SOPP 8406: CBER Processing of PDUFA Application Payments

Version: 6
Effective Date: October 1, 2017

I. Purpose

A. 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 the Center Director, Associate Director for Review Management, Business Operations Staff (OD/ADRM/BOS) is responsible.

II. Scope

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

1. BLAs submitted for licensure under Section 351(a) of the Public Health Service 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 FDA to collect fees from the pharmaceutical industry to augment appropriations spent on FDA's human drug review process. The Food and Drug Administration (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 exclusions apply to the following product types:

1. A drug that is not distributed commercially and is the subject of an application submitted by a state or United States government entity.

2. An application for orphan designated product that includes only an orphan designated indication.

D. An electronic PDUFA User Fee Cover Sheet is used to submit payment information on human drug applications subject to PDUFA. A web link to the cover sheet appears in the Reference Section.

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. A web link to the current user fee rates appears in the Reference Section.

IV. Definitions

A. **Application -** A submission for licensure of a BLA submitted under Section 351 of the Public Health Service Act or an NDA submitted under Section 505 of the FD&C Act.

B. **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. Note: The fees are used to hire review staff and for other related drug and biologic review purposes to help assure application review timeline goals are met.

C. **PDUFA Payment and Arrears Report -** A daily email report from the Office of Financial Management (OFM) which provides a running 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. Note: the PDUFA Payment and Arrears Report is posted for reference in CBER's Outlook Public Folder, *PDUFA Arrears List & General Information*.

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

E. **Unacceptable for Filing -** The application is not accepted by the FDA for review. Note: PDUFA requires this action when the applicant has not submitted payment for the application, or when the applicant is determined to be in arrears for non-payment of annual program fees.

V. Policy

A. Each original application should 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 on FDA's User Fee website.

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

1. A large volume parenteral drug product approved under Section 505 of the FD&C Act before September 1, 1992

2. The application qualifies for the orphan 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 a small business waiver

C. The PDUFA User Fee Cover Sheet need not be included with applications for the following product types (exemptions):

1. Whole blood or blood components for transfusion,

2. Blood bags,

3. Bovine blood products for topical application licensed before September 1, 1992,

4. Cord blood and peripheral blood stem cells separated from whole blood by physical or mechanical means for transfusion,

5. Crude allergenic extracts,

6. An in vitro diagnostic biologic product (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.*

7. Biological products for further manufacturing use only

D. The Guidance for Industry: *Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees* should 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 OD/ADRM/BOS by emailing '*CBER PDUFA 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 applications and supplements including manufacturing and labeling supplements received by an applicant in arrears for non-payment of fees invoiced are deemed Unacceptable for Filing and should not be reviewed.

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 five (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 for filing as long as the required fees are received.

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 PDUFA Staff.*

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

C. Office of the Center Director, Associate Director for Review Management, Business Operations Staff (OD/ADRM/BOS)

1. Monitors the *CBER PDUFA 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 exclusion checked on the PDUFA User Fee Cover Sheet is accurate. Enters user fee payment data in RMS-BLA 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 daily PDUFA Payment and Arrears Report for CBER applicants and notifies review offices of firms 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 RMS-BLA when payment is received for an application that is deemed Unacceptable for Filing.
9. Posts current user fee rates and list of firms in arrears in CBER's Outlook public folder: *PDUFA Arrears List & General Information.*
10. 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.
11. Drafts letters in response to applicant refund and waiver requests for application and program fees.
12. Maintains the User Fee Billable Biologic Products and Potencies List on FDA's Internet website.
13. 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 a user fee.

2. Notifies CBER user fee staff (OD/ADRM/BOS via the *CBER PDUFA 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 exclusion 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 RMS-BLA. (Note: 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. Compares 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, contacts review office management and/or OD/ADRM/BOS via the *CBER PDUFA Staff* email account for guidance.

    b. If the application is subject to user fees, verifies payment receipt with OD/ADRM/BOS via the *CBER PDUFA Staff* email account. If payment was received and there is a discrepancy in the payment amount, OD/ADRM/BOS resolves it. Note: Payment discrepancies do not affect the review clock.

2. Verifies that any application fee exclusion checked on the PDUFA User Fee Cover Sheet is accurate (e.g., orphan drug designation, small business waiver, etc.). See list of exclusions

under the policy section, item B, above. **[RPM or designee and OD/ADRM/BOS]**

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

1. Contacts the applicant and requests 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 follows the procedures under Section A above. **[RPM or designee]**

2. Contacts the applicant to obtain the necessary information or relay the inaccuracy, if an incomplete or inaccurate form is submitted with an application. An application should not proceed to a filing action until the information is obtained. **[OD/ADRM/BOS]**

C. Processing submissions received without Payment

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

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

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

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

d. Enters the *Acknowledgement letter* into RMS-BLA, which stops the review clock. The letter entry also changes the status of the application in RMS-BLA to *Unacceptable for Filing*. **[RPM or designee]**

2. Once payment has been received the review process is reactivated.

a. Notifies the RPM when fees owed have been paid. [**OD/ADRM/BOS]**

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

c. Enters the payment date into RMS-BLA based on the payment date identified in the PDUFA Receipts Report, and resets the STN status to pending. **[OD/ADRM/BOS]**

Note: RMS-BLA automatically calculates the new action due dates based on the payment receipt date.

VIII. Appendix

A. N/A

IX. References

A. The reference below is located on CBER's Intranet Web Page:

1. RMS-BLA Data Dictionary (assessed via RMS-BLA)

B. References below can be found on the Internet:

1. PDUFA User Fee Cover Sheet

https://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm119184.htm

2. PDUFA Rates

https://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/default.htm

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

https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf

4. CBER User Fee Billable Products List

https://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm151732.htm

X. History

Written/ Revised	Approved By	Approval Date	Version Number	Comment
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 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.