SOPP 8406: CBER Processing of PDUFA Application Payments

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I. Purpose

This Standard Operating Policy and Procedure (SOPP) serves as a guide for Center for Biologics Evaluation and Research (CBER) staff on the procedures for verifying application payments in accordance with the Prescription Drug User Fee Act (PDUFA). In addition, this SOPP identifies billing activities for which CBER's Office of Regulatory Operations (ORO), Division of Regulatory Operations and Programs (DROP), Regulatory Programs Branch (RPB) is responsible.

II. Scope

A. This SOPP applies to original Biologics License Applications (BLAs) and New Drug Applications (NDAs) regulated by CBER which are subject to PDUFA. These include:

1. BLAs submitted for licensure under Section 351(a) of the Public Health Service (PHS) Act. (See exemptions below in the policy section, item C).

2. NDAs submitted under Section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

III. Background

A. The FD&C Act as amended by PDUFA, authorizes the Food and Drug Administration (FDA) to collect fees from the pharmaceutical industry to augment appropriations spent on FDA's human drug review process. The FDA spends fee revenues to hire, support, and maintain personnel for the review of human drug applications to ensure safe and effective prescription drugs reach the American public more quickly.

B. PDUFA authorizes FDA to assess and collect fees for certain drug and biologic license applications as well as program fees for approved products. Because user fee application payments are required to be submitted concurrently with applications, review of an application cannot begin until the fee is received.

C. In certain circumstances, application fees do not apply, but the applications are still subject to PDUFA requirements. These PDUFA user fee exceptions apply to the following application types:

1. A drug that is not distributed commercially and is the subject of an application or supplement submitted by a State or Federal Government entity.

2. A human drug application for a prescription drug product that has been designated as a drug for a rare disease or condition pursuant to section 526 of the FD&C Act, also commonly referred to as an orphan drug. The application for orphan drug is not subject to an application fee unless the application also includes an indication that is not for a rare disease or condition.

D. An electronic PDUFA User Fee Cover Sheet, FDA Form 3397, is completed and submitted online through the User Fee System with each new original NDA or BLA application submitted to the FDA. In addition, a cover sheet is required for resubmissions of original NDAs and BLAs after a Refuse to File (RTF) and resubmissions of original NDAs and BLAs withdrawn before the FDA filing date. A cover sheet is not required for application supplements.

E. Each fiscal year, FDA is required to announce prescription drug user fee rates for the coming fiscal year. Rates are set for application and program fees. The rates are published in the Federal Register approximately 60 days before the start of the fiscal year.

IV. Definitions

A. Affiliate – 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 power to control, both of the business entities.

B. Application - A submission for licensure of a BLA submitted under Section 351 of the PHS Act or an NDA submitted under Section 505 of the FD&C Act.

C. PDUFA - A United States law enacted in 1992, which is reviewed and revised every 5 years, authorizing FDA to collect fees from companies that apply for approval and market certain human drug and biological products.

D. PDUFA Payment and Arrears Report - A daily email report from the Office of Financial Management (OFM) which provides a list of applicants who have made an application payment as well as a list of applicants in arrears for non-payment of annual program fees.

E. PDUFA Receipts Report - A daily email report from OFM which provides payment information for applications.

F. Unacceptable for Filing (UN) – An action taken by FDA to not accept an application for review as required by PDUFA because an applicant has not submitted payment for the application, or because an applicant or affiliate is determined to be in arrears for non-payment of annual program fees.

V. Policy

A. Each original application will include a completed PDUFA User Fee Cover Sheet (FDA Form 3397), unless specifically exempted below, under C. The cover sheet is completed by the applicant by using FDA's User Fee System..

B. The PDUFA User Fee Cover Sheet is to be included with original applications which meet one of the following user fee exceptions under the FD&C Act. The exception is entered by the applicant when completing the PDUFA User Fee Cover Sheet:

1. The application qualifies for the skin test diagnostic product exception under section 736 of the FD&C Act.
2. The application qualifies for the orphan drug exception under Section 736(a)(1)(F) of the FD&C Act
3. The application is submitted by a State or Federal government entity for a drug that is not distributed commercially

4. The applicant has been granted awaiver. A copy of the official FDA notification is to be included with the application submission.

C. Human drug applications submitted under section 505(b) of the FD&C Act or section 351 of the PHS Act will not be assessed an application fee for the following applications:

1. A supplement to such an application,

2. An application with respect to whole blood or blood component for transfusion,

3. An application with respect to a large volume parenteral drug product approved before September 1, 1992,

4. An application with respect to bovine blood product for topical application licensed before September 1, 1992,

5. An application with respect to an allergenic extract product licensed before October 1, 2022,

6. An application with respect to a standardized allergenic extract product submitted pursuant to a CBER notification to the applicant in accordance with 21 CFR 680.3(e) regarding the existence of a potency test that measures the allergenic activity of an allergenic extract product licensed by the applicant before October 1, 2022,

7. An application with respect to an in vitro diagnostic biologic product licensed under section 351 of the PHS Act (these BLAs are for biologics that are also medical devices and are subject to the Medical Devices User Fee Act (MDUFA)). Refer to *SOPP 8704: Managing MDUFA User Fee Payments and Billing Activities*,

8. An application for licensure of a biological product for further manufacturing use only,

9. An application or supplement submitted by a State or Federal Government entity for a drug that is not distributed commercially.

D. The Guidance for Industry: *Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees* is to be referenced when there is a question about whether an applicant's proposed submission should be submitted as an original application or a supplement. This guidance also describes what changes may be bundled in one application and what changes should be submitted in separate applications. Contact ORO/DROP/RPB by emailing *CBER User Fee Staff* for guidance.

E. When an applicant fails to submit timely payment of an invoice issued by FDA, the applicant is listed on OFM's PDUFA Payment and Arrears Report. All original applications and supplements including manufacturing and labeling supplements received by an applicant or affiliate in arrears for non-payment of fees invoiced are deemed Unacceptable for Filing and will not be reviewed until all user fees are paid in full.

F. When an applicant fails to submit payment for a BLA or NDA that is subject to a user fee, the application is considered Unacceptable for Filing. There is a 5 (calendar) day grace period within which the applicant's payment must be received before the application is deemed Unacceptable for Filing. Note: failure to submit payment for a specific application does *not* result in the applicant being placed on OFM's PDUFA Payment and Arrears Report**.** Other applications received from the applicant may be accepted as long as the required fees are received and the applicant or affiliate is not listed on the PDUFA Payments and Arrears Report.

VI. Responsibilities

A. FDA/Office of the Commissioner (OC)

1. Annually establishes PDUFA user fee rates and publishes them in the Federal Register.

B. FDA/Office of Financial Management (OFM)

1. Receives notice of PDUFA payments from the U.S. Bank.

2. Sends daily PDUFA Payment and Arrears Report to *CBER User Fee Staff*.

3. Sends daily PDUFA Receipts Report to *CBER User Fee Staff*.

C. Office of Regulatory Operations, Division of Regulatory Operations and Programs, Regulatory Programs Branch (ORO/DROP/RPB)

1. Monitors the *CBER User Fee Staff* email account.

2. Provides guidance to review offices on whether or not a submission is subject to user fees.

3. Reviews the PDUFA Receipts Report and notifies the Regulatory Project Manager (RPM) of payment receipts for incoming applications.

4. Verifies that any exception checked on the PDUFA *User Fee Cover Sheet* is accurate. Enters user fee payment data in the appropriate regulatory system based on reconciliation of the subject PDUFA User Fee Cover Sheet with the PDUFA Receipts Report.

5. Contacts the applicant if there are any payment discrepancies, e.g., applicant did not pay current fiscal year rate. Coordinates with OFM until resolved.
6. Monitors the CBER Submission Weekly Receipts Report and the PDUFA Payment and Arrears Report for CBER applicants and notifies review offices of applicants or affiliates in arrears when applicable.
7. Monitors status of all applications that have been designated as Unacceptable for Filing. Notifies the RPM when payment is received.
8. Restarts the review clock in the appropriate regulatory system when payment is received for an application that is deemed Unacceptable for Filing.
9. Identifies biologic products subject to annual program fees and provides product and applicant information to the Center for Drug Evaluation and Research (CDER) for invoicing.
10. Drafts letters in response to applicant waivers, reductions, exemptions, and refund (WER)requests for user fees assessed under section 736 of the FD&C Act.
11. Maintains the User Fee Billable Biologic Products and Potencies List on FDA's Internet website.
12. Maintains the CBER Discontinued Products List on FDA's Internet website.

D. Regulatory Project Manager (RPM or designee)

1. Receives the application and determines whether it is subject to a user fee.
2. Notifies CBER User Fee Staff (ORO/DROP/RPB via the *CBER User Fee Staff* email account) that it has received a PDUFA application to verify receipt of user fee payment.
3. Notifies the applicant when a user fee has not been received for the application that the review is on hold pending receipt of payment.
4. Verifies that any exception checked on the PDUFA *User Fee Cover Sheet* is accurate.
5. Alerts the review committee when the application is Unacceptable for Filing that review may not begin.
6. Issues an *Acknowledgment* letter to the applicant making certain to include the *unacceptable for filing* paragraph, when user fee payment is not received within 5 calendar days of the CBER receipt date.
7. Enters the *Acknowledgement* letter into the appropriate regulatory system. (Note: if UN included, entry of this communication stops the review clock.)

8. Notifies review committee to resume review when payment for the application is received.

VII. Procedures

A. Routine Processing of Submission Cover Sheets

1. Compare the PDUFA *User Fee Cover Sheet* with the submission to determine if the application is subject to user fees. **[RPM or designee]**

   a. If there is a question about whether the application is subject to a user fee, is properly classified, or is inappropriately bundled, contact review office management and/or ORO/DROP/RPB via the *CBER User Fee Staff* email account for guidance.

   b. If the application is subject to user fees, verify payment receipt with ORO/DROP/RPB via the *CBER User Fee Staff* email account. If payment was received and there is a discrepancy in the payment amount, ORO/DROP/RPB resolves it. Note: Payment discrepancies do not affect the review clock**.**

2. Verify that any application fee exception checked on the PDUFA *User Fee Cover Sheet* is accurate (e.g., orphan drug designation, small business waiver, etc.). See list of exceptions under the policy section, item B, above. **[RPM or designee and ORO/DROP/RPB]**

B. Processing submissions Received Without a PDUFA User Fee Cover Sheet or With an Incomplete Cover Sheet

1. Contact the applicant and request immediate submission of a completed form if an application is received without a PDUFA *User Fee Cover Sheet*. Once the PDUFA Cover Sheet is received, follow the procedures under Section A above. **[RPM or designee]**

2. Contact the applicant to obtain the necessary information or relay the inaccuracy, if an incomplete or inaccurate form is submitted with an application. **[ORO/DROP/RPB] Note:** An application should not proceed to a filing action until the information is obtained.

C. Processing submissions received without Payment

1. If payment is not received within **5 calendar** days of the CBER receipt date of the application:

   a. Notify the review committee to halt the review. **[RPM or designee]**

b. Notify the applicant that the application is Unacceptable for Filing (by phone and/or email). **[RPM or designee]**

c. Prepare and issue an a*cknowledgement* letter with the *Unacceptable for Filing* paragraph, using the CBER Acknowledgment letter template. **[RPM or designee]**

d. Enter the *Acknowledgement letter* into the appropriate regulatory system, which stops the review clock and changes the status of the application to *Unacceptable for Filing*. **[RPM or designee]**

2. Once payment has been received, reactivate the review process.

a. Notify the RPM when fees owed have been paid. **[ORO/DROP/RPB]**

b. Notify the review committee that the review process may proceed. **[RPM or designee]**

c. Enter the payment date into the appropriate regulatory system based on the payment date identified in the PDUFA Receipts Report and reset the STN status to pending. **[ORO/DROP/RPB]**

Note: The regulatory system automatically calculates the new action due dates based on the payment receipt date.

VIII. Appendix

A. Not Applicable

IX. References

A. References below can be found on the Internet:

1. User Fee System

2. PDUFA User Fee Rates

3. Guidance to Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees

4. CBER User Fee Billable Biologic Products and Potencies Approved Under Section 351 of the PHS Act

X. History

Written/Revised	Approved By	Approval Date	Version Number	Comment
F. Mesarina	Martha Monser, RRDL, RABOB/DROP /ORO	June 3, 2026	11	Minor revisions: corrected terminology of exemptions, exceptions and exclusion, corrected exception types, clarified which products are not assessed UFs, and wordsmithing throughout for clarity.
F. Mesarina	Martha Monser RRDL Coordinator, RABOB/DROP /ORO	September 30, 2025	10	Updated to include the definition of affiliate in accordance with 21 USC 379g: Definitions and updated RPB's responsibilities to include monitoring of the CBER Submission Weekly Receipts Report.
C. Vincent	Darlene Martin, MS, PMP ORO/DROP Director (acting)	September 28, 2022	9	Updated for PDUFA VII
M. Monser	N/A	February 27, 2022	8	Technical update for changes due to 2022 CBER reorganization
M. Monser	N/A (technical review by Job Aid Coordinator)	September 24, 2019	7	Technical Change to update hyperlinks and to current font/format
C. Vincent	Christopher Joneckis, PhD	September 11, 2017	6	Updated to reflect changes effective under PDUFA VI
C. Vincent	Robert Yetter, PhD	10/7/2013	5	Updated to new standard SOPP format and to reflect minor changes in process since last revision.
C. Vincent	Robert Yetter, PhD	10/5/2009	4	Updated to reflect changes to the process due to the on-line user fee cover sheet and FDAAA and to include

Written/Revised	Approved By	Approval Date	Version Number	Comment
				other user fee activities for which RIMS is responsible. Comments from BPWG and RMCC incorporated.
R. Eastep	Robert Yetter, PhD	8/10/2001	3	Removal of plasma volume expanders from the non-User Fee list in Section 5.
G. Conley D. Bigelow R.Eastep C. Nemoff C. Vincent	Robert Yetter, PhD	4/11/2001	2	This revision further clarifies the responsibilities and procedures. It supersedes version 1 of this SOPP.
CBER Application Policy Task Force	M. Beatrice	3/23/1994	1	Reissued as SOPP 8406 in August 1997. No change to Guide content.