U.S. FOOD & DRUG ADMINISTRATION

WELCOME

We'll begin the meeting promptly at 9:00am.

U.S. FOOD & DRUG ADMINISTRATION

Public Meeting on the Recommendations for BsUFA III

Tuesday, November 2nd, 2021

Note: A video recording and transcription of today's meeting will be published on the FDA website after this meeting.

Tasha Ray

Center for Drug Evaluation and Research, FDA

Meeting Moderator, Program Evaluation and Implementation Staff,
Office of Program and Strategic Analysis, Office of Strategic Programs

AGENDA

- Welcome and Introduction
- Opening Remarks
- BsUFA Background and Reauthorization Process
- BsUFA III Agreement Overview
- **Break**
- Industry Comments
- Open Public Comment
- Closing Remarks

Patrizia Cavazzoni

Center for Drug Evaluation and Research, FDA

Center Director

BsUFA
Background and Reauthorization Process

Andrew Kish

Center for Drug Evaluation and Research, FDA

Director, Office of Program and Strategic Analysis, Office of Strategic Programs

Basic User Fee Construct

- Congress directed FDA to establish a user fee program for the process for the review of biosimilar biological product applications. Fee funds are added to non-fee appropriated funds and are intended to increase staffing and other resources to speed and enhance review process.
- User fees pay for services that directly benefit fee payers.*
- Fee discussions with industry focus on desired enhancements in terms of specific aspects of activities related to review of biosimilar biological products.
  - What new or enhanced process will the FDA want or industry seek to include in the next 5 years?
  - What is technically feasible?
  - What resources are required to implement and sustain these enhancements?
  - **No discussion of policy** (e.g., FDA does not discuss what its policy decisions will be in guidance)
- Fee discussions also include mechanics of user-fee program (e.g., how fees are collected, fee types, products covered by each fee).
- Medical product user fee programs must be reauthorized every 5 years.

** OMB Circular A-25; direct benefit distinguishes user fees from tax*

BsUFA is still a relatively new program.

- The Biologics Price Competition and Innovation Act of 2009 (BPCI Act) directed FDA to develop recommendations for a user fee program for 351(k) applications for FY 2013 – FY 2017.
- After consultation with regulated industry and public stakeholders, FDA transmitted recommendations to Congress on January 13th, 2012. The Food and Drug Administration Safety and Innovation Act (FDASIA) of 2012 included the first authorization of BsUFA.
- In 2011-2012, there were no marketing applications or products on the market, established drug development process or history related to biosimilar biological products.
- BsUFA is in its 9th year; PDUFA is in its 28th year.
- Since its creation, BsUFA facilitated the approval of 31 biosimilar biological products for the American public.

BsUFA I to BsUFA II

BsUFA I (FDASIA) | 2013-2017

- Referenced PDUFA fee amounts and included fees for products in the development phase in order to generate fee revenue to support FDA's review work during development and enable sponsors to have meetings with FDA early in development.
- Introduced predictable timelines and review process performance goals, primarily modeled on PDUFA, that increased over the course of BsUFA I.

BsUFA II (FDARA) | 2018-2022

- Established an independent, efficient user fee structure based on program costs.
- Implemented a review program ("the Program") to promote the efficiency and effectiveness of the first review cycle and minimize the number of review cycles necessary for biosimilar approval.
- Added commitments to assess the Program, clarify the regulatory pathway, and enhance staff capacity.

This public meeting is one of the last steps in the reauthorization process.

BsUFA REAUTHORIZATION AND REPORTING REQUIREMENTS

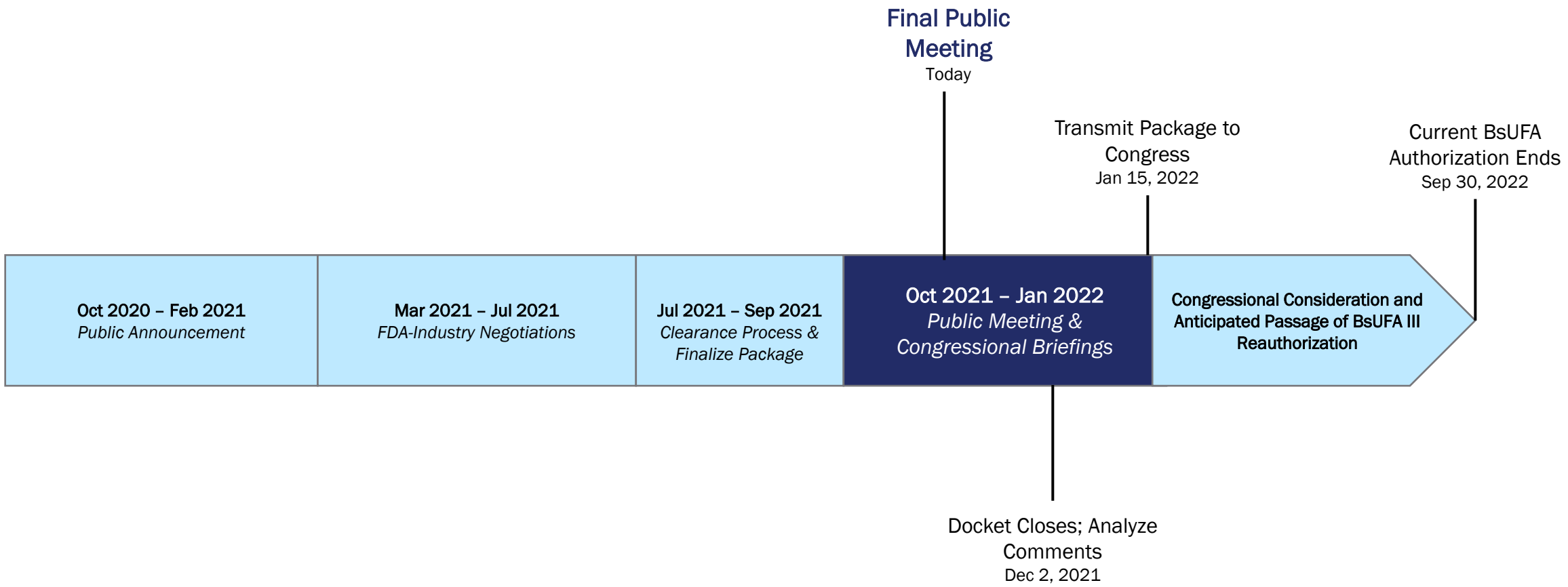
(f) REAUTHORIZATION

(1) CONSULTATION - In developing recommendations to present to the Congress with respect to the goals described in subsection (a), and plans for meeting the goals, for the process for the review of biosimilar biological product applications for the first 5 fiscal years after fiscal year 2022, and for the reauthorization of this subpart for such fiscal years, the Secretary shall consult with- (A) the Committee on Energy and Commerce of the House of Representatives; (B) the Committee on Health, Education, Labor, and Pensions of the Senate; (C) scientific and academic experts; (D) health care professionals; (E) representatives of patient and consumer advocacy groups; and (F) the regulated industry.

(2) PUBLIC REVIEW OF RECOMMENDATIONS - After negotiations with the regulated industry, the Secretary shall- (A) present the recommendations developed under paragraph (1) to the congressional committees specified in such paragraph; (B) publish such recommendations in the Federal Register; (C) provide for a period of 30 days for the public to provide written comments on such recommendations; (D) hold a meeting at which the public may present its views on such recommendations; and (E) after consideration of such public views and comments, revise such recommendations as necessary.

(3) TRANSMITTAL OF RECOMMENDATIONS - Not later than January 15, 2022, the Secretary shall transmit to the Congress the revised recommendations under paragraph (2), a summary of the views and comments received under such paragraph, and any changes made to the recommendations in response to such views and comments.

BsUFA III Reauthorization Timeline



BsUFA III
Agreement Overview

BsUFA III Enhancement Areas

Supplements | Introducing new supplement types and expedited review timelines

Meeting Management | Enhancing communication and feedback during the biosimilar biological development process

Best Practices| Implementing best practices in communication during application review

URRA and Human Factors Timelines | Introducing timelines for review of URRA and Human Factors studies

Inspections| Enhancing pre-licensure inspection communication and clarifying use of alternative tools

Interchangeable Products| Introducing focused effort to advance the development of interchangeable products

Regulatory Science | Introducing new pilot program to enhance regulatory decision-making and facilitate science-based recommendations

Finance | Enhancing financial management and transparency

Hiring and Retention | Focusing on the strategic hiring and retention of world-class technical and scientific staff

Information Technology| Investing in modern technology to support enhanced and streamlined biosimilar product development and review

Sarah Yim

Center for Drug Evaluation and Research, FDA

Director, Office of Therapeutic Biologics and Biosimilars, Office of New Drugs

Supplements (1)

- Introduces new supplement categories and timelines to expedite the review of supplements.
- Includes faster review timelines for safety labeling updates and labeling updates to add or remove an indication where FDA does not need to review efficacy data.
- Depending on the content of the supplement submission, the new timelines are 3 months, 4 months, 6 months, and 10 months from the supplement receipt date.

Supplements (2)

Category	Goal
Category A Supplements	Supplements seeking to update the labeling for a licensed biosimilar or interchangeable product with regards to safety information that has been updated in the reference product labeling and is applicable to one or more indications for which the biosimilar or interchangeable product is licensed.
Category B Supplements	Supplements seeking licensure for an additional indication for a licensed biosimilar or interchangeable product when the submission does not include new data sets (other than analytical in vitro data obtained by use of physical, chemical and/or biological function assays, if needed to support the scientific justification for extrapolation), provided that: 1) The supplement does not seek a new route of administration, dosage form, dosage strength, formulation or presentation; and 2) If the supplement is subject to section 505B(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), the supplement contains an up-to-date agreed initial pediatric study plan (iPSP).

Supplements (3)

Category	Goal
Category C Supplements	Supplements seeking to remove an approved indication for a licensed biosimilar or interchangeable product.
Category D Supplements	Supplements seeking licensure for an additional indication for a licensed biosimilar or interchangeable product when the submission: 1) Contains new data sets (other than efficacy data, data to support a supplement seeking an initial determination of interchangeability, or only analytical in vitro data obtained by use of physical, chemical and/or biological function assays); or 2) Does not contain new data sets (other than analytical in vitro data obtained by use of physical, chemical and/or biological function assays) but is subject to section 505B(a) of the FD&C Act, and the supplement does not contain an up-to-date agreed iPSP.
Category E Supplements	Supplements seeking licensure for an additional indication for a licensed biosimilar or interchangeable product and containing efficacy data sets.
Category F Supplements	Supplements seeking an initial determination of interchangeability.

Supplements (4)

Category	Goal
Original Biosimilar Biological Product Applications	90% in 10 months of the 60 day filing date
Resubmitted Original Biosimilar Biological Product Applications	90% in 6 months of the receipt date
Category A Supplements (original and resubmitted)	• FY 2023: 70% in 3 months of the receipt date • FY 2024: 80% in 3 months of the receipt date • FY 2025-2027: 90% in 3 months of the receipt date
Category B and C Supplements (original and resubmitted)	• FY 2023: 70% in 4 months of the receipt date • FY 2024: 80% in 4 months of the receipt date • FY 2025-2027: 90% in 4 months of the receipt date
Category D Supplements (original and resubmitted)	• FY 2023: 70% in 6 months of the receipt date • FY 2024: 80% in 6 months of the receipt date • FY 2025-2027: 90% in 6 months of the receipt date
Original Category E and F Supplements	90% in 10 months of the receipt date
Resubmitted Category E and F Supplements	90% in 6 months of the receipt date

Meeting Management

- Modifies the Biosimilar Initial Advisory (BIA) meeting to specify that preliminary comparative analytical data is not required to meet with FDA. BIA meetings are an initial assessment limited to a general discussion regarding whether licensure under the 351 (k) pathway may be feasible for a particular product.
- Introduces a new BPD meeting type, Type 2a, focused on a narrow set of issues requiring input from no more than 3 disciplines or review divisions. The new meeting type reduces the meeting scheduled or written response time from 90 to 60 calendar days compared to traditional Type 2 meetings under BsUFA II. Maintains the traditional type 2 meetings, now called Type 2b meetings in BsUFA III.
- Modifies timing of background packages for BPD Type 4 meetings, so they may be submitted up to 14 days after FDA receipt of the written meeting request (previously packages were submitted with the written request).
- Consistent with the PDUFA VII Commitment Letter, introduces a new follow-up opportunity for sponsors to submit clarifying questions after meetings or Written Response Only (WRO) responses to ensure sponsors' understanding of FDA feedback.
- Includes updating meetings guidance, MAPPs, and SOPPs accordingly.

Best Practices in Communication During Application Review

- Building on lessons learned during BsUFA II, commits to **updating relevant guidances, MAPPs, and SOPPs** to reflect best practices in communication during application review.

Improving Predictability in Human Factors (HFs) and Use-Related Risk Analyses (URRAs) Reviews

- New procedures and review timelines for use-related risk analysis and human factor validation study protocols to advance the development of biosimilar biologic-device combination products.
- Includes guidance on considerations related to combination products.

These commitments are consistent with the PDUFA VII Commitment Letter.

Laurie Graham

Center for Drug Evaluation and Research, FDA

Director, Division of Internal Policies and Programs, Office of Policy for Pharmaceutical Quality, Office of Pharmaceutical Quality

Enhancing Inspection Communication and Alternative Tools

- Includes goal for FDA to notify sponsors at least 60 days in advance and no later than mid-cycle of the pre-licensure inspections for applications, not including supplements, where FDA needs to see the product being manufactured. FDA reserves the right to conduct inspections at any time during the review cycle, whether or not they've communicated to the facility the intent to inspect.
- Commits to guidance on FDA's thinking on the use of alternative tools to assess manufacturing facilities named in pending applications beyond the COVID-19 pandemic. Examples of alterative tools include requesting existing inspection reports from other trusted foreign regulatory partners through mutual recognition and confidentiality agreements, requesting information from applicants, requesting records and other information directly from facilities and other inspected entities, and, as appropriate, utilizing new or existing technology platforms to assess manufacturing facilities.

These commitments are consistent with the PDUFA VII Commitment Letter.

Advancing the Development of Interchangeable Products (1)

- Introduces focused effort to further advance the development of safe and effective interchangeable biosimilar biological products.
- **Research:**
  - Leverages the BsUFA III Regulatory Science Pilot Program *(covered in upcoming slide).*
- **Stakeholder engagement:**
  - Includes a scientific workshop on the development of interchangeable products to help identify future needs.
  - Issuance of draft and final strategy documents that outline the specific actions the agency will take to facilitate the development of interchangeable biosimilar biological products.

Advancing the Development of Interchangeable Products (2)

- **Foundational guidance development:**
  - Includes 4 draft guidances, with revised/final guidances published within 18 months after the close of the public comment period.
    1. Guidance describing considerations for developing presentations, container closure systems and device constituent parts for proposed interchangeable biosimilar biological products
    2. Guidance on labeling for interchangeable biosimilar biological products
    3. Guidance on promotional labeling and advertising considerations for interchangeable biosimilar biological products
    4. Guidance on the nature and type of information, for different reporting categories, a sponsor should provide to support post-approval manufacturing changes to approved biosimilar and interchangeable biosimilar biological products

Steven Kozlowski

Center for Drug Evaluation and Research, FDA

Director, Office of Biotechnology Products, Office of Pharmaceutical Quality

Regulatory Science (1)

- Pilots a BsUFA regulatory science program broadly applicable to biosimilar and interchangeable biological product development, with project goals not specific to a product or product class.
- **Two demonstration projects:**
  - Advancing the Development of Interchangeable Products
    - Investigate and evaluate the data and information (including Real World Evidence) needed to meet the safety standards for determining interchangeability under section 351(k)(4) of the PHS Act.
  - Improving the Efficiency of Biosimilar Product Development
    - Research to advance the efficiency of biosimilar product development, enhance regulatory decision-making based on the latest scientific knowledge, and advance the use of innovative scientific methodologies and experience with biosimilars.

Regulatory Science (2)

- **Stakeholder engagement:**
  - Includes a public meeting at the midpoint to review progress and solicit input on future priorities and issuing an interim report on project progress, in advance of the meeting.
  - Includes publishing a final summary report on pilot outcomes.
- **Deliverables:**
  - Includes publication of a comprehensive strategy document within 12 months of completing the projects.

Joshua Barton

Center for Drug Evaluation and Research, FDA

Director, Resource Capacity Planning Staff, Office of Program and Strategic Analysis, Office of Strategic Programs

Finance: Maturing the Capacity Planning Function

- Includes publication of an implementation plan outlining continual improvement of the Capacity Planning Adjustment (CPA) and integration of resource capacity planning analyses in the Agency's resource and operational decision-making processes.
- Provides annual updates on progress made on the activities outlined in the implementation plan and documentation of how CPA funds are used in the annual financial report.
- Includes a 3rd party evaluation of the resource capacity planning capability.

These commitments are consistent with the PDUFA VII Commitment Letter.

Finance: Continuing Transparency on Financial Plan and Commitments

- Continues the BsUFA II commitments of publishing a 5-year financial plan and holding a public meeting to discuss the plan and other financial commitments every fiscal year.
- Includes new commitments to share information in 5-year financial plan on the following:
    - Personnel compensation and benefits (PC&B) costs that exceed the funds provided by the PC&B portion of the inflation adjustment. This is related to the new strategic hiring and retention adjustment.
    - FDA's plan for managing costs related to personnel beyond BsUFA III.
    - Provide updates on its progress towards implementing its plan to reduce the carryover balance as outlined in the FY 2022 BsUFA financial report and the five-year financial plan.

Finance: Modifications to Fee Adjustments

- Introduces modifications to the capacity planning adjustment to clarify the scope of the inputs used in the methodology.
- Includes a new strategic hiring and retention adjustment to provide funding to cover costs for retaining and hiring highly qualified scientific and technical staff for the BsUFA program.
- Includes enhancements to the operating reserve adjustment to manage financial risks to the program by establishing a minimum amount and maximum amount of available operating reserves to be maintained each year.
    - The defined minimum amount is equivalent to 10 weeks of operations.
    - The defined maximum amount is 21 weeks phased in over the first three years of BsUFA III: 33 weeks in FY23, 27 weeks in FY24, 21 weeks in FY25 and each subsequent year.

Hiring and Retention: Continuing Transparency on Hiring Progress

- Continues quarterly reporting on FDA’s progress toward meeting annual hiring goals in BsUFA III on FDA's website.
- Includes a third-party assessment of hiring and retention practices.

These commitments are consistent with the PDUFA VII Commitment Letter.

Information Technology Goals

- Establishes a **Data and Technology Modernization Strategy** that reflects the FDA's Technology and Data Modernization Action Plan.
- Includes monitoring and modernizing the **Electronic Submission Gateway (ESG).**

These commitments are consistent with the PDUFA VII Commitment Letter.

U.S. FOOD & DRUG ADMINISTRATION

BREAK

We'll return promptly at 10:05am (ET).

Note: A video recording and transcription of today's meeting will be published on the FDA website after this meeting.

Industry Comments

Cory Wohlbach

Association for Accessible Medicines

Global Vice President, Biosimilar & Gx Steriles Regulatory Affairs, Teva Pharmaceuticals

Camelia Thompson

Biotechnology Innovation Organization

Senior Director, Science & Regulatory Affairs

Lucy Vereshchagina

Pharmaceutical Research and Manufacturers of America

Vice President, Science and Regulatory Advocacy

Meaghan Smith

Biosimilars Forum

Executive Director

Public Comment

Public Commenters

Cate Lockhart
Biologics & Biosimilars Collective Intelligence Consortium

Radia Hocini
El Kendi Pharmaceutical

Geetanjali Saini
Abhilashi College of Pharmacy

Andrew Spiegel
Global Colon Cancer Association

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THANK YOU