is necessary. The legislative history of PDUFA I states 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.[17] It also expressly notes that FDA should consider the "limited resources" of the applicant when evaluating a request for a fee waiver or reduction under section 736(d).[18] Therefore, the Agency believes that a financial test is appropriate for the public health waiver provision. The Agency considers the relationship between the annualized cost of user fees and the financial resources of the applicant, including affiliates, requesting the waiver or reduction. The financial considerations are discussed in section IV.C below.

B. Barrier to Innovation

Under section 736(d)(1)(B) of the Act, an applicant may qualify for a waiver of or reduction in application, product, and/or establishment 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 may grant a waiver of or reduction in user fees if:

- The product or other products or technologies under development by the applicant are innovative; and
- The fee(s) would 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 must meet both criteria.

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 asks the following questions:

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

[17] House Report 102-895 (1992) at 17.

[18] Id.

- 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?

- 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?

- Is the drug product designated as a priority drug, has it been granted fast track status, or has it been 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 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 applicant recently received a Federal grant for innovation? Two examples of such Federal grant programs that may qualify as innovative are: (1) the National Institutes of Health's Small Business Innovative Research Program and (2) the National Institute of Standards and Technology's Advanced Technology 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 annualized cost of user fees and the gross annual revenues and financial resources of the applicant and its affiliates. The revenue considerations are discussed below.

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

1. Whose revenues are considered when evaluating a waiver or reduction request?

When evaluating requests for waivers of 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, regardless of who submits a request for a waiver or reduction of user fees.

Section 736(d)(2) of the Act states that, in determining whether to grant a waiver or reduction of a user fee, FDA shall consider only the circumstances and financial resources of the applicant and any affiliate of the applicant. Under the Act, the applicant is the ***person*** who is responsible for payment of the fees and the ***person*** who must qualify for a waiver or reduction of user fees. 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. How does the agency determine whether an applicant has 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.[19] FDA will consider the total annual revenue of an applicant and its affiliates in determining whether the applicant has limited financial resources. Total annual revenue is an objective measure of the resources available to the applicant and is defined by generally accepted accounting principles. FDA does not intend to deduct marketing costs, including expenses in foreign markets that are often incurred because of an applicant's marketing decisions, when calculating total annual revenue.

In addition to total annual revenue of the applicant and its affiliates, FDA considers other available financial assets, including net proceeds, cash, and total assets. FDA may also consider the results of recent issuances of stock and the recently available capital raised from the sales of shares in the applicant company.

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.

Ordinarily, beginning with fees assessed for FY 2011, the Agency expects to determine that an applicant with financial resources, including the financial resources of affiliates, of less than $20 million has limited resources for user fee purposes.[20] 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 considers the financial resources of applicants that are State or Federal government entities differently. The agency will consider State or Federal government entities with less than $20 million in total annual revenues ***from the sale of drug*** 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, if any, 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

[19] As noted above, the legislative history states that FDA should consider the "limited resources" of an applicant when evaluating a request for a fee waiver or reduction under section 736(d). *See* House Report 102-895 (1992) at 17. FDA therefore believes that a financial test is appropriate for both the public health and barrier-to-innovation waiver provisions.

[20] For waivers regarding fees for fiscal years prior to 2011, the agency intends to continue to use as its general marker of limited resources the $10 million benchmark cited in the 1993 interim guidance, adjusted for inflation.

on their drug development revenues, not the overall revenues of the entity or the State or Federal government.[21]

3. Why did FDA choose $20 million as a marker?

When the 1993 interim guidance was issued, the Agency used $10 million as a financial marker for evaluating whether a waiver or reduction was *necessary* to protect the public health and whether the fees were a *significant barrier* to innovation. Since 1993, the Agency has received several requests to adjust the $10 million financial marker for inflation. As stated in Section II, the more fee waivers and reductions FDA grants, the more the fees for other applications, products, and establishments must be increased to ensure that FDA obtains the total annual fee revenues specified in the Act. However, the Agency believes that the $10 million figure is outdated and should be adjusted. Based on almost 20 years of experience in implementing the user fee program, FDA has determined that most applicants that have annual revenues and financial resources of less than $20 million are those least able to pay the fees. Therefore, the Agency intends to use $20 million as its marker for evaluating whether an applicant and its affiliate have limited resources such that a waiver or reduction is *necessary* to protect the public health and/or whether the fees are a *significant barrier* to innovation.[22]

D. Small Business

Under section 736(d)(1)(D) of the 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. An applicant is eligible for a small business waiver when:

- The applicant employs fewer than 500 employees, including employees of affiliates;
- The applicant does not have a drug product that has been approved under a human drug application and introduced or delivered for introduction into interstate commerce; and
- The applicant, including its affiliates, is submitting its first human drug application.

To qualify for a small business waiver, an applicant must meet all of these criteria.

To determine the size of an applicant and its affiliates, the FDA works with the Small Business Administration (SBA). FDA asks the SBA to determine what companies are affiliates of the applicant and the total number of employees for the applicant and its affiliates. After receiving a request from the FDA, the SBA consults with the applicant and determines the number of

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

[22] If the $10 million benchmark in the 1993 guidance, which was written to be used under PDUFA I, were adjusted solely for inflation since the conclusion of the PDUFA I period in 1998, it would be less than $15 million in FY 2011 dollars, so this adjustment to $20 million would be expected to anticipate and eliminate the need for any further adjustments for inflation for at least the next 10 years.

employees the applicant and its affiliates have, based on SBA regulations. According to these regulations, SBA may contact the applicant to request the following information in the appropriate formats and detail:

- An application for size determination;
- A copy of the company's Articles of Incorporation and Bylaws;
- The company's last annual statement to shareholders; and
- A breakdown of the number of persons employed full time, part time, temporarily, or otherwise during each of the pay periods for the 12 months preceding the company's certification.

Companies should not submit the information requested by the SBA to FDA, nor should they submit this information to SBA until contacted. If the information is not submitted to the SBA, the request for a small business waiver will be denied.

The SBA recognizes, as does FDA, that some information provided by companies may be confidential. Both the SBA and FDA will treat confidential commercial or financial information consistent with applicable federal laws and regulations. See Section IX.

Once the SBA has identified and confirmed the affiliates of the applicant and determined whether the applicant qualifies as a small business, FDA will evaluate whether the applicant meets the other criteria for the small business waiver. Specifically, FDA searches its records to determine whether the applicant or its affiliates have previously submitted a human drug application or 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. If the waiver applicant meets all the criteria for a small business waiver, then FDA will notify the applicant that the waiver is granted.

1. Does a small business waiver have an expiration date?

If a small business waiver is granted, the applicant should submit its human drug application within 1 year after the date of the SBA determination. The reason for the 1 year timeframe is that the circumstances supporting a small business waiver may 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.

FDA understands that unforeseen circumstances may delay submission of an application. If an applicant is granted a small business waiver and is not able to submit the application within 1 year of the SBA determination, the applicant may ask FDA to extend the expiration date.

If an extension is requested, the Agency will examine its records and will work with SBA to confirm that the applicant still meets the criteria for a small business waiver. If the criteria are no longer met, the extension request will be denied.

2. Can a small business receive a waiver 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 or a supplement to an application.[23]

After an applicant or its affiliate is granted a small business waiver and submits its first human drug application, the applicant or affiliate is ineligible for another small business waiver even if the application is withdrawn or refused for filing. 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.

3. Can a small business receive a waiver or reduction of product and establishment fees?

There is no specific provision in the Act for a waiver or reduction of product and establishment fees for small businesses. However, small businesses may apply for a waiver or reduction of product and establishment fees through the public health or barrier-to-innovation waiver provisions. See discussions in sections IV.A, IV.B, and IV.C above.

V. EXEMPTIONS AND REFUNDS

A. Orphan Designated Products

1. Application Fees

Under section 736(a)(1)(F) of the 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 Act is not subject to an application fee unless the human drug application includes an indication for other than a rare disease or condition. A supplement proposing to include a new indication for a rare disease or condition in a human drug application shall not be subject to an application fee if the drug has been designated under section 526 as a drug for a rare disease or condition with regard to the indication proposed in the supplement.

If an application or supplement 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 Coversheet, Form FDA 3397.[24]

[23] Section 736(d)(4)(B) of the Act.

The User Fee Coversheet should be included with the application or supplement, and a brief statement claiming the orphan exception should be included in the cover letter.

2. Product and Establishment Fees

Under section 736(k) of the Act, a drug product designated under section 526 of the Act for a rare disease or condition and approved under section 505 of the Act or section 351 of the Public Health Service Act is exempt from the product and establishment fees if it meets the public health requirements contained in the Act as such requirements are applied to requests for waivers of product and establishment fees. In addition, the applicant must have less than $50 million in gross worldwide revenue during the year preceding the request for exemption. 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. See sections VI for information about how to submit a request for an exemption from product and establishment fees.

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 Act. If the application is not considered a human drug application, then application fees are not assessed and product and establishment fees do not apply.

For the purposes of the State and Federal exemption from user fees under the Act, ***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. Any recovery by the applicant of all or part of the costs of manufacture or distribution of a product makes the distribution commercial.

C. No Substantial Work

Under section 736(a)(1)(G) of the Act, if an application or supplement is withdrawn after the application or supplement is filed, FDA may refund the fee or a portion of the fee if no substantial work was performed on the application or supplement after the application or supplement was filed.

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

VI. SUBMITTING REQUESTS FOR WAIVERS, REDUCTIONS AND REFUNDS

A. Timing of Requests

1. Is there a statutorily mandated deadline for requesting a waiver or reduction?

Yes. Under section 736(i) of the Act, to qualify for a waiver of 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 or reduction no later than 180 calendar days after the fee is due.

For example, if an applicant receives a product and establishment fee invoice from FDA, we expect 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 days from the date when the invoice is due. If the request is submitted within 180 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 waiver or reduction in advance of when the product and establishment fee invoice is due to be paid, or in advance of submitting an application. See section VI.A.3 and 4 below.

2. Are there consequences if user fees are not paid because an applicant has not yet submitted a waiver or reduction request or because FDA has not yet responded to a waiver or reduction request?

Yes. According to section 736(e) of the Act, a human drug application or supplement submitted by a person subject to fees under section 736(a) is considered incomplete and will not be accepted for filing until all fees have been paid. That means that if the applicant submits an application or a supplement without the application fee or is in arrears for non-payment of an establishment or product fee, then the submission is incomplete and FDA will not review it. However, the review status of an application or supplement submitted before the invoice due date would not be affected (the review would continue and there would be no effect on the review goal date).[25]

*3. Is there a recommended time frame to submit a waiver or reduction request if an applicant wants to avoid paying the **application** fee and then seeking a refund?*

Yes. FDA encourages applicants to submit a request for a waiver of 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 and the fee is due.

[25] See CDER's MAPP 6050.1, *Refusal to Accept Application for Filing From Applicants in Arrears*.

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, and FDA considers it unreasonable to assume that those circumstances will continue to exist for longer than 4 months prior to the submission of an application. For example, if an applicant submits an application fee waiver request on July 1 and plans to submit its application on March 1 of the next year, FDA considers it unreasonable to assume that the facts stated on July 1 will remain the same 8 months later, in the following March. Therefore, FDA encourages sponsors to submit their waiver or reduction requests no more than 4 months prior to the submission of the application.

*4. Is there a recommended time frame to submit a waiver or reduction request if the applicant wants to avoid paying the **product and establishment fees** and then seeking a refund?*

Yes. The time frame is the same as for an advance request for an application fee waiver or reduction: an applicant seeking a waiver or reduction of product and establishment fees may submit a request for a waiver or reduction 3 to 4 months before the fee is due. Annual product and establishment fees are usually assessed in August and are due on October 1.[26] 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 product and establishment fees.

The 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 product and establishment fees will be paid without regard to a pending request for a fee waiver or reduction. This approach will ensure 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 product or establishment fee only for the current year. If an applicant wishes to have a product or establishment 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

1. General Information for All Requests

Requests for CDER and CBER user fee waivers, reductions, and refunds will be reviewed and granted or denied by CDER's Associate Director for Policy.[27] However, reductions and refunds for products regulated by CBER will be reviewed and granted or denied by CBER's Center Director.

[26] The fiscal year begins October 1 and ends September 30.

[27] Waivers and reductions under the fees-exceed-the-costs waiver provision are the responsibility of FDA's Office of Financial Management.

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,[28] including company name, address, contact, telephone and facsimile numbers, and e-mail address
- Identification of the specific fee(s) for which the waiver, refund, or reduction is requested
- Date on which payment was made or will be made of the fee for which a waiver or reduction is requested
- Statutory provision under which a waiver or reduction is requested
- Information and analyses showing that the criteria for the waiver or reduction have been met
- Rationale for why the waiver, reduction or refund request should be granted
- A list of the applicant's affiliates
- 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 annual revenues, net proceeds, cash, and total assets.

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

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

- NDA number (including supplement number and type if there is one) or BLA number
- Trade and established names of products covered by the waiver request
- Date the application was or will be submitted
- Whether or not clinical data are required for approval

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

[28] If an agent is submitting a waiver request on behalf of the waiver applicant, authorization from the waiver applicant for the agent to act on its behalf should also be included.

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

- NDA or BLA number
- Trade and established names of the product
- National Drug Code (NDC) number
- Name of the application holder
- Specific strength, dosage form, and route of administration
- Invoice date and number (or copy of the invoice sheet)

4. Additional Specific Information Requested for Establishment Fee Waiver and Reduction Requests

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

- Name of the establishment
- Address of the manufacturing site (not a business, office, or headquarters address, but the actual address of the manufacturing site)
- Establishment number as listed on the invoice
- Invoice date and number (or a copy of the invoice sheet)

C. Address for Submitting Requests

Original user fee waiver or reduction requests should be submitted in writing to:

Associate Director for Policy
Attention: User Fee Waiver Office, Michael D. Jones
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue
Bldg. 51, Room 6216
Silver Spring, MD 20993-0002

VII. FDA RESPONSES TO REQUESTS FOR WAIVERS AND REDUCTIONS

FDA will review the waiver or reduction request, consulting with relevant Agency officials as appropriate. FDA may request additional information from the applicant during the review period. The Agency will respond to requests for waivers and reductions in a timely fashion based on available resources and collection time for additional information.

VIII. RECONSIDERATIONS AND APPEALS

A. Reconsideration Request

If FDA fully or partially denies a request for a waiver or reduction of user fees, the applicant may request reconsideration of that decision. A request for reconsideration should be made within 30 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 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.

All requests for reconsiderations should be submitted in writing to:

Associate Director for Policy
Attention: User Fee Waiver Office, Michael D. Jones
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue
Bldg. 51, Room 6216
Silver Spring, MD 20993-0002

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 days of the issuance of FDA's decision to affirm its denial of a request for a waiver, 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

The appeal request should also contain particular references to information or analyses already submitted to the Agency that the applicant believes is relevant to its position. No new information should be presented in the appeal request.

All requests for appeals should be submitted in writing to:

Chief Scientist and Deputy Commissioner for Science and Public Health
User Fee Appeals Officer
Food and Drug Administration
c/o Matthew Warren
10903 New Hampshire Avenue
Bldg. 32, Room 4210
Silver Spring, MD 20993-0002Fax: 301-847-8617

A copy of the request for appeal should also be submitted to the CDER Associate Director for Policy as noted in section VIII above. After FDA reviews the information submitted in the appeal request, the Deputy Commissioner will issue a written decision on the applicant's request. The written decision issued by the Deputy Commissioner will constitute final Agency action on that request.

IX. DISCLOSURE OF PUBLIC INFORMATION

FDA plans to disclose to the public information about its actions granting or denying waivers and reductions. This disclosure will be consistent with the laws and regulations governing the disclosure of confidential commercial or financial information.