May 14, 2018

Dear Colleague:

The Prescription Drug User Fee Amendments of 2017 (PDUFA VI) amended the Federal Food, Drug, and Cosmetic Act (the FD&C Act) authorizing the Food and Drug Administration (FDA) to assess and collect two types of user fees – human drug application fees and prescription drug program fees (program fees). Under PDUFA VI, a program fee is assessed annually for each prescription drug product identified in an approved human drug application, with a limit of five program fees for a single approved application.[1,2]

This letter notifies you of certain changes in FDA's policies for prescription drug products under PDUFA VI and requests you verify the data that will be used for your fiscal year (FY) 2019[3] program fee invoice. Because we plan to issue the FY 2019 program fee invoices in August 2018,[4] we ask that you confirm or correct your company's contact information and PDUFA program fee-eligible products according to the instructions below by **Friday, June 15, 2018**.

I. Policy Changes Under PDUFA VI

The changes described below affect (1) what prescription drug products are considered to be the "same product as another product" for the purpose of the program fee exception and (2) what products are considered to be separate prescription drug products subject to separate program fees.[5]

1. "Same Product as Another Product" Program Fee Exception

Section 736(a)(2)(B)(ii) of the FD&C Act provides that a prescription drug product will not be assessed a program fee if it is the same product as another product that was approved under an application filed under section 505(b) or 505(j) of the FD&C Act and is not in the list of discontinued products compiled under section 505(j)(7) of the FD&C Act.

To be considered the "same product as another product," a product must be determined by FDA to be therapeutically equivalent to another drug product. Therapeutically equivalent products are

[1] Section 736(a)(2)(A) of the FD&C Act.
[2] Section 736(a)(2)(C) of the FD&C Act.
[3] FY 2019 = October 1, 2018, through September 30, 2019.
[4] The FY 2019 fees will be published in a *Federal Register* notice anticipated in August 2018.
[5] For additional information, please refer to the guidance for industry *Assessing User Fees Under the Prescription Drug User Fee Amendments of 2017* (PDUFA VI guidance). The PDUFA VI guidance is available on the Internet at www.fda.gov/Drugs under Guidance (Drugs).

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approved drug products that are pharmaceutical equivalents[6] for which bioequivalence[7] has been demonstrated and that can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling.

FDA publishes its conclusions regarding therapeutic equivalence in the *Approved Drug Products with Therapeutic Equivalence Evaluations* (the Orange Book) available at https://www.accessdata.fda.gov/scripts/cder/ob/. Therapeutically equivalent products are identified by "A" codes.[8] Therefore, FDA considers a product to be the same product as another product for the purpose of the program fee exception if a product has been assigned an "A" code published in the Orange Book.

2. Liquid Parenteral Biological Products Approved under Section 351 of the PHS Act

- Assessing the Strength or Potency of a Drug in Final Dosage Form

When evaluating the specific strength or potency of a drug in final dosage form for purposes of assessing program fees for liquid parenteral biological products approved under section 351 of the Public Health Service (PHS) Act, FDA intends to take into consideration both the total amount of drug substance in mass or units of activity in a product and the concentration of drug substance (mass or units of activity per unit volume of product). Biological products considered to have a different strength or potency in a final dosage form will be given separate entries in the Biologics List[9] and assessed separate program fees.

- Auto-Injectors, Prefilled Syringes, and Vials

An auto-injector that has the same strength or potency as a prefilled syringe or vial will generally be given a separate entry on lists[10] maintained by the FDA for biological products and assessed a separate program fee.

This change for liquid parenteral biological products is intended to align the FDA's assessment of program fees for products approved under section 351 of the PHS Act with its assessment of fees for products approved under section 505 of the FD&C Act, providing consistency in implementation of the program fee.

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[6] Pharmaceutical equivalents are drug products in identical dosage forms and routes of administration that contain identical amounts of the identical active drug ingredient. 21 CFR § 314.3.

[7] Bioequivalence is the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study. 21 CFR § 314.3.

[8] See the Orange Book Preface to the 38th Edition at section 1.7, available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm079068.htm.

[9] See section IV of this letter.

[10] *Id.*

II. Review Your Company's Contact Information

Attachment A – Company Contact Information

Attachment A contains the contact information FDA has for the person designated by your company to receive correspondence, invoices, and inquiries concerning prescription drug user fees. Please review and make corrections to Attachment A or confirm that the information is correct as listed, and return the signed form by email to the PDUFA User Fee staff at CDERCollections@fda.hhs.gov.

Attachment B – Product List

Considering the information in section I of this letter, please review your existing product list, cross out any products that you believe should not be assessed a program fee, and include the reason why it should not be assessed a fee (e.g., generic competition for new drug application (NDA) products, revocation or discontinuation of a biological product).

If any product is omitted that should be included on the existing product list, please add the relevant product information on the "Missing PDUFA Eligible Products List" and include the reason why it should be assessed a fee. **Please make your changes directly on the lists provided in Attachment B rather than by creating a separate list.**

III. Confirm Your NDA Prescription Drug Products in the Orange Book

A list of user fee-eligible *prescription drug products* for which the Center for Drug Evaluation and Research (CDER) has regulatory responsibility can be found in the "Prescription Drug Product List" of the Orange Book, available at https://www.accessdata.fda.gov/scripts/cder/ob/.

After making necessary updates to the list of your products in Attachment B, we recommend reviewing your company's current list of drug products in the Orange Book and notifying the Orange Book staff (OrangeBook@fda.hhs.gov) in writing about any changes (e.g., drug products that are no longer marketed) to the Prescription Drug Product List **no later than June 30, 2018**. For the Orange Book staff to receive changes in a consistent format, please print your company's list of products from the FDA website and note any changes directly on the printed list. Please send the User Fee staff (CDERCollections@fda.hhs.gov) a courtesy copy of any information sent to the Orange Book staff.

If you notify the Orange Book staff of a drug product's marketing status after June 30, 2018, the product may be included on your FY 2019 invoice. You may be eligible for a refund of the assessed program fee provided the Orange Book staff receives the notification to move the product from the Prescription Drug Product List to the "Discontinued Drug Product List" no later than **September 30, 2018**. To be eligible for a refund, you must submit a refund request in writing to the User Fee staff no later than 180 days after the fee is due.[11]

[11] Section 736(i) of the FD&C Act (21 U.S.C. § 379h(i)).

Failure to move a product to the Discontinued Drug Product List of the Orange Book could result in the assessment of fees, even if the product is not marketed. If you plan to resume marketing your drug product and the product is on the Discontinued Drug Product List, you should notify the Orange Book staff to move the drug product to the Prescription Drug Product List.

IV. Confirm Your Biological Products on the CDER and CBER Lists

For a current list of user fee-eligible licensed therapeutic biological products for which **CDER** has regulatory responsibility, please see the *CDER Billable Biologic List* at https://www.fda.gov/downloads/forindustry/userfees/prescriptiondruguserfee/ucm164641.pdf.

For a current list of user fee-eligible licensed biological products for which the Center for Biologic Evaluation and Research (**CBER**) has regulatory responsibility, please see CBER's list of *User Fee Billable Biologic Products and Potencies Approved Under Section 351 of the PHS Act* (CBER Billable Biologic List) at https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/UCM606472.pdf.

We recommend reviewing the information on both websites to obtain a complete list of your biological products. If you are no longer marketing a biological product and have delisted it under § 510 of the FD&C Act (21 U.S.C. § 360), but the product is on the CDER or CBER Billable Biologic List, please do the following:

- For CDER regulated products, contact the CDER User Fee staff and request in writing that FDA move the product to the *CDER Discontinued Product List*.

- For CBER regulated products, submit a Product Correspondence to the Product Review Office requesting that the product be moved to the *CBER Discontinued Products List* and copy the CBER User Fee staff.

Please notify FDA by **June 30, 2018**, if changes need to be made:

- For CDER biological products, email the CDER User Fee staff at CDERCollections@fda.hhs.gov.

- For CBER biological products, email the CBER User Fee staff at CBERPDUFAstaff@fda.hhs.gov. Please include CDERCollections@fda.hhs.gov on correspondence sent to the CBER User Fee staff.

If you notify the User Fee staff to discontinue marketing a biological product after June 30, 2018, the product may be included on the invoice for the next fiscal year. You may be eligible for a refund of the assessed program fee provided the User Fee staff receives notificaction to move the product to the Discontinued Product List no later than **September 30, 2018**. To be eligible for a refund, you must submit the refund request in writing to the User Fee staff no later than 180 days after the fee is due.[11]

Failure to move a product to the Discontinued Product List could result in the assessment of a program fee, even if the product is not marketed. If you plan to resume marketing your biological product and it is on the Discontinued Product List, you should notify the User Fee staff so the product can be moved to the appropriate CDER or CBER Billable Biologic Product List.

V. How to Provide the Requested Information

Please return Attachments A and B (including the updated product list) by **June 15, 2018**, by email to the PDUFA User Fee staff at CDERCollections@fda.hhs.gov.

If you have any questions, please email CDERCollections@fda.hhs.gov.

We look forward to receiving your response by **June 15, 2018**.

Sincerely,

Jeen Min, R.Ph.
CDR, United States Public Health Service
Branch Chief, Division of User Fee Management
and Budget Formulation
Office of Management
Center for Drug Evaluation and Research

Attachments:

Attachment A – Company Contact Information
Attachment B – List of User Fee Eligible Products