



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2015-N-3326]

Biosimilar User Fee Act; Public Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public meeting; request for comments.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing a public meeting to discuss proposed recommendations for the reauthorization of the Biosimilar User Fee Act (BsUFA) for fiscal years (FYs) 2018 through 2022. BsUFA authorizes FDA to collect fees and use them for the process for the review of biosimilar biological product applications. The current legislative authority for BsUFA expires in September 2017. At that time, new legislation will be required for FDA to continue collecting biosimilar biological product user fees in future fiscal years. Following an initial consultation with public stakeholders and discussions with the regulated industry, the Federal Food, Drug, and Cosmetic Act (the FD&C Act) directs FDA to publish the recommendations for the reauthorized program in the Federal Register, hold a meeting at which the public may present its views on such recommendations, and provide for a period of 30 days for the public to provide written comments on such recommendations. FDA will then consider the public views and comments and revise the recommendations as necessary.

DATES: The public meeting will be held on October 20, 2016, from 9 a.m. to 2 p.m. Please register for the meeting by October 19, 2016, at <http://bsufapublicmeeting.eventbrite.com>.

Submit electronic or written comments to the public docket by [INSERT DATE 30 DAYS AFTER PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: The meeting will be held at the FDA White Oak Campus, 10903 New Hampshire Ave., Bldg. 31 Conference Center, the Great Room (rm. 1503, Section A), Silver Spring, MD 20993-0002. Participants must enter through Building 1 and undergo security screening. For more information on parking and security procedures, please refer to <http://www.fda.gov/AboutFDA/WorkingatFDA/BuildingsandFacilities/WhiteOakCampusInformation/ucm241740.htm>.

You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <http://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <http://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Division of Dockets Management, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2015-N-3326 for "Biosimilar User Fee Act; Public Meeting." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <http://www.regulations.gov> or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <http://www.regulations.gov>. Submit both copies to the Division of

Dockets Management. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at:

<http://www.fda.gov/regulatoryinformation/dockets/default.htm>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <http://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FDA will post the agenda approximately 5 days before the meeting at:

<http://www.fda.gov/ForIndustry/UserFees/BiosimilarUserFeeActBsUFA/ucm461774.htm>.

FOR FURTHER INFORMATION CONTACT: Amanda Roache, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 1176, Silver Spring, MD 20993, 301-796-4548, FAX: 301-847-8443, amanda.roache@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Introduction

FDA is announcing a public meeting to discuss proposed recommendations for the reauthorization of BsUFA, the legislation that authorizes FDA to collect user fees and use them for the process for the review of biosimilar biological product applications. The current

authorization of the program (BsUFA I) expires in September 2017. Without new legislation, FDA will no longer be able to collect user fees for future fiscal years to fund the process for the review of biosimilar biological product applications. Section 744I(e)(2) of the FD&C Act (21 U.S.C. 379j-53(e)(2)) requires that after FDA holds negotiations with regulated industry, we do the following: (1) Present recommendations to the relevant Congressional committees, (2) publish recommendations in the Federal Register, (3) provide a period of 30 days for the public to provide written comments on the recommendations, (4) hold a meeting at which the public may present its views on the recommendations, and (5) after consideration of public views and comments, revise the recommendations as necessary.

This notice, the 30-day comment period, and the public meeting will satisfy some of these requirements.

The purpose of the meeting is to hear the public's views on the proposed recommendations for the reauthorization of BsUFA II. The following information is provided to help potential meeting participants better understand the history and evolution of the BsUFA program and the proposed BsUFA II recommendations.

II. What is BsUFA and What Does It Do?

BsUFA is a law that authorizes FDA to collect fees from drug companies that submit marketing applications for certain biosimilar biological products. BsUFA was originally enacted in 2012 as the Biosimilar User Fee Act (Pub. L. 112-144) for a period of 5 years.

BsUFA's intent is to provide additional revenues so that FDA can hire more staff, improve systems, and establish a better-managed biosimilar biological product review process to make important therapies available to patients sooner without compromising review quality or FDA's high standards for safety, efficacy, and quality. As part of FDA's agreement with industry

during each reauthorization, the Agency agrees to certain performance goals. These goals apply to the process for the review of new biosimilar biological product applications, resubmissions of original applications, and new and resubmitted supplements to approved applications. Phased in over the 5 years of BsUFA I, the goals were to review and act on 90 percent of original biosimilar biological product application submissions within 10 months of receipt and resubmitted original biosimilar biological product applications within 6 months of receipt; to review and act on 90 percent of original supplements with clinical data within 10 months of receipt and resubmitted supplements with clinical data within 6 months of receipt; and review and act on 90 percent of manufacturing supplements within 6 months of receipt.

III. Proposed BsUFA II Recommendations

In preparing the proposed recommendations to Congress for BsUFA reauthorization, FDA conducted discussions with the regulated industry and consulted with stakeholders, as required by the law. We began the BsUFA reauthorization process by publishing a notice in the Federal Register requesting public input on the reauthorization and announcing a public meeting that was held on December 18, 2015. The meeting included presentations by FDA and a series of panels with representatives of different stakeholder groups, including patient advocates, consumer groups, regulated industry, health professionals, and academic researchers. The materials from the meeting, including a transcript and Webcast recording, can be found at <http://www.fda.gov/ForIndustry/UserFees/BiosimilarUserFeeActBsUFA/ucm461774.htm>.

Following the December 2015 public meeting, FDA conducted negotiations with the regulated industry from March 2016 through May 2016. FDA posted minutes of these meetings on its Web site at <http://www.fda.gov/ForIndustry/UserFees/BiosimilarUserFeeActBsUFA/ucm461774.htm>.

The proposed enhancements for BsUFA II address many of the top priorities identified by public stakeholders, the regulated industry, and FDA. While some of the proposed enhancements are new, many either build on successful enhancements or refine elements from the existing program. The enhancements are proposed in the following areas: Review performance, meeting management, guidance development, and administrative areas (hiring and financial management). The full text of the proposed BsUFA II commitment letter can be found here at

<http://www.fda.gov/ForIndustry/UserFees/BiosimilarUserFeeActBsUFA/ucm461774.htm>. Each significant new or modified enhancement is described briefly in sections III.A through III.K.

A. The Review Cycle

FDA and the regulated industry jointly identified an opportunity to reduce multiple review cycles for biosimilar biological products by increasing transparency and communication during the review process of a 351(k) application. For BsUFA II, it is therefore proposed to establish a model for the review of biosimilar biological products similar to the Program for Enhanced Review Transparency and Communication for New Molecular Entity New Drug Applications and original Biologics License Applications (the Program) that was established in the fifth authorization of the Prescription Drug User Fee Act (PDUFA).

The Program was first established for PDUFA in 2012. An interim assessment of the Program suggested that it has created conditions that enhance the ability of applicants and FDA reviewers to work toward application approval in the first cycle (see

<http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm327030.htm>).

Likewise, it is anticipated that the review model will promote efficiency and effectiveness of the

first cycle review process and minimize the number of review cycles necessary for approval for 351(k) applications.

The Program will allow for additional communication between FDA review teams and the applicants of biosimilar biological products in the form of pre-submission meetings, mid-cycle communications, and late-cycle meetings, while also adding 60 days to the review timeframe to accommodate this additional interaction.

This enhancement is described in section I.B. of the proposed BsUFA II commitment letter.

B. Review Goal Extension for Missing Manufacturing Facilities

When manufacturing facilities are not adequately identified, this may result in the need for FDA to conduct inspections late in the review process. This can adversely impact FDA's ability to complete application review within the performance goal timeframes. Accordingly, FDA proposes to extend the goal date for an original application or a supplement when FDA identifies a need to inspect a facility that was not included in a comprehensive and readily located list of manufacturing facilities. This enhancement is described in section I.A.5.b of the proposed BsUFA II commitment letter.

C. Special Protocol Assessment and Agreement

Further clarity is needed regarding the types of clinical study protocols that may qualify for a Special Protocol Assessment and Agreement under BsUFA. Pharmacokinetic (PK) and Pharmacodynamic (PD) similarity studies should be added to the examples provided in the goals letter. It is proposed that the language in the goals is revised to include PK and PD similarity studies. This enhancement is described in section I.H.1.c of the proposed BsUFA II commitment letter.

D. Prior Approval Manufacturing Supplements

The review goal date for biosimilar prior approval manufacturing supplements is currently 6 months under BsUFA I, compared to 4 months for stand-alone biologics under PDUFA. Therefore, to increase consistency among user fee programs, it is proposed that prior approval manufacturing supplements are reviewed in 4 months, instead of 6 months, with a phased-in performance goal. The language for prior approval supplements is included in section I.A.3 of the proposed BsUFA II commitment letter.

E. Meeting Management

The enhancements in this section focus on FDA's ability to better manage meetings with sponsors of 351(k) applications. The details for these enhancements can be found in section I.I of the proposed BsUFA II commitment letter.

1. Addition of a Written Response Meeting Format for Biosimilar Initial Advisory (BIA) and Biosimilar Program Development (BPD) Type 2 Meetings

Currently, there is no mechanism to grant a meeting request and provide a written response in place of a face-to-face meeting, videoconference, or teleconference. From FY 2013 to FY2015, FDA provided written responses to sponsors for 16 out of 22 meetings that were denied or cancelled due to incomplete, premature, or unnecessary requests in order to support biosimilar development programs. Such responses are not on a user fee clock and are not tracked work. For BsUFA II, it is proposed that for BIA and BPD Type 2 meetings, the sponsor may request a written response to questions rather than a face-to-face meeting, videoconference, or teleconference. If a written response is deemed appropriate, FDA will notify the requester of the date it intends to send the written response. This date will be consistent with the timeframes specified for the specific meeting type.

2. Increase the Scheduling Timeframe for BPD Type 2 Meetings

The FDA has had challenges scheduling BPD type 2 meetings within the 75-day timeframe. Scheduling challenges occur due to an increasing number of Type 2 meetings to discuss novel and complex aspects of development that require extensive internal discussion. A review committee must address many of these aspects to ensure implementation of consistent scientific advice and policy concerning biosimilar development. Consequently, FDA is unable to answer and provide comprehensive responses to such questions at meetings within the 75-day timeframe. This results in unresolved issues and additional followup questions that ultimately leads to a delay in a sponsor's overall development program. To provide the necessary time for FDA discussions and to develop comprehensive responses, it is proposed that BPD Type 2 Meetings occur within 90 calendar days, instead of 75 days, from receipt of the meeting request and meeting package with a phased in performance goal. Additionally, it is proposed that the Agency will send preliminary responses to the sponsor's questions contained in the background package no later than five calendar days before the face-to-face videoconference or teleconference meeting date for BPD Type 2 and Type 3 meetings.

3. Reduce the Scheduling Timeframe for Biosimilar Initial Advisory (BIA) Meetings

On average, five BIA meetings were scheduled per fiscal year from 2013 to 2015. The content of a BIA meeting is limited to a general discussion on whether a proposed product could be developed as a biosimilar product and to provide high-level advice on the expected content of the development program. Targeted advice on the adequacy of any comparative data or extensive advice for any aspect of an ongoing biosimilar development program is not expected to be provided in a BIA meeting. The current 90-day scheduling timeframe may no longer be

appropriate and should be shortened. Therefore, it is proposed for BIA meetings to occur within 75 calendar days, instead of 90 days, from receipt of the meeting request and meeting package.

F. Guidance Development

FDA has received feedback that additional clarity is needed on regulatory processes and the scientific criteria for biosimilar development and approval to provide certainty to industry and other stakeholders related to Agency expectations. Therefore, it is proposed that FDA revise its guidance entitled "Formal Meetings Between the FDA and Biosimilar Biological Product Sponsors or Applicants" and update the draft guidance entitled "Best Practices for Communication Between IND Sponsors and FDA During Drug Development" to include communications between IND sponsors and FDA during biosimilar biological product development. Additionally, it is proposed that FDA publish draft or final guidance on several issues related to biosimilar biological product development including considerations in demonstrating interchangeability with a reference product; statistical considerations for analytic similarity for biosimilar biological products; processes and further considerations related to post-approval manufacturing changes for biosimilar biological products; clinical pharmacology data to support a demonstration of biosimilarity to a reference product; nonproprietary naming of biological products; and labeling for biosimilar biological products. The proposed goals related to guidance development are described in sections I.I.6 and II of the proposed BsUFA II commitment letter.

G. Improving FDA Hiring and Retention of Review Staff

To speed and improve development of safe and effective biosimilar biological products for patients, FDA must hire and retain sufficient numbers and types of technical and scientific experts to efficiently conduct reviews of 351(k) applications. In order to strengthen this core

function during BsUFA II, FDA proposes to implement a full time equivalent staff-based position management system capability and an online position classification system. In addition, FDA will complete implementation of corporate recruiting practices, augment hiring capacity with expert contractor support, establish a dedicated function for staffing of the human drug review program, establish clear goals for biosimilar review program hiring, and conduct comprehensive and continuous assessments of hiring and retention performance. These enhancements are described in section V of the proposed BsUFA II commitment letter.

H. Enhancing Capacity for Biosimilar Guidance Development, Reviewer Training, and Timely Communication

In order to accelerate patient access to safe and effective biosimilar biological products and ensure accuracy, consistency, and timeliness FDA needs a more focused and better resourced capacity to coordinate key legal, scientific, review, and outreach functions in FDA's development phase advice and premarket review. It is proposed that FDA strengthen its staff capacity to: (1) Develop new regulations and guidance to clarify scientific criteria for biosimilar development and approval, and to provide certainty to industry and other stakeholders on key regulatory issues including the scope of eligible biosimilar biological products; (2) develop or revise manuals of policy and procedures, standard operating procedures, and review templates to facilitate rapid update and application of new policies and guidance by review staff, and to develop and deliver timely, comprehensive training to all Center for Drug Evaluation and Research and Center for Biologics Evaluation and Research review staff and special government employees involved in the review of 351(k) BLAs; (3) deliver timely information to the public to improve public understanding of biosimilarity and interchangeability; and (4) deliver information concerning the date of first licensure and the reference product exclusivity expiry date, to be

included in the Purple Book¹. The language for enhanced capacity is included in section III of the proposed BsUFA II commitment letter.

I. Enhancing Management of User Fee Resources

FDA is committed to enhancing management of BsUFA resources and ensuring BsUFA user fee resources are administered, allocated, and reported in an efficient and transparent manner. In BsUFA II, FDA proposes to establish a resource capacity planning function to improve its ability to analyze current resource needs and project future resource needs, to modernize its time reporting approach, to conduct an evaluation of BsUFA program resource management, to publish a 5-year BsUFA financial plan with annual updates, and to convene an annual public meeting, beginning in FY 2019, to discuss the financial plan and progress towards the financial management enhancements. FDA also proposes to reduce the carryover balance to no greater than 21 weeks of the FY 2022 target revenue by the end of FY 2022. These enhancements are described in section IV of the proposed BsUFA II commitment letter.

J. Enhancements to Fee Structure and Related Mechanisms for Increased Predictability, Stability, and Efficiency

The current BsUFA fee structure references PDUFA fees each fiscal year and calculates biosimilar biological product development program (BPD) fees based on the PDUFA application fee. FDA and industry agreed that the BsUFA II fee structure and the fee setting process could be updated to enhance the predictability and stability of fee amounts and revenues in a manner to improve FDA's ability to engage in long-term financial planning. To address these issues, FDA proposes to discontinue the reduction of the biosimilar biological product application fee by the cumulative BPD fees paid by sponsors, to discontinue the establishment and supplement fees, to

¹ The "Purple Book" lists biological products, including any interchangeable biological products, licensed by FDA under the Public Health Service Act.

rename the product fee as the BsUFA Program fee, to modify the Program fee billing date to minimize the need for multiple billing cycles, and to add a limitation that a sponsor shall not be assessed more than five BsUFA Program fees for a fiscal year for products identified in each distinct approved biosimilar biological product application held by that sponsor.

K. Enhancements to User Fee Revenue Amounts and Adjustments

FDA and industry agreed that the BsUFA II user fee revenue amounts and fee amounts should be independent of PDUFA and based on BsUFA program costs. FDA proposes to establish fees to generate a total of \$45 million in user fee revenue for FY 2018. However, FDA also proposes that it can adjust this amount when setting the user fee amounts published in the FY 2018 Federal Register notice to reflect an updated assessment of the BsUFA workload, with the limitation that this adjustment cannot increase user fee revenue by more than \$9 million (i.e. relative to the \$45 million specified for FY 2018 user fee revenue). To enhance the predictability of user fee amounts, FDA proposes that the amount for each BsUFA fee cannot increase more than 25 percent from the respective FY2018 fee amount until the capacity planning adjustment is effective and that FDA can otherwise modify the amount of the user fee revenue generated from each fee type each fiscal year. FDA proposes to adjust the annual user fee revenue amount for inflation, to develop a robust methodology for adjusting fees based on the capacity needs of the program, and to introduce an annual operating reserve adjustment to provide for adequate carryover resources.

IV. Purpose and Scope of the Meeting

If you wish to attend this meeting, visit <http://bsufapublicmeeting.eventbrite.com>. Please register by October 19, 2016. If you are unable to attend the meeting in person, you can register to view a live Webcast of the meeting. You will be asked to indicate in your registration if you

plan to attend in person or via the Webcast. Seating will be limited, so early registration is recommended. Registration is free and will be on a first-come, first-served basis. However, FDA may limit the number of participants from each organization based on space limitations. Registrants will receive confirmation once they have been accepted. Onsite registration on the day of the meeting will be based on space availability. If you need special accommodations because of a disability, please contact Amanda Roache (see FOR FURTHER INFORMATION CONTACT) at least 7 days before the meeting.

The meeting will include a presentation by FDA and a series of invited panels representing different stakeholder groups identified in the statute (such as patient advocacy groups, consumer advocacy groups, health professionals, and regulated industry). We will also provide an opportunity for other organizations and individuals to make presentations at the meeting or to submit written comments to the docket before the meeting.

FDA will also hold an open public comment period at the meeting to give the public an opportunity to present their comments. Registration for open public comment will occur at the registration desk on the day of the meeting and workshop on a first-come, first-served basis.

Transcripts: As soon as a transcript is available, FDA will post it at <http://www.fda.gov/ForIndustry/UserFees/BiosimilarUserFeeActBsUFA/ucm461774.htm>.

Dated: September 13, 2016.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2016-22442 Filed: 9/16/2016 8:45 am; Publication Date: 9/19/2016]