Assessing User Fees Under the Biosimilar User Fee Amendments of 2017

Guidance for Industry

DRAFT GUIDANCE

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For questions regarding this draft document, contact (CDER) Office of Communication, Division of Drug Information, Phone: 855-543-3784 or (CBER) Office of Communication, Outreach and Development, 800-835-4709-or 240-402-8010.

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)

November 2017
User Fees

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Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353; Email: druginfo@fda.hhs.gov
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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance provides stakeholders information regarding FDA's implementation of the Biosimilar User Fee Amendments of 2017 (BsUFA II) under Title IV of the FDA Reauthorization Act of 2017. Because BsUFA II created changes to the user fee program, this guidance serves to provide an explanation about the new fee structure and types of fees for which entities are responsible.

This guidance describes the types of user fees authorized by BsUFA II, the process for submitting payments to FDA, the consequences for failing to pay BsUFA fees, and the process for requesting a reconsideration of a user fee assessment. This guidance also describes how FDA determines which products are subject to a fee and discusses certain changes to FDA's policies under the new law. This guidance does not address how FDA determines and adjusts fees each fiscal year; nor does it address FDA's implementation of other user fee programs (e.g., Prescription Drug User Fee Amendments, Generic Drug User Fee Amendments).[2] Throughout this guidance, references to *user fees* or the *user-fee program* are to the user fee program for biosimilar biological products under section 744H of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations unless specific regulatory or statutory requirements are cited. The use of

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

[2] FDA will publish in the *Federal Register* the fee revenue and fees resulting from adjustment not later than 60 days before the start of each fiscal year. Section 744H(c)(5) of the FD&C Act, as amended by the FDA Reauthorization Act of 2017.

the word *should* in Agency guidances means that something is suggested or recommended, but not required.

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

II. BACKGROUND

The Biosimilar User Fee Act of 2012 (BsUFA I) added sections 744G and 744H to the FD&C Act, authorizing FDA to collect user fees for a 5-year period from persons that develop biosimilar biological products. Fees authorized by this legislation help fund the process for the review of biosimilar biological product applications, and have played an important role in expediting the review and approval process. BsUFA was reauthorized for a five-year period in 2017 under Title IV of the FDA Reauthorization Act of 2017 (BsUFA II), enacted on August 18, 2017.

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

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 ***biosimilar biological product*** means a specific strength of a biological product in final dosage form for which a biosimilar biological product application has been approved.[5]

- Except as provided by section 744G(4)(B), the term ***biosimilar biological product application*** means an application for licensure of a biological product under section 351(k) of the Public Health Service Act (PHS Act).[6]

[3] FDA's fiscal year begins on October 1 and ends on September 30.
[4] Section 744G(2) of the FD&C Act.
[5] Section 744G(3) of the FD&C Act.
[6] Section 744G(4)(A) of the FD&C Act.

- The term ***final dosage form*** means, with respect to a biosimilar biological product, a finished dosage form which is approved for administration to a patient without substantial further manufacturing (such as lyophilized products before reconstitution).[7]

- The term ***financial hold*** means an order issued by the Secretary to prohibit the sponsor of a clinical investigation from continuing the investigation if the Secretary determines that the investigation is intended to support a biosimilar biological product application and the sponsor has failed to pay any of the biosimilar biological product development program fees for the product.[8]

- The term ***person*** includes an affiliate of such person.[9] The term ***person*** includes an individual, partnership, corporation, or association.[10] This document will also use the term ***person*** when referring to a sponsor or applicant.

- The term ***supplement*** means a request to the Secretary to approve a change in a biosimilar biological product application which has been approved, including a supplement requesting that the Secretary determine that the biosimilar biological product meets the standards for interchangeability described in section 351(k)(4) of the PHS Act.[11]

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

BsUFA II authorizes the collection of three types of fees: (1) biosimilar biological product development program fees (BPD fees), (2) biosimilar biological product application fees (application fees), and (3) biosimilar biological product program fees (program fees).

Previously, section 744H of the FD&C Act authorized FDA to collect (1) biosimilar development program fees, (2) biosimilar biological product application and supplement fees, (3) biosimilar biological product establishment fees, and (4) biosimilar biological product fees. BsUFA II eliminates fees for supplements as well as for establishments. Applicants will be assessed annual biosimilar biological product program fees, rather than the biosimilar biological product fees assessed under BsUFA I.

Additionally, BsUFA II eliminates the reduction of an application fee by the cumulative amount of fees paid by the applicant under the BPD program.

The Agency will establish BPD fees, biosimilar biological product application fees, and the biosimilar biological product program fees for each fiscal year as set forth in the statute, and will

[7] Section 744G(10) of the FD&C Act.
[8] Section 744G(11) of the FD&C Act.
[9] Section 744G(12) of the FD&C Act.
[10] Section 201(e) of the FD&C Act.
[11] Section 744G(14) of the FD&C Act.

publish the fees and fee revenue amounts for a fiscal year in the Federal Register not later than 60 days before the start of that year.[12]

V. BIOSIMILAR BIOLOGICAL PRODUCT DEVELOPMENT FEES

BsUFA II BPD fees are assessed for products in FDA's BPD program. BPD fees include the initial BPD fee, the annual BPD fee, and the reactivation fee.

A. Initial BPD Fee

Under section 744H(a)(1)(A) of the FD&C Act, an ***initial BPD fee*** is a one-time fee that is assessed to a sponsor to enter the BPD program. A sponsor can enter the BPD program through one of two ways:

- The sponsor submits to FDA a meeting request for a BPD meeting for a product; or
- The sponsor submits a clinical protocol for an investigational new drug application (IND) describing an investigation that FDA determines is intended to support a biosimilar biological product application.

There is no fee for a biosimilar initial advisory meeting.

The initial BPD fee is due within 5 calendar days after FDA grants the first BPD meeting for the product or upon submission of an IND for the product that FDA determines is intended to support a biosimilar biological product application, whichever occurs first.[13] Refer to section VIII of this guidance for consequences of failing to pay the required fees.

B. Annual BPD Fee

Beginning in the next fiscal year after a sponsor has paid the initial BPD fee, the sponsor must pay an ***annual BPD fee***[14] for the product in each fiscal year. The annual BPD fee for a product is due on the first business day on or after October 1 of each fiscal year[15] or the first business day after the enactment of an appropriations Act providing for the collection and obligation of such fees for the year, whichever is later, unless the sponsor has discontinued participation in the BPD program for the product or has submitted a marketing application for the product that was accepted for filing.[16]

[12] Section 744H(c)(5) of the FD&C Act.
[13] Section 744H(a)(1)(A)(iv) of the FD&C Act.
[14] Section 744H(a)(1)(B) of the FD&C Act.
[15] Section 744H(a)(1)(B)(ii) of the FD&C Act.
[16] Section 744H(a)(1)(B)(iii) of the FD&C Act.

C. Request for Refund of Annual BPD Fee

If a person submits a biosimilar biological product application before October 1 of the fiscal year and the application is accepted for filing on or after October 1 of that fiscal year, the applicant may request a refund of the annual BPD fee paid by the applicant for such fiscal year.[17] FDA must receive a written request for a refund not later than 180 calendar days after the application is accepted for filing.[18]

For example, if an applicant submits a biosimilar biological product application for a product in the BPD program on September 15, 2017, the annual BPD fee for the product for FY 2018 is due on the first business day on or after October 1, 2017 (unless one of the exceptions applies; *see* section V.B of this guidance). If the application is accepted for filing by FDA on or after October 1, 2017, the applicant may submit Form FDA 3913 (User Fee Payment Refund Request)[19] to CDERCollections@fda.hhs.gov to request a refund of the annual BPD fee paid for the product for fiscal year 2018 within 180 calendar days from the date the application was accepted for filing.

D. Discontinuation of Annual BPD Fee Obligation

A sponsor may discontinue participation in the BPD program for a product, effective October 1 of a fiscal year, by notifying FDA ***on or before August 1 of the preceding fiscal year*** as follows:[20]

- If the sponsor has not yet submitted an IND – By submitting a written declaration to FDA that the sponsor has no present intention of further developing the product as a biosimilar biological product.[21] The sponsor should send a courtesy copy to CDERCollections@fda.hhs.gov and include the following information in the letter:
    - Sponsor's contact information including name, address, email, and telephone number
    - Identification of the request at the top of the cover letter as "Request to Discontinue Participation in the BPD Program"
    - Name of product
    - Pre-IND number
- If the sponsor has already submitted an IND and wishes to discontinue participation in the BPD program – By withdrawing the IND for the product in accordance with Part 312 of Title 21 of the Code of Federal Regulations (available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=312).[22]

[17] Section 744H(a)(1)(B)(iv) of the FD&C Act.
[18] Section 744H(a)(1)(B)(iv) of the FD&C Act.
[19] https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM492188.pdf.
[20] Section 744H(a)(1)(C) of the FD&C Act.
[21] Section 744H(a)(1)(C)(i) of the FD&C Act.
[22] Section 744H(a)(1)(C)(ii) of the FD&C Act.

In addition to withdrawing the IND, a sponsor who has already submitted an IND and wishes to discontinue participation should also submit to FDA a written request to discontinue participation in the BPD program, as described above, with a courtesy copy to CDERCollections@fda.hhs.gov.

Requests to discontinue participation in the BPD program can be submitted to the FDA Electronic Submissions Gateway or mailed to:

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

FDA must receive the request by August 1 of the preceding fiscal year to avoid assessment of the annual BPD fee. If FDA receives a request to discontinue participation in the BPD program after August 1 of the fiscal year, the sponsor will receive an annual BPD fee invoice for the upcoming fiscal year and must pay the invoice amount by the due date. Under section 744H(a)(1)(F)(i), FDA shall not refund any BPD fee (initial, annual, or reactivation), except as provided in section 744H(a)(1)(B)(iv) (see section V.C of this guidance).

E. Reactivation Fee

A sponsor that has discontinued participation in the BPD program for a product and wants to resume participation in the BPD program for the product must pay a ***reactivation fee***.[23] A sponsor may resume participation in the BPD program for a product in one of two ways:

- The sponsor requests a BPD meeting for the product; or
- The sponsor submits a clinical protocol for an IND describing an investigation that FDA determines is intended to support a biosimilar biological product application for the product.

The ***reactivation fee*** is due within 5 calendar days after FDA grants a BPD meeting for the product or upon submission of an IND describing an investigation that FDA determines is intended to support a biosimilar biological product application for the product, whichever occurs first. The reactivation fee for a fiscal year will be equal to twice the amount of the annual BPD fee established for that fiscal year.[24] Refer to section VIII of this guidance for consequences of failing to pay the required fees.

Beginning in the next fiscal year after a sponsor has paid the reactivation fee, the sponsor must pay an annual BPD fee.

[23] Section 744H(a)(1)(D) of the FD&C Act.
[24] Section 744H(b)(3)(D) of the FD&C Act.

VI. BIOSIMILAR BIOLOGICAL PRODUCT APPLICATION FEES

FDA assesses a user fee for each biosimilar biological product application. Under BsUFA II, application fees are not assessed for supplements to approved biosimilar biological product applications.

Beginning in FY 2018, each person that submits an application is assessed an application fee as follows:

- A biosimilar biological product application for which clinical data (other than comparative bioavailability studies) with respect to safety or effectiveness are required for approval is assessed a full application fee.[25]

- A biosimilar biological product application for which clinical data (other than comparative bioavailability studies) with respect to safety or effectiveness are not required for approval is assessed one-half of a full application fee.[26]

Under BsUFA II, application fees are not reduced by the cumulative amount of BPD fees paid for the product that is the subject of the application.[27] Application fees are due when the application is submitted.[28]

A. Exception to the Application Fee

If a biosimilar biological product application:

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

the submission of a biosimilar biological product application for the same product by the same person (or the person's licensee, assignee, or successor) does not require an application fee.[29]

[25] Section 744H(a)(2)(A)(i) of the FD&C Act.
[26] Section 744H(a)(2)(A)(ii) of the FD&C Act.
[27] See section 744H(a)(2)(B) of the FD&C Act. For application fees assessed under BsUFA I, the application fee was reduced by the cumulative amount of BPD fees paid for a product that was the subject of the application.
[28] Section 744H(a)(2)(C) of the FD&C Act.
[29] Section 744H(a)(2)(D) of the FD&C Act.

B. Refund of the Application Fee

If an application is refused for filing or is withdrawn without a waiver before filing, FDA will refund seventy-five percent of the application fee paid.[30] A written refund request is not required. An application that was withdrawn before filing or refused for filing will be subject to the full application fee when resubmitted, unless a waiver applies.[31]

C. Waiver of Application Fees

Under section 744H(d)(1) 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 biosimilar biological product application to the Agency for review and does not have another product that has been approved under a human drug application or a biosimilar biological product application and introduced or delivered for introduction into interstate commerce.

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

- 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 or a biosimilar biological product application and introduced or delivered for introduction into interstate commerce; and
- The applicant, including its affiliates, is submitting its first biosimilar biological product application.

1. Small Business Waiver and Refund Request

To qualify for a small business waiver of the biosimilar biological product application fee,[32] an applicant should submit to FDA Form FDA 3971, attached as Appendix I, at least four months prior to the submission of the application. If an applicant submitted an application with payment and would like to request a small business waiver and refund, the applicant should complete and submit Form FDA 3971 to request the refund. Such a request must be made within 180 calendar days of when the application fee was due.[33] The completed form should be submitted via email to CDERCollections@fda.hhs.gov.

Upon receipt of Form FDA 3971, FDA may contact the applicant to request additional information and to clarify information provided in Form FDA 3971. Examples of requested information include, but are not limited to, the following:

- An application for size determination;

[30] Section 744H(a)(2)(E) of the FD&C Act.
[31] Section 744H(a)(2)(F) of the FD&C Act.
[32] Section 744H(d)(1) of the FD&C Act.
[33] Section 744H(h) of the FD&C Act.

- A copy of the applicant's Articles of Incorporation and Bylaws;
- The applicant's most recent annual financial statement to shareholders; or
- 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 applicant's certification.

Occasionally, FDA finds entities affiliated with the applicant that the applicant did not identify as one of its affiliates. 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.

If the requested information is not submitted, FDA may deny the small business waiver request because there is insufficient evidence that the applicant meets the criteria described in section 744H(d)(1) of the FD&C Act.

2. Expiration Date of the Small Business Waiver

If a small business waiver is granted, the applicant should submit its biosimilar biological product application within 1 year after the date of the small business determination since 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 a new drug application (NDA) or biologics license application (BLA) from an unaffiliated company and, therefore, would have a drug product that has been approved under a human drug application or a biosimilar biological product 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. The Agency will examine its records to confirm that the applicant still meets the criteria for a small business waiver. If the criteria are no longer met, the small business waiver request will be denied. If the criteria are still met, the Agency will renew the small business waiver for another year.

3. Small Business Waivers of Application Fees for Future Biosimilar Biological Product Applications

After an applicant or its affiliate is granted a small business waiver and submits its first biosimilar biological product application, the applicant cannot receive another small business waiver.[34] That means the applicant or its affiliate is not eligible to receive a small business waiver for any subsequent biosimilar biological product application. In addition, 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.

[34] See section 744H(d)(1) of the FD&C Act.

VII. BIOSIMILAR BIOLOGICAL PRODUCT PROGRAM FEES

The biosimilar biological product program fee is assessed annually for each eligible biosimilar biological product. Program fees are assessed for a fiscal year to each person[35] who is named as the applicant in a biosimilar biological product application for each biosimilar biological product identified in a biosimilar biological product application approved as of October 1 of such fiscal year,[36] where the product does not appear on a list of discontinued biosimilar biological products (as of October 1 of such fiscal year).[37] For example, if approval of a biosimilar biological product application occurs on or before October 1, 2017 and the products identified in the approved application are not on the discontinued list as of October 1, 2017, then program fees will be assessed for the products for FY 2018. However, if approval of a biosimilar biological product application occurs after October 1, 2017, then program fees are not assessed for the products identified in the application for FY 2018.

The program fees are due on the first business day on or after October 1 of each fiscal year or the first business day after the enactment of an appropriations Act providing for the collection and obligation of such fees for the year, whichever is later.[38]

Applicants may not be assessed more than five program fees for biosimilar biological products identified in each approved application for each fiscal year.[39] For example, if seven biosimilar biological products are approved under the same BLA, the applicant would be assessed five program fees for the fiscal year.

Program fees for liquid parenteral biosimilar biological products. BsUFA II clarifies the definition of a "biosimilar biological product" to mean "a specific strength of a biological product in final dosage form for which a biosimilar biological product application has been approved."[40] For the purposes of assessing program fees for liquid parenteral biosimilar biological products, FDA intends to take into consideration both the total quantity of drug substance in mass or units of activity in a product and the concentration of the drug substance in mass or units of activity per unit volume of product. For example, two biosimilar biological products in final dosage form with the same concentration but with different fill volumes would be considered two separate biosimilar biological products for the purpose of assessing program fees. The applicant would be assessed two program fees for these products. If the applicant has more than five concentrations or fill volumes approved in the BLA, it will not be assessed more than five program fees for each fiscal year for products identified in such application.

[35] "The term 'person' includes an affiliate of such person." Section 744G(12) of the FD&C Act. See section III of this document for more information on the meaning of the term "person" for purposes of this guidance.
[36] Section 744H(a)(3)(A)(i) of the FD&C Act.
[37] Section 744H(a)(3)(A)(ii) of the FD&C Act.
[38] Section 744H(a)(3)(B) of the FD&C Act.
[39] Section 744H(a)(3)(D) of the FD&C Act.
[40] Section 744G(3) of the FD&C Act.

An auto-injector that has the same strength or potency in final dosage form as a prefilled syringe or vial will generally be assessed a separate program fee. This is intended to align the Agency's assessment of fees for biological products approved under section 351(k) of the PHS Act with its assessment of fees for products approved under section 351(a) of the PHS Act or section 505 of the FD&C Act.[41, 42]

VIII. FAILURE TO PAY FEES

Under section 744H(a)(1)(E) of the FD&C Act, if a person has failed to pay any BPD fee (initial, annual, or reactivation) for a product as required:

- FDA shall not provide a BPD meeting relating to the product for which fees are owed.[43]
- Except in extraordinary circumstances, FDA shall not consider an IND submitted for the product to have been received under section 505(i)(2) of the FD&C Act if FDA determines that the investigation is intended to support a biosimilar biological product application.[44]
- Except in extraordinary circumstances, FDA shall prohibit the sponsor of a clinical investigation from continuing the investigation (this is referred to as a "financial hold") if FDA determines that the investigation is intended to support a biosimilar biological product application.[45]

Under sections 744H(a)(1)(E)(iv) and 744H(e) and of the FD&C Act, a biosimilar biological product application or supplement submitted by a person subject to BsUFA fees shall be considered incomplete and shall not be accepted for filing until all BsUFA fees owed by such person have been paid.

IX. PAYMENT INFORMATION AND PROCEDURES

This section briefly describes the procedures for assessing and issuing annual invoices for the annual BPD fee and the biosimilar biological product program fees under BsUFA II. More detailed instructions will be provided in FDA's direct notice to affected persons by issuing a "Notification of Annual BsUFA Fees" correspondence.

[41] See draft guidance for industry *Assessing User Fees Under the Prescription Drug User Fee Amendments of 2017.*
[42] The distinction in this guidance between (1) auto-injectors and (2) prefilled syringes or vials is for the purposes of assessing the biosimilar biological product program fee only and not for any other purpose.
[43] Section 744H(a)(1)(E)(i) of the FD&C Act.
[44] Section 744H(a)(1)(E)(ii) of the FD&C Act.
[45] Section 744H(a)(1)(E)(iii) of the FD&C Act.

A. Initial BPD Fees, Reactivation Fees, and Application Fees

Applicants should complete a Biosimilar User Fee Cover Sheet (Form FDA 3792) online and pay by electronic check, wire transfer, money order, or bank draft. Instruction on accessing and completing the Biosimilar User Fee Cover Sheet is located on the BsUFA website (https://www.fda.gov/bsufa).

B. Annual Billing Cycle

1. BPD Sponsor Survey

FDA intends to send sponsors an annual survey to gather pertinent information to assist with fee setting for the next fiscal year. FDA anticipates sending the survey in the third quarter of each fiscal year.

2. Notification of Annual BsUFA Fees Correspondence

FDA will issue a "Notification of Annual BsUFA Fees" correspondence to affected sponsors in July of each fiscal year regarding their active BPD programs and approved biosimilar biological products. Sponsors should review the correspondence and notify FDA of any changes in contact information, changes in the status of Pre-IND/INDs in the BPD program, changes in biosimilar biological product marketing status, and any other information pertinent for the Agency to issue an accurate invoice to the proper person.

3. Annual Invoicing

FDA expects to issue annual invoices in September. Because sponsors are invoiced for annual BPD fees and program fees in advance of the upcoming fiscal year, the invoices may not reflect the actual data available as of October 1. FDA will issue additional invoices by December of the fiscal year to capture any new BPD sponsors and program fee-eligible biosimilar biological products that should have been invoiced. For example, if a sponsor pays a FY 2017 initial BPD fee on September 15, 2017, the sponsor can expect to receive a FY 2018 annual BPD fee invoice by December 2017.

Payment instructions are included on the invoice.

4. Moving a Product to the Discontinued Section of the Biosimilar List

FDA will maintain a list of approved biosimilar biological products that are user fee-eligible and products that are not marketed (discontinued). FDA intends to make this list available on the BsUFA website (https://www.fda.gov/bsufa) after this guidance is finalized. A biosimilar biological product is not assessed a program fee if it is in the discontinued section of the biosimilar list on the date that fees are assessed as of October 1 of the fiscal year. Applicants who have decided to stop marketing a product, or have decided to delay launch of a product after its approval date, should request to have the product moved to the discontinued section. If a biosimilar biological product remains on the biosimilar list, and has not been moved to the

discontinued section, on the date that fees are assessed for a fiscal year, the applicant will be assessed a program fee for the product even if it is no longer being marketed.[46]

Requests to move an approved biosimilar biological product to the discontinued section of the biosimilar list should be submitted to CDERCollections@fda.hhs.gov no later than September 30 of the preceding fiscal year. The request should clearly identify the product to be moved and the date that its not-marketed status begins and, if applicable, would end. If the applicant submits a request as set forth in this paragraph, FDA intends to consider the product to have been moved to the discontinued section on the date that the request was received or on the date the product is no longer marketed, whichever is later.

Please note that applicants seeking to move a biosimilar biological product to the discontinued section should clearly indicate the date on which their product is no longer marketed. Applicants should not rely on communications with a review division. Communication with the wrong division of FDA, or in a manner that does not make clear when a product is no longer marketed, may mean that the biosimilar biological product is not moved to the discontinued section of the biosimilar list before the date program fees are assessed, and may result in the applicant being required to pay a program fee for the product.

C. Waiver or Refund Requests

An applicant may request a waiver of the application fee, and may request a refund of fees it has paid, if it meets the applicable statutory criteria.[47] The written waiver or refund request must be submitted not later than 180 calendar days after such fee is due.[48] To request a small business waiver of the application fee, see section VI.C of this guidance. To request a refund of fees paid, the applicant should complete Form FDA 3913 (User Fee Payment Refund Request) and submit to CDERCollections@fda.hhs.gov. This form can be accessed from the User Fees website (https://www.fda.gov/ForIndustry/UserFees/). Any questions can be directed to CDERCollections@fda.hhs.gov.

X. APPEALS PROCESS

A. Reconsideration Request

If FDA fully or partially denies a request for a waiver or refund 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 or refund of user fees.

[46] Section 744H(a)(3)(A) of the FD&C Act.

[47] Sections 744H(a)(1)(F) and 744H(d)(1) of the FD&C Act. The FD&C Act does not provide for deferral of user fees, and FDA does not grant deferral of user fees based on pending requests for a refund. FDA therefore expects that all BsUFA fees assessed will be paid when due without regard to a pending request for a refund.

[48] Section 744H(h) of the FD&C Act.

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

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

Division of User Fee Management and Budget Formulation
Attention: Division Director
Center for Drug Evaluation and Research

Alternatively, an applicant can mail the request to FDA via the carrier of its choice. For the most updated mailing address, visit the following FDA website: https://www.fda.gov/bsufa.

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

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

All requests for appeals for either CDER or CBER products should be submitted to the Director of CDER's Office of Management via CDERCollections@fda.hhs.gov and a copy should be submitted to the CDER Formal Dispute Resolution Project Manager. The contact information can be found on the CDER Formal Dispute Resolution Web page.[49] Alternatively, an applicant can mail the request to FDA via carrier of its choice. For the most updated mailing address, visit the following FDA website: https://www.fda.gov/bsufa.

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

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

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 of Food and Drugs (Commissioner) under 21 C.F.R §10.75(c). Requests for review by the Commissioner should be submitted to FDA's Ombudsman, with a copy provided to the Center. Review of such matters by the Commissioner is discretionary.[50]

CBER Products

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

XI. OTHER RESOURCES

The following guidance documents may be helpful:

- Guidance for Industry - Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees[51]

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

- MAPP 6050.1 Refusal to Accept Applications for Filing From Applicants in Arrears[52]

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

[50] See 40 FR 40682, 40693 (September 3, 1975).

[51] See https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf.

[52] See https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM082029.pdf.

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. xxxx-xxxx
Expiration Date: Xxxxxxxx xx, 20xx
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

If 'No", list all previously submitted application numbers and the corresponding submission dates.

Application Number	*Submission Date*	*Application Number*	*Submission Date*

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

If 'Yes', list application number and approval date for each approved drug product.

Application Number: _____ Approval Date: _____
Application Number: _____ Approval Date: _____
Application Number: _____ Approval Date: _____
Application Number: _____ Approval Date: _____
Application Number: _____ Approval Date: _____

Click for an additional pair of Application Number/Approval Date entries. May be repeated. Add Application #

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

If 'Yes', select the user fee program (PDUFA and/or BsUFA), and provide Small Business Waiver number and date waiver was granted.

	If PDUFA, check the following: ☐ PDUFA	Small Business Waiver Number	Waiver Approval Date
	If BsUFA, check the following: ☐ BsUFA	Small Business Waiver Number	Waiver Approval Date

Has the Waiver been redeemed? ☐ Yes ☐ No

Section II: Affiliate Information *(Enter information for <u>each</u> 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 *(<u>No P.O. boxes allowed</u>)*

Address 1 *(Street address)*

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

City | State/Province/Region

Country | ZIP or Postal Code

14. DUNS Number

15. Number of Employees

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

If 'Yes', select the user fee program (PDUFA and/or BsUFA), and provide Small Business Waiver number and waiver approval date.

	If PDUFA, check the following: ☐ PDUFA	Small Business Waiver Number	Waiver Approval Date
	If BsUFA, check the following: ☐ BsUFA	Small Business Waiver Number	Waiver Approval Date

Has the Waiver been redeemed? ☐ 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

If 'Yes', list all submitted human drug or biosimilar biological product application numbers, and the corresponding submission dates.

Application Number	*FDA Submission Date*	*Application Number*	*FDA Submission Date*

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)

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)*

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 averagr 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."