

POLICY AND PROCEDURES

OFFICE OF MANAGEMENT

Effect of Failure to Pay BsUFA Fees

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PURPOSE

This Manual of Policies and Procedures (MAPP) establishes:

- The Center for Drug Evaluation and Research (CDER) policy for assessing biosimilar biological product development (BPD) fees and failure to pay any required BPD fees, in accordance with the Federal Food, Drug, and Cosmetic Act (the FD&C Act), as amended by the Biosimilar User Fee Amendments of 2022 (BsUFA III).
- CDER’s policy concerning Unacceptable for Filing (UN)¹ in cases where the sponsor or its affiliates are in arrears with respect to the biosimilar user fees (user fees) assessed and owed, in accordance with BsUFA III.
- CDER’s standard procedures for notifying sponsors participating in FDA’s BPD program of a failure to pay BPD fees.

¹ The terms “unacceptable for filing” and “refused for filing” are not the same. This MAPP only addresses the former, “unacceptable for filing,” which applies when applications or supplements are not suitable for evaluation by FDA because of outstanding Biosimilar User Fee Act (BsUFA) fees. An application for a biologics license, for which the applicant has met all applicable user fee obligations (paid or waived), shall not be considered as filed until all pertinent information and data have been received by the FDA (See 21 CFR 601.2). The applicant for such an application that is not considered filed may receive a “refused for filing” notice.

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- CDER’s standard procedures for recognizing and processing applications submitted by applicants subject to user fees, and for communicating to applicants that their applications² and/or supplements³ have not been accepted by CDER for filing.
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BACKGROUND

The Biosimilar User Fee Act of 2012 (BsUFA I) added sections 744G and 744H to the FD&C Act, authorizing FDA to assess and collect user fees for a 5-year period from persons that develop biosimilar biological products. BsUFA has been reauthorized by Congress every 5 years since 2012. The most recent reauthorization is under the Biosimilar User Fee Amendments of 2022 (BsUFA III), authorized as part of the FDA User Fee Reauthorization Act of 2022. BsUFA III extends FDA’s authority to collect user fees for fiscal years (FYs) 2023 through 2027.

BsUFA III authorizes the collection of three types of fees: (1) BPD fees; (2) biosimilar biological product application fees (application fees); and (3) biosimilar biological product program fees (program fees). BPD fees include the initial BPD fee, the annual BPD fee, and the reactivation fee.

POLICY

- A sponsor can enter or resume participation in the BPD program through one of the following two ways:⁴
 - A 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.
 - A sponsor submits a BPD meeting⁵ request for a product.

² For the purposes of this MAPP, the term “application” refers to an application for licensure of a biological product under section 351(k) of the Public Health Service Act that meets the definition of a biosimilar biological product application. See section 744G(4) of the FD&C Act.

³ Section 744G(14) of the FD&C Act defines the term “supplement” to mean 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 in section 351(k)(4) of the Public Health Service Act.

⁴ See sections 744H(a)(1)(A) and 744H(a)(1)(D) of the FD&C Act.

⁵ A BPD meeting is defined as any meeting other than a Biosimilar Initial Advisory (BIA) meeting, regarding the content of a development program, including a proposed design for, or data from, a study intended to support a biosimilar biological product application. See section 744G(5) of the FD&C Act. Note that there is no fee for a BIA meeting.

- The initial BPD fee or reactivation fee, as applicable, is due within 7 calendar days after FDA grants such BPD meeting request or upon submission of such IND, whichever occurs first.⁶
- Beginning in the next fiscal year after a sponsor has paid the initial BPD fee, the sponsor owes an annual BPD fee for the product until the sponsor discontinues participation in the BPD program for the product, submits a marketing application for the product that is accepted for filing, or is administratively removed from the BPD program for the product.⁷
- If a sponsor fails to pay an initial BPD fee, an annual BPD fee, or a reactivation fee by the due date, then any pending BPD meeting request or scheduled BPD meeting relating to the product for which fees are owed is denied or canceled,⁸ and no further BPD meetings relating to the product are granted until the fees are paid.
- If a sponsor fails to pay an initial or annual BPD fee or a reactivation fee by the due date, then, except in extraordinary circumstances, an IND submitted for the product for which fees are owed is not considered to be received if FDA determines that the investigation is intended to support a biosimilar biological product application.^{9, 10}
- If FDA determines that an investigation is intended to support a biosimilar biological product application, and the sponsor fails to pay any applicable BPD fee for the product by the due date, then the IND is placed on financial hold,¹¹ except in extraordinary circumstances.¹² Additionally, the sponsor (including its affiliates) is placed on the arrears list.¹³
- Applications and supplements are not accepted for filing from applicants (including their affiliates) who are in arrears.¹⁴ An applicant will be deemed to be in arrears for any BsUFA fees invoiced (i.e., annual BPD fee, annual program fee) by FDA if the applicant or its affiliate(s) have not paid all invoiced fees by the payment due date. An applicant is placed on the arrears list the calendar day after

⁶ Sections 744H(a)(1)(A)(iv) and 744H(a)(1)(D) of the FD&C Act.

⁷ Section 744(H)(a)(1)(B)(iii) of the FD&C Act.

⁸ See section 744H(a)(1)(E)(i) of the FD&C Act.

⁹ See section 744H(a)(1)(E)(ii) of the FD&C Act.

¹⁰ In the system of record, the status change reason will reflect “unacceptable for receipt.”

¹¹ The term “financial hold” means an order issued by FDA to prohibit the sponsor of a clinical investigation from continuing the investigation if FDA determines that the investigation is intended to support a biosimilar biological product application and the sponsor has failed to pay any of the BPD fees for the product. See section 744G(11) of the FD&C Act. When an IND is placed on financial hold, the investigation(s) covered by such IND is prohibited from continuing.

¹² See sections 744G(11) and 744H(a)(1)(E)(iii) of the FD&C Act.

¹³ In the system of record, the status change reason will reflect “financial hold.”

¹⁴ See section 744H(e) of the FD&C Act.

the annual fees are due if the invoice is not paid in full by the due date. When an applicant is on the arrears list, an application or supplement submitted by the applicant or its affiliates will be deemed UN on the FDA receipt date of the submission.

- When an applicant submits an application for which an application fee is owed, and the applicant (including its affiliates) is not on the arrears list, FDA will deem the application UN if the user fee obligation is not met within 5 calendar days of the application receipt date (e.g., the full fee is paid or has been waived).
- FDA's Office of Financial Management (OFM) and the BsUFA Team within the Brands Branch of the Division of User Fee Management (hereafter referred to as user fee staff) maintain a list of applicants and their affiliates that are in arrears (i.e., the arrears list) due to failure to pay user fees. This arrears list is used as a reference for determining whether an application or supplement should be accepted for filing review or deemed UN by FDA, and the list is updated as appropriate, if applicants pay any outstanding fees. In addition, OFM maintains a list of applicants that have paid the annual invoiced user fees for a given fiscal year.
- To initiate the UN process, the user fee staff notifies the appropriate regulatory staff aligned with the review division (e.g., regulatory project manager (RPM), regulatory business process manager (RBPM), or Chief of Project Management Staff) that an application or supplement has been deemed UN or is expected to be deemed UN. The notification should be provided as soon as possible. In general, the review team ceases all work on the application and/or supplement upon notification.

PROCEDURES

- OFM and the user fee staff maintain the arrears list that will serve as a reference for determining if BPD meeting requests will be granted or an IND will be considered received.

BPD Program

- Sponsors who have not paid the annual BPD fee by the payment due date are placed on the arrears list. The user fee staff will notify the application RPM and the Office of Therapeutic Biologics and Biosimilars (OTBB) via email within 2 business days of a sponsor being placed on the arrears list. The appropriate system of record is updated to indicate that the user fee obligation is "Not Met."

- The RPM, in collaboration with OTBB, issues a *BPD Fee Not Received Letter* to the sponsor. Any pending BPD meeting request or scheduled BPD meeting relating to the product for which the fees are owed is denied or canceled, regardless of whether the meeting was granted before the sponsor was placed on the arrears list. Additionally, except in extraordinary circumstances:
 - A new IND submission for the product for which the fees are owed is not considered received if FDA determines that the investigation is intended to support a biosimilar biological product application¹⁵; and
 - The IND for the product is placed on financial hold if FDA determines that the investigation is intended to support a biosimilar biological product application.¹⁶
- Once the sponsor pays the annual BPD fee, the following steps are taken.
 - The user fee staff:
 - Notifies the RPM and OTBB.
 - Removes the sponsor from the arrears list.
 - Updates the system of record to indicate that the user fee obligation is “Met.”
 - The RPM, in collaboration with OTBB, issues a *BPD Fee Received Letter* to the sponsor. The sponsor may submit a new meeting request for any BPD meeting request that was denied or scheduled meeting that was cancelled, resubmit a new IND for any IND submission that was not considered to have been received, or resubmit a new review request for any pending submission not reviewed under the existing IND due to a financial hold.
- If a sponsor is in arrears for non-payment of BPD fees, FDA may grant a BPD meeting or receive an IND if the meeting or IND, as applicable, is not related to the product for which the fees are owed.

Application/Supplement

- When FDA receives a new application or supplement, the user fee staff conducts a user fee assessment within 10 calendar days to determine: (1) whether the applicant (including its affiliates) is in arrears; and (2) in the case of an application, whether any user fee obligation for that application has been met

¹⁵ See section 744H(a)(1)(E)(ii) of the FD&C Act.

¹⁶ See sections 744G(11) and 744H(a)(1)(E)(iii) of the FD&C Act.

(e.g., appropriate application fee has been received by FDA, or application fee was waived).

- If the applicant (including its affiliates) is not in arrears and has satisfied any fee requirements for the application, then the RPM /RBPM aligned with the review division sends an Acknowledgement Letter within 14 calendar days¹⁷ of receipt of submission to the applicant.
- If the applicant is in arrears for non-payment of invoiced fees and an application or supplement is received, the user fee staff, in consultation with the OTBB or appropriate regulatory staff aligned with the review division, notifies the applicant that the application is UN due to non-payment of fees. The user fee staff prepares the Applicant in Arrears Letter, also known as the Unacceptable for Filing Letter (UN Letter), to be approved by the BsUFA Team Lead of the user fee staff for the DUFM Division Director and enters it into the appropriate system of record. This letter informs the applicant that the application or supplement has not been accepted for filing because the applicant or its affiliate is in arrears for previously invoiced fees. If a UN Letter has been issued, the RPM/RBPM should not send the standard Acknowledgement Letter to the applicant.
- If the applicant is not in arrears but has not paid the appropriate application fee (e.g., only paid one-half of a full application fee or partial payment missing due to wire transfer fees), the user fee staff notifies the applicant by email that FDA will deem the application UN if the appropriate fee is not received or otherwise met (e.g., waived) within 5 calendar days of the date of notification. If the user fee obligation is not met within 5 calendar days, the user fee staff prepares the UN Letter to be approved by the BsUFA Team Lead of the user fee staff for the DUFM Division Director and enters it into the appropriate system of record. This letter informs the applicant that the application has been deemed UN because the user fee obligation has not been met and the review clock of the application will not begin until the user fee obligation has been met (e.g., appropriate payment is made). The user fee staff sends the UN Letter by email notifying the applicant that the application is deemed UN due to non-payment of the appropriate application fee. If a UN Letter has been issued, the RPM should not send the standard Acknowledgement Letter to the applicant.
- When the UN Letter is issued by the user fee staff, the system of record updates to indicate that the application or supplement has been deemed UN, and informs appropriate regulatory staff aligned with the review division.

¹⁷ Acknowledgement letters for Office of Pharmaceutical Quality managed chemistry, manufacturing, and controls supplements may be issued within 30 calendar days.

- Once an applicant satisfies its user fee obligation for a previously deemed UN submission, the date that the user fee obligation is met is the date that starts the review clock. The user fee staff reopens the submission in the appropriate system of record and indicates that the user fee obligation has been met. The user fee staff notifies the RPM/RBPM/OTBB via email that the submission has been reopened and the appropriate regulatory staff aligned with the review division sends a User Fees Received or Waived Letter instead of the standard Acknowledgment Letter. The User Fees Received or Waived Letter is an acknowledgement letter after a UN action. The receipt date that starts the review clock is not set until the user fee obligations have been met. The date that starts the review clock may not be the same as the date that the User Fees Received or Waived Letter issues.
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RESPONSIBILITIES

User fee staff:

- Checks Payment and Arrears Report for user fee payment.
- Conducts user fee assessment.
- Issues UN Letter.
- Notifies applicant that payment is required.
- Re-opens application deemed UN after payment is paid.

RPM/RBPM:

- Issues Acknowledgment Letter (if not notified of UN) by the 14-day date.
 - Issues User Fee Received or Waived Letter.
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REFERENCES

- Federal Food, Drug and Cosmetic Act, Sections 744G and 744H.
 - FDA Guidance for Industry: Assessing User Fees Under the Biosimilar User Fee Amendments of 2022.
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DEFINITIONS

- **Affiliate** – Under section 744G(2) of the FD&C Act, this term means a business entity that has a relationship with a second business entity if, directly or indirectly: (1) one business entity controls, or has the power to control, the other business entity; or (2) a third-party controls, or has the power to control, both of the business entities.
- **In Arrears** – A sponsor/applicant is deemed to be in arrears for any annual BPD fees or biosimilar biological product program fees invoiced by FDA if the sponsor/applicant or its affiliate has not paid all fees by the payment due date.
- **Unacceptable for Filing** – This is **not** the same as *refuse to file*. For more on “refuse to file,” refer to 21 CFR 601.2(a), which states that a biologics license application “shall not be considered as filed until all pertinent information and data have been received by the Food and Drug Administration.” Unacceptable for filing means that the application or supplement is not suitable for evaluation by FDA because of outstanding BsUFA fees. Section 744H(e) of the FD&C Act requires that applications be considered incomplete and not be accepted for filing in situations in which an applicant is determined to be in arrears for BsUFA user fees.¹⁸

EFFECTIVE DATE

This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
12/3/2021	N/A	Initial
10/10/2023	1	Updates information from BsUFA II to BsUFA III.

¹⁸ See section 744H(e) of the FD&C Act (stating that applications and supplements from applicants that owe a BsUFA fee will “be considered incomplete and shall not be accepted for filing ... until all such fees are owed by such person have been paid.”).