POLICY AND PROCEDURES

OFFICE OF MANAGEMENT

Effect of Failure to Pay PDUFA Fees

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PURPOSE

This Manual of Policies and Procedures (MAPP) establishes:

- The Center for Drug Evaluation and Research (CDER) policy concerning the effect of failure to pay prescription drug user fees in accordance with the Prescription Drug User Fee Amendments.[1]

- CDER's policy concerning what is Unacceptable for Filing (UN)[2] in cases where the applicant or its affiliates are in arrears for the prescription drug user fees (user fees) assessed and owed in accordance with the Prescription Drug User Fee Amendments.

[1] See sections 735 and 736 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act). The Prescription Drug User Fee Act of 1992 (PDUFA I) authorized the Food and Drug Administration (FDA) to collect user fees for a 5-year period from persons that submit certain human drug applications for review, or that are named in approved applications as the applicant of certain prescription drug products. Since 1992, Congress has revised and extended PDUFA five times, each time for a 5-year period. The most recent reauthorization is Title I of the FDA Reauthorization Act of 2017 (PDUFA VI).

[2] 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 Prescription Drug User Fee Amendments (PDUFA) fees. The latter, "refused for filing," applies when the applicant has met all user fee obligations (paid or waived), but the Agency does not make a threshold determination that the application is sufficiently complete to permit a substantive review (see 21 CFR 314.101 for new drug applications) or all pertinent information and data has not been received by the Agency (see 21 CFR 601.2 for biologics license applications).

- CDER's standard procedures in recognizing and processing applications and supplements submitted by applicants subject to user fees, and for communicating to applicants that their applications[3] and/or supplements[4] are UN and have not been accepted by CDER for filing.

BACKGROUND

- The Prescription Drug User Fee Act of 1992 (PDUFA) added sections 735 and 736 to the Federal Food, Drug, and Cosmetic Act (the FD&C Act), authorizing the Food and Drug Administration (FDA) to collect user fees from persons that submit certain human drug applications for review or that are named in approved applications as the applicant of certain prescription drug products. Since 1992, Congress has reauthorized PDUFA five times, each time for a 5-year period.

- PDUFA was last reauthorized under Title I of the FDA Reauthorization Act of 2017, enacted on August 18, 2017 (PDUFA VI). PDUFA VI extends FDA's authority to collect user fees for fiscal years (FYs) 2018 through 2022.

- Prior to PDUFA VI, FDA was authorized to collect 3 types of prescription drug user fees: (1) human drug application and supplement fees; (2) prescription drug establishment fees; and (3) prescription drug product fees.

- PDUFA VI authorizes the collection of two types of user fees: (1) human drug application fees due at the time certain human drug applications are submitted; and (2) prescription drug program user fees collected annually. PDUFA VI eliminates user fees for supplements and establishments but does not eliminate prior outstanding invoiced user fees.

POLICY

- Although PDUFA VI eliminated user fees for supplements, the total number of supplements that FDA receives and reviews contributes to capacity planning adjustments. It is expected that the appropriate regulatory staff aligned with the review division and Division of User Fee Management (DUFM) staff will

[3] For the purposes of this MAPP, the term "application" refers to new drug applications and biologics license applications that are human drug applications. See section 735(1) of the FD&C Act.
[4] Section 735(2) defines the term "supplement" to mean a request to the Secretary to approve a change to a human drug application that has been approved.

coordinate to ensure that applications and supplements are bundled appropriately.[5]

- Human drug applications and supplements are accepted for filing from applicants (including their affiliates) who are not in arrears.[6] An applicant will be deemed to be in arrears for any prescription drug user fees invoiced by FDA if the applicant has not paid all invoiced user fees[7] by the payment due date.

- An applicant is placed on the arrears list the calendar day after the annual user fees are due if the invoice is unpaid in full by the due date and the fee has not been waived by FDA. If an applicant is on the arrears list, an application or supplement submitted by the applicant or its affiliates is deemed UN on the FDA receipt date of the application or supplement. Please note that submissions received prior to a firm (or its affiliates) going into arrears would not be deemed UN.

- When an applicant not on the arrears list submits an application for which an application fee is owed, FDA will deem the application UN if the user fee obligation is not met within 5 calendar days of the date the application is submitted (e.g., the full fee is paid or has been waived).

- FDA's Office of Financial Management (OFM) and the Office of Management, DUFM, Brands Branch, user fee staff (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 the reference for determining whether an application or supplement should be accepted for filing review or deemed UN by FDA, and is updated, as appropriate, if applicants pay all outstanding fees or all fees are waived. 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 (CPMS)), 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, if the submission is deemed UN, the review team ceases all work on the application or supplement.

[5] Guidance for applicants regarding what should be contained in separate marketing applications are described in FDA's Guidance for Industry, *Submitting Separate Marketing Application and Clinical Data for Purposes of Assessing User Fees* (bundling guidance) (https://www.fda.gov/media/72397/download).
[6] Section 736(e) of the FD&C Act.
[7] Invoiced prescription drug user user fees may include annual prescription drug program fees, application fees, and previously invoiced product and establishment fees. See section 736(a) of the FD&C Act.

- If FDA (user fee staff in consultation with the appropriate regulatory staff aligned with the review division) determines at the time of application receipt or during the course of the review of a submission that the application needs to be separated into more than one application,[8] the Agency communicates with the applicant to determine which application will be placed into review status and which application(s) will require additional fees. The remaining application(s) is UN if the appropriate fees are not received by FDA within 5 calendar days of notifying the applicant via email.

- FDA may determine after approval that the application or supplement should have been separated into more than one application or supplement. If this determination is made, FDA may separate the submission into more than one application or supplement. The appropriate regulatory staff aligned with the review division, in consultation with the user fee staff, is responsible for informing the applicant of the administrative separation of the application or supplement, and the user fee staff is responsible for determining whether an invoice will be issued to the applicant. The user fee staff coordinates with OFM to issue an invoice to the applicant for any additional fees determined to be due. The RPM/RBPM works with the document room to administratively separate the application in appropriate FDA databases.

PROCEDURES

- 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) for an application, whether any user fee obligation for the application has been met (e.g., appropriate application fee has been received by FDA, or application fee was waived).

- If the applicant and/or 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 days[9] 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 RPM/RBPM 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

[8] The appropriate regulatory staff aligned with the review division should consult with the user fee staff for bundling issues.

[9] Acknowledgement letters for Office of Pharmaceutical Quality managed Chemistry, Manufacturing, and Controls supplements may be issued within 30 days.

Unacceptable for Filing letter (UN Letter), to be approved by the PDUFA Fees 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 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 half fee paid or entire payment missing due to wiring issues), the user fee staff notifies the applicant by email that FDA will deem the application UN if the appropriate fee is not received or is otherwise met (e.g., exempted, waived) within 5 calendar days of the date of notification. If the prescription drug user fee obligation is not met within 5 calendar days, the user fee staff notifies the applicant by email that the application is deemed UN due to non-payment of the appropriate application fee. The user fee staff prepares the UN Letter to be approved by the Fees Team Lead of the user fee staff for the DUFM Division Director. This letter informs the applicant that the application has been deemed UN because the prescription drug user fee obligation has not been met, and the review clock of the application will not begin until the prescription drug user fee obligation has been met (e.g., appropriate payment is made). If a UN Letter has been issued, the RPM should not send the standard an Acknowledgement Letter to the applicant.

- When the applicable UN Letter is issued, the user fee staff updates the system(s) of record to reflect that the application or supplement has been deemed UN and informs appropriate regulatory staff aligned with the review division.

- 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 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 Fee Received or Waived Letter is an acknowledgement letter after an UN action.[10] 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.

[10] User Fee Received or Waived Letter Types: User Fees Received or Waived, Receipt of User Fees-Prior Approval Supplement, Receipt of User Fees-Presubmission, Receipt of User Fees- CBE Supplement.

RESPONSIBLITIES

RPM/RBPM:

- Issues Acknowledgement Letter (if not notified of UN) by the 14-day date.
- Issues User Fee Received or Waived Letter.
- Notifies applicant of bundling issues if application/supplement is already approved.

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.

REFERENCES

- Federal Food, Drug, and Cosmetic Act (FD&C Act):
  1. Sections 735 and 736 — Fees Relating to Drugs.
  2. Section 736(e) — Effect of Failure to Pay Fees.
- FDA Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees. December 2004 (Bundling Guidance).
- Assessing User Fees Under the Prescription Drug User Fee Amendments of 2017 Guidance for Industry.

DEFINITIONS

- **Affiliate** — Under section 735(11) 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.

- **Applicant** — Any person[11] who submits an application[12] or an amendment or supplement to an application to obtain FDA approval of a new drug (21 CFR 314.3(b)) and any person who owns an approved application; or any legal person or entity who submits an application to obtain a biologics license under section 351 of the Public Health Service Act or who holds the biologics license and assumes responsibility for compliance with the applicable product and establishment standards (21 CFR. 600.3(t)).

- **In Arrears** — An applicant is deemed to be in arrears for any annual prescription drug program fees invoiced by FDA if the applicant or its affiliate has not paid all fees by the payment due date. Applicants are not deemed to be in arrears for an unpaid human drug application fee unless a fee has been invoiced for that application.

- **Unacceptable for Filing** — This is **not** the same as *refusal to file* defined under 21 CFR. 314.101 and 21 CFR 601.2(a). Unacceptable for filing means that the application or supplement is not suitable for evaluation by FDA because of outstanding prescription drug user fees. Section 736(e) of the FD&C Act requires that applications be considered incomplete and shall not be accepted for filing in situations in which an applicant is determined to be in arrears for any PDUFA user fees.[13]

EFFECTIVE DATE

This MAPP is effective upon date of publication.

[11] For the purposes of this MAPP, the term *person* includes affiliates. See section 735(9) of the FD&C Act.
[12] Abbreviated new drug applications are **not** *human drug applications* as defined in section 735(1) of the FD&C Act. The procedures for generic drug user fees and biosimilar user fees are not affected by or addressed in this MAPP.
[13] See section 736(e) of the FD&C Act (stating that applications and supplements from applicants that owe a fee will "be considered incomplete and shall not be accepted for filing... until all such fees are owed by such person have been paid.").

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
7/17/2007	N/A	Initial
12/3/2021	Rev. 2	• Changes Title from *Refusal to Accept Application for Filing From Applicants in Arrears.* • Moves the responsibilities of the MAPP to the Office of Management, DUFM. • Revises the Purpose, Policy, Procedures, References, and Definitions sections. • Adds Background section and Responsibilities section.