

1 **BIOSIMILAR BIOLOGICAL PRODUCT**  
2 **REAUTHORIZATION PERFORMANCE GOALS**  
3 **AND PROCEDURES FISCAL YEARS 2023**  
4 **THROUGH 2027**

5 **I. ENSURING THE EFFECTIVENESS OF THE BIOSIMILAR BIOLOGICAL**  
6 **PRODUCT REVIEW PROGRAM**

7 A. Review Performance Goals

8 B. Program for Enhanced Review Transparency and Communication for Original 351(k)  
9 BLAs

10 C. Guidance

11 D. Review of Proprietary Names to Reduce Medication Errors

12 E. Major Dispute Resolution

13 F. Clinical Holds

14 G. Special Protocol Question Assessment and Agreement

15 H. Meeting Management Goals

16 **II. ENHANCING BIOSIMILAR AND INTERCHANGEABLE BIOLOGICAL**  
17 **PRODUCT DEVELOPMENT AND REGULATORY SCIENCE**

18 A. Promoting Best Practices in Communication between FDA and Sponsors During  
19 Application Review

20 B. Inspections and Alternate Tools to Evaluate Facilities

21 C. Advancing Development of Biosimilar Biological-Device Combination Products  
22 Regulated by CDER and CBER

23 D. Advancing Development of Interchangeable Biosimilar Biological Products

24 E. Regulatory Science to Enhance the Development of Biosimilar and Interchangeable  
25 Biological Products

26 **III. CONTINUED ENHANCEMENT OF USER FEE RESOURCE MANAGEMENT**

27 A. Resource Capacity Planning

28	<b>B.</b>	Financial Transparency
29	<b>C.</b>	Management of Carryover Balance
30	<b>IV.</b>	<b>IMPROVING FDA HIRING AND RETENTION OF REVIEW STAFF</b>
31	<b>A.</b>	Set Clear Goals for Biosimilar Biological Product Review Program Hiring
32	<b>B.</b>	Comprehensive and Continuous Assessment of Hiring and Retention
33	<b>V.</b>	<b>INFORMATION TECHNOLOGY GOALS</b>
34	<b>A.</b>	Develop Data and Technology Modernization Strategy
35	<b>B.</b>	Monitor and Modernize Electronic Submission Gateway (ESG)
36	<b>VI.</b>	<b>DEFINITIONS AND EXPLANATION OF TERMS</b>

# **BIOSIMILAR BIOLOGICAL PRODUCT AUTHORIZATION PERFORMANCE GOALS AND PROCEDURES FOR FISCAL YEARS 2023 THROUGH 2027**

This document contains the performance goals and procedures for the Biosimilar User Fee Act (BsUFA) reauthorization for fiscal years (FYs) 2023-2027, known as BsUFA III. It is commonly referred to as the “goals letter” or “commitment letter.” The goals letter represents the product of FDA’s discussions with the regulated industry and public stakeholders, as mandated by Congress. The performance and procedural goals and other commitments specified in this letter apply to aspects of the biosimilar biological product review program that are important for facilitating timely access to safe and effective biosimilar medicines for patients. FDA is committed to meeting the performance goals specified in this letter, enhancing management of BsUFA resources, and ensuring BsUFA user fee resources are administered, allocated, and reported in an efficient and transparent manner.

Under BsUFA III, FDA is committed to ensuring effective scientific coordination and review consistency, as well as efficient governance and operations across the biosimilar biological product review program.

FDA and the regulated industry will periodically and regularly assess the progress of the biosimilar biological product review program throughout BsUFA III. This will allow FDA and the regulated industry to identify emerging challenges and develop strategies to address these challenges to ensure the efficiency and effectiveness of the biosimilar biological product review program.

# I. ENSURING THE EFFECTIVENESS OF THE BIOSIMILAR BIOLOGICAL PRODUCT REVIEW PROGRAM

## A. REVIEW PERFORMANCE GOALS

### 1. Original and Resubmitted Biosimilar Biological Product Applications

- a. Review and act on 90 percent of original biosimilar biological product application submissions within 10 months of the 60 day filing date.
- b. Review and act on 90 percent of resubmitted original biosimilar biological product applications within 6 months of receipt.

### 2. Original and Resubmitted Supplemental Biosimilar Biological Product Applications

- a. Review and act on the following supplements within 3 months of receipt:
  - i. **Category A:** 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.
- b. Review and act on the following supplements within 4 months of receipt:
  - i. **Category B:** 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).
  - ii. **Category C:** Supplements seeking to remove an approved indication for a licensed biosimilar or interchangeable product.
- c. Review and act on the following supplements within 6 months of receipt:
  - i. **Category D:** 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.
- d. Review and act on the following supplements within 10 months of receipt for the original submissions, and within 6 months of receipt for resubmissions:
- i. **Category E:** Supplements seeking licensure for an additional indication for a licensed biosimilar or interchangeable product and containing efficacy data sets.
  - ii. **Category F:** Supplements seeking an initial determination of interchangeability.
- e. FDA will issue a letter to the applicant for 90% of original Category A through D supplements within 60 calendar days of receipt. The letter will acknowledge receipt of the submission and provide the date for FDA to take action on the supplement.
- i. Applicants may include in their cover letter a request that FDA not approve the supplement before a certain date, as long as that date is not later than the BsUFA goal date.
- f. A filing letter will be issued to the applicant for 90% of original Category E and F supplements within 74 calendar days of receipt. Consistent with the underlying principles articulated in the Good Review Management Principles and Practices (GRMP) guidance, the letter will acknowledge receipt of the submission and inform the applicant of the planned review timeline and whether substantive review issues were identified. If no substantive review issues were identified during the filing review, FDA will so notify the applicant.

### **3. Original Manufacturing Supplements**

- a. Review and act on 90 percent of manufacturing supplements requiring prior approval within 4 months of receipt.
- b. Review and act on 90 percent of all other manufacturing supplements within 6 months of receipt.

### **4. Goals Summary Tables**

**Table 1: Original and Resubmitted Applications and Category A- F Supplements**

<p><b>Original Biosimilar Biological Product Application Submissions</b></p>	<p>90% in 10 months of the 60 day filing date</p>
<p><b>Resubmitted Original Biosimilar Biological Product Applications</b></p>	<p>90% in 6 months of the receipt date</p>
<p><b>Category A Supplements</b></p> <ul style="list-style-type: none"> <li>• (original and resubmitted)</li> </ul>	<ul style="list-style-type: none"> <li>• FY 2023: 70% in 3 months of the receipt date</li> <li>• FY 2024: 80% in 3 months of the receipt date</li> <li>• FY 2025: 90% in 3 months of the receipt date</li> <li>• FY 2026: 90% in 3 months of the receipt date</li> <li>• FY 2027: 90% in 3 months of the receipt date</li> </ul>
<p><b>Category B and C Supplements</b></p> <ul style="list-style-type: none"> <li>• (original and resubmitted)</li> </ul>	<ul style="list-style-type: none"> <li>• FY 2023: 70% in 4 months of the receipt date</li> <li>• FY 2024: 80% in 4 months of the receipt date</li> <li>• FY 2025: 90% in 4 months of the receipt date</li> <li>• FY 2026: 90% in 4 months of the receipt date</li> <li>• FY 2027: 90% in 4 months of the receipt date</li> </ul>
<p><b>Category D Supplements</b></p> <ul style="list-style-type: none"> <li>• (original and resubmitted)</li> </ul>	<ul style="list-style-type: none"> <li>• FY 2023: 70% in 6 months of the receipt date</li> <li>• FY 2024: 80% in 6 months of the receipt date</li> <li>• FY 2025: 90% in 6 months of the receipt date</li> <li>• FY 2026: 90% in 6 months of the receipt date</li> <li>• FY 2027: 90% in 6 months of the receipt date</li> </ul>
<p><b>Original Category E and F Supplements</b></p>	<p>90% in 10 months of the receipt date</p>

<b>Resubmitted Category E and F Supplements</b>	90% in 6 months of the receipt date
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**Table 2: Manufacturing Supplements**

	<b>PRIOR APPROVAL</b>	<b>ALL OTHER</b>
<b>Manufacturing Supplements</b>	90% in 4 months of the receipt date	90% in 6 months of the receipt date

**5. Review Performance Goal Extensions**

a. Major Amendments

- i. A major amendment to an original application, supplement with clinical data, or resubmission of any of these applications, submitted at any time during the review cycle, may extend the goal date by three months.
- ii. A major amendment may include, for example, a major new clinical study report; major re-analysis of previously submitted study(ies); submission of a risk evaluation and mitigation strategy (REMS) with elements to assure safe use (ETASU) not included in the original application; or significant amendment to a previously submitted REMS with ETASU. Generally, changes to REMS that do not include ETASU and minor changes to REMS with ETASU will not be considered major amendments.
- iii. A major amendment to a manufacturing supplement submitted at any time during the review cycle may extend the goal date by two months.
- iv. Only one extension can be given per review cycle.
- v. Consistent with the underlying principles articulated in the Good Review Management Principles and Practices (GRMP) guidance, FDA’s decision to extend the review clock should, except in rare circumstances, be limited to occasions where review of the new information could address outstanding deficiencies in the application and lead to approval in the current review cycle.

b. Inspection of Facilities Not Adequately Identified in an Original Application or Supplement

- i. All original applications and supplements are expected to include a comprehensive and readily located list of all manufacturing facilities included or referenced in the application or supplement. This list provides FDA with information needed to schedule inspections of manufacturing facilities that may be necessary before approval of the original application or supplement.
- ii. If, during FDA’s review of an original application or supplement, the Agency identifies a manufacturing facility that was not included in the comprehensive and readily located list, the goal date may be extended.
  - 1) If FDA identifies the need to inspect a manufacturing facility that is not included as part of the comprehensive and readily located list in an original application or supplement with clinical data, the goal date may be extended by three months.
  - 2) If FDA identifies the need to inspect a manufacturing facility that is not included as part of the comprehensive and readily located list in a manufacturing supplement, the goal date may be extended by two months.

## **B. PROGRAM FOR ENHANCED REVIEW TRANSPARENCY AND COMMUNICATION FOR ORIGINAL 351(k) BLAs**

To promote transparency and communication between the FDA review team and the applicant, FDA will apply the following model (“the Program”) to the review of all original Biologics License Applications (BLAs) submitted under section 351(k) of the Public Health Service Act (“351(k) BLAs”), including applications that are resubmitted following a Refuse-to-File decision, received from October 1, 2022, through September 30, 2027.<sup>1</sup> The goal of the Program is to promote the efficiency and effectiveness of the first cycle review process and minimize the number of review cycles necessary for approval, ensuring that patients have timely access to safe, effective, and high quality biosimilar and interchangeable biological products.

The standard approach for the review of original 351(k) BLAs is described in this section. However, the FDA review team and the applicant may discuss and reach mutual agreement on an alternative approach to the timing and nature of interactions and information exchange between the applicant and FDA, i.e., a Formal Communication Plan for the review of the original 351(k) BLA. The Formal Communication Plan may include elements of the standard approach (e.g., a mid-cycle communication or a late-cycle meeting) as well as other interactions that

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<sup>1</sup> The “Program for Enhanced Review Transparency and Communication for Original 351(k) BLAs” (referred to as “the Program” and described in this goals letter) is distinct from the statutory term, “biosimilar biological product development program,” which is defined in section 744G of the Federal Food, Drug, and Cosmetic (FD&C Act) as “the program under [the statutory BsUFA fee provisions] for expediting the process for the review of submissions in connection with biosimilar biological product development.” Section 744G(6) of the FD&C Act.



sometimes occur during the review process (e.g., a meeting during the filing period to discuss the application, i.e., an “application orientation meeting”). If appropriate, the Formal Communication Plan should specify those elements of the Program that FDA and the sponsor agree are unnecessary for the application under review. If the review team and the applicant anticipate developing a Formal Communication Plan, the elements of the plan should be discussed and agreed to at the pre-submission meeting (see Section I.B.1) and reflected in the meeting minutes. The Formal Communication Plan may be reviewed and amended at any time based on the progress of the review and the mutual agreement of the review team and the applicant. For example, the review team and the applicant may mutually agree at any time to cancel future specified interactions in the Program (e.g., the late-cycle meeting) that become unnecessary (e.g., because previous communications between the review team and the applicant are sufficient). Any amendments made to the Formal Communication Plan should be consistent with the goal of an efficient and timely first cycle review process and not impede the review team’s ability to conduct its review.

The remainder of this Section I.B. describes the parameters that will apply to FDA’s review of applications in the Program.

1. **Pre-submission meeting:** The applicant is strongly encouraged to discuss the planned content of the application with the appropriate FDA review division at a BPD Type 4 (pre-351(k) BLA) meeting. This meeting will be attended by the FDA review team, including appropriate senior FDA staff.
  - a. The BPD Type 4 (pre-351(k) BLA) meeting should be held sufficiently in advance of the planned submission of the application to allow for meaningful response to FDA feedback and should generally occur not less than 2 months prior to the planned submission of the application.
  - b. In addition to FDA’s preliminary responses to the applicant’s questions, other potential discussion topics include preliminary discussions regarding the approach to developing the content for REMS, where applicable, patient labeling (e.g., Medication Guide and Instructions For Use) and, where applicable, the development of a Formal Communication Plan. These discussions will be summarized at the conclusion of the meeting and reflected in the FDA meeting minutes.

The FDA and the applicant will agree on the content of a complete application for the proposed indication(s) at the pre-submission meeting. The FDA and the applicant may also reach agreement on submission of a limited number of application components not later than 30 calendar days after the submission of the original application. These submissions must be of a type that would not be expected to materially impact the ability of the review team to begin its review. These agreements will be summarized at the conclusion of the meeting and reflected in the FDA meeting minutes.

- i. Examples of application components that may be appropriate for delayed submission include; stability updates, the final audited report of a preclinical study (e.g., toxicology) where the final draft report is submitted with the original application, or a limited amount of the data from an assessment of a single transition from the reference product to the proposed biosimilar biological product, where applicable.
  - ii. Major components of the application (e.g., the complete analytical similarity assessment, the complete study report of a comparative clinical study or the full study report of necessary immunogenicity data) are expected to be submitted with the original application and are not subject to agreement for late submission.
2. **Original application submission:** Applications are expected to be complete, as agreed between the FDA review team and the applicant at the BPD Type 4 (pre-351(k) BLA) meeting, at the time of original submission of the application. If the applicant does not have a BPD Type 4 (pre-351(k) BLA) meeting with FDA, and no agreement exists between FDA and the applicant on the contents of a complete application or delayed submission of certain components of the application, the applicant's submission is expected to be complete at the time of original submission.
  - a. All applications are expected to include a comprehensive and readily located list of all clinical sites and manufacturing facilities included or referenced in the application.
  - b. Any components of the application that FDA agreed at the pre-submission meeting could be submitted after the original application are expected to be received not later than 30 calendar days after receipt of the original application.
  - c. Incomplete applications, including applications with components that are not received within 30 calendar days after receipt of the original submission, will be subject to a Refuse-to-File decision.
  - d. The following parameters will apply to applications that are subject to a Refuse-to-File decision and are subsequently filed over protest:
    - i. The original submission of the application will be subject to the review performance goal as described in Section I.A.1.a.
    - ii. The application will not be eligible for the other parameters of the Program (e.g., mid-cycle communication, late-cycle meeting).
    - iii. FDA generally will not review amendments to the application during any review cycle. FDA also generally will not issue information requests to the applicant during the agency's review.

- iv. The resubmission goal described in Section I.A.1.b will not apply to any resubmission of the application following an FDA complete response action. Any such resubmission will be reviewed as available resources permit.
  - e. Since applications are expected to be complete at the time of submission, unsolicited amendments are expected to be rare and not to contain major new information or analyses. Review of unsolicited amendments, including those submitted in response to an FDA communication of deficiencies, will be handled in accordance with the GRMP guidance. This guidance includes the underlying principle that FDA will consider the most efficient path toward completion of a comprehensive review that addresses application deficiencies and leads toward a first cycle approval when possible.
3. **Day 74 Letter:** FDA will follow existing procedures regarding identification and communication of substantive review issues identified during the initial filing review to the applicant in the “Day 74 letter.” If no substantive review issues were identified during the filing review, FDA will so notify the applicant. FDA’s filing review represents a preliminary review of the application and is not indicative of deficiencies that may be identified later in the review cycle.

For applications subject to the Program, the timeline for this communication will be within 74 calendar days from the date of FDA receipt of the original submission. The planned timeline for review of the application included in the Day 74 letter for applications in the Program will include:

- a. the planned date for the internal mid-cycle review meeting,
  - b. preliminary plans on whether to hold an Advisory Committee (AC) meeting to discuss the application,
  - c. a target date for communication of feedback from the review division to the applicant regarding proposed labeling and any postmarket requirements or postmarket commitments the Agency will be requesting.
4. **Review performance goals:** For original 351(k) BLA submissions that are filed by FDA under the Program, the BsUFA review clock will begin at the conclusion of the 60 calendar day filing review period that begins on the date of FDA receipt of the original submission. The review performance goals for these applications are as follows:
- a. Review and act on 90 percent of original 351(k) BLA submissions within 10 months of the 60 day filing date.
5. **Mid-Cycle Communication:** The FDA Regulatory Project Manager (RPM), and other appropriate members of the FDA review team (e.g., Cross Discipline Team Leader (CDTL)), will call the applicant, generally within 2 weeks following the Agency’s internal mid-cycle review meeting, to provide the applicant with an

update on the status of the review of their application. An agenda will be sent to the applicant prior to the mid-cycle communication. Scheduling of the internal mid-cycle review meeting will be handled in accordance with the GRMP guidance. The RPM will coordinate the specific date and time of the telephone call with the applicant.

The update should include any significant issues identified by the review team to date, any information requests, and information regarding major concerns with the following:

- a. The analytical similarity data, including the potential relevance of any issues (e.g. data analysis issues or potential clinical impact of observed analytical differences), intended to support a demonstration that the proposed biosimilar biological product is highly similar to the reference product.
- b. The data intended to support a demonstration of no clinically meaningful differences, including discussion of any immunogenicity issues.
- c. The data intended to support a demonstration of interchangeability.
- d. CMC issues.

In addition, the update should include preliminary review team thinking regarding the content of the proposed REMS, where applicable, proposed date(s) for the late-cycle meeting, updates regarding plans for the AC meeting (if an AC meeting is anticipated), and other projected milestone dates for the remainder of the review cycle.

6. **Late-Cycle and Advisory Committee Meetings:** A meeting will be held between the FDA review team and the applicant to discuss the status of the review of the application late in the review cycle. Late-cycle meetings will generally be face-to-face meetings; however, the meeting may be held by teleconference if FDA and the applicant agree. Since the application is expected to be complete at the time of submission, FDA intends to complete primary and secondary reviews of the application in advance of the planned late-cycle meeting.
  - a. FDA representatives at the late-cycle meeting are expected to include the signatory authority for the application, review team members from appropriate disciplines, and appropriate team leaders and/or supervisors from disciplines for which substantive issues have been identified in the review to date.
  - b. For applications that will be discussed at an Advisory Committee (AC) meeting, the following parameters apply:
    - i. FDA intends to convene AC meetings no later than 2 months prior to the BsUFA goal date. The late-cycle meeting will occur not less than 12 calendar days before the date of the AC meeting.

- ii. FDA intends to provide final questions for the AC to the sponsor and the AC not less than 2 calendar days before the AC meeting.
  - iii. Following an AC meeting, FDA and the applicant may agree on the need to discuss feedback from the committee for the purpose of facilitating the remainder of the review. Such a meeting will generally be held by teleconference without a commitment for formal meeting minutes issued by the agency.
- c. For applications that will not be discussed at an AC meeting, the late-cycle meeting will generally occur not later than 3 months prior to the BsUFA goal date.
- d. Late-Cycle Meeting Background Packages: The Agency background package for the late-cycle meeting will be sent to the applicant not less than 10 calendar days before the late-cycle meeting. The package will consist of any discipline review (DR) letters issues to date, a brief memorandum from the review team outlining substantive application issues (e.g., deficiencies identified by primary and secondary reviews), the Agency's background package for the AC meeting (incorporated by reference if previously sent to the applicant), potential questions and/or points for discussion for the AC meeting (if planned) and the current assessment of the content of proposed REMS or other risk management actions, where applicable.
- e. Late-Cycle Meeting Discussion Topics: Potential topics for discussion at the late-cycle meeting include:
  - i. major deficiencies identified to date;
  - ii. analytical similarity data, including the potential relevance of any issues (e.g. data analysis issues or potential clinical impact of observed analytical differences), intended to support a demonstration that the proposed biosimilar biological product is highly similar to the reference product;
  - iii. data intended to support a demonstration of no clinically meaningful differences, including discussion of any immunogenicity issues;
  - iv. data intended to support a demonstration of interchangeability;
  - v. CMC issues;
  - vi. inspectional findings identified to date;
  - vii. issues to be discussed at the AC meeting (if planned);
  - viii. current assessment of the content of proposed REMS or other risk management actions, where applicable;

- ix. information requests from the review team to the applicant; and additional data or analyses the applicant may wish to submit.

With regard to submission of additional data or analyses, the FDA review team and the applicant will discuss whether such data will be reviewed by the Agency in the current review cycle and, if so, whether the submission will be considered a major amendment and trigger an extension of the BsUFA goal date.

- 7. **Inspections:** FDA's goal is to complete all GCP, GLP, and GMP inspections for applications in the Program within 10 months of the date of original receipt of the application. This will allow 2 months at the end of the review cycle to attempt to address any deficiencies identified by the inspections.

### **C. GUIDANCE**

FDA and industry share a commitment to ensuring an efficient and effective review process for all applications subject to the BsUFA program.

In light of the new, expedited timelines for supplements, FDA will issue guidance and/or a MAPP on classifying supplements to a licensed 351(k) BLA for purposes of determining review timelines. FDA will publish a draft guidance for public comment and/or a MAPP no later than the end of FY 2023. FDA will work toward the goal of publishing a revised draft or final guidance within 18 months after the close of the public comment period.

### **D. REVIEW OF PROPRIETARY NAMES TO REDUCE MEDICATION ERRORS**

To enhance patient safety, FDA is committed to various measures to reduce medication errors related to look-alike and sound-alike proprietary names and such factors as unclear label abbreviations, acronyms, dose designations, and error prone label and packaging design. The following performance goals apply to FDA's review of biosimilar biological product proprietary names during the biosimilar biological product development (BPD) phase and during FDA's review of a marketing application:

#### **1. Proprietary Name Review Performance Goals During The BPD Phase**

- a. Review 90% of proprietary name submissions filed within 180 days of receipt. Notify sponsor of tentative acceptance or non-acceptance.
- b. If the proprietary name is found to be unacceptable, the sponsor can request reconsideration by submitting a written rebuttal with supporting data or request a meeting within 60 days to discuss the initial decision (meeting package required).

- c. If the proprietary name is found to be unacceptable, the above review performance goals also would apply to the written request for reconsideration with supporting data or the submission of a new proprietary name.
- d. A complete submission is required to begin the review clock.

**2. Proprietary Name Review Performance Goals During Application Review**

- a. Review 90% of biosimilar biological product proprietary name submissions filed within 90 days of receipt. Notify sponsor of tentative acceptance/non-acceptance.
- b. A supplemental review will be done meeting the above review performance goals if the proprietary name has been submitted previously (during the BPD phase) and has received tentative acceptance.
- c. If the proprietary name is found to be unacceptable, the sponsor can request reconsideration by submitting a written rebuttal with supporting data or request a meeting within 60 days to discuss the initial decision (meeting package required).
- d. If the proprietary name is found to be unacceptable, the above review performance goals apply to the written request for reconsideration with supporting data or the submission of a new proprietary name.
- e. A complete submission is required to begin the review clock.

**E. MAJOR DISPUTE RESOLUTION**

- 1. **Procedure:** For procedural or scientific matters involving the review of biosimilar biological product applications and supplements (as defined in BsUFA) that cannot be resolved at the signatory authority level (including a request for reconsideration by the signatory authority after reviewing any materials that are planned to be forwarded with an appeal to the next level), the response to appeals of decisions will occur within 30 calendar days of the Center's receipt of the written appeal.
- 2. **Performance goal:** 90% of such responses are provided within 30 calendar days of the Center's receipt of the written appeal.
- 3. **Conditions:**
  - a. Sponsors should first try to resolve the procedural or scientific issue at the signatory authority level. If it cannot be resolved at that level, it should be appealed to the next higher organizational level (with a copy to the signatory authority) and then, if necessary, to the next higher organizational level.

- b. Responses should be either verbal (followed by a written confirmation within 14 calendar days of the verbal notification) or written and should ordinarily be to either grant or deny the appeal.
- c. If the decision is to deny the appeal, the response should include reasons for the denial and any actions the sponsor might take to persuade the Agency to reverse its decision.
- d. In some cases, further data or further input from others might be needed to reach a decision on the appeal. In these cases, the “response” should be the plan for obtaining that information (e.g., requesting further information from the sponsor, scheduling a meeting with the sponsor, scheduling the issue for discussion at the next scheduled available advisory committee).
- e. In these cases, once the required information is received by the Agency (including any advice from an advisory committee), the person to whom the appeal was made, again has 30 calendar days from the receipt of the required information in which to either deny or grant the appeal.
- f. Again, if the decision is to deny the appeal, the response should include the reasons for the denial and any actions the sponsor might take to persuade the Agency to reverse its decision.
- g. Note: If the Agency decides to present the issue to an advisory committee and there are not 30 days before the next scheduled advisory committee, the issue will be presented at the following scheduled committee meeting to allow conformance with advisory committee administrative procedures.

## **F. CLINICAL HOLDS**

1. **Procedure:** The Center should respond to a sponsor’s complete response to a clinical hold within 30 days of the Agency’s receipt of the submission of such sponsor response.
2. **Performance goal:** 90% of such responses are provided within 30 calendar days of the Agency’s receipt of the sponsor’s response.

## **G. SPECIAL PROTOCOL QUESTION ASSESSMENT AND AGREEMENT**

1. **Procedure:** Upon specific request by a sponsor (including specific questions that the sponsor desires to be answered), the Agency will evaluate certain protocols and related issues to assess whether the design is adequate to meet scientific and regulatory requirements identified by the sponsor.
  - a. The sponsor should submit a limited number of specific questions about the protocol design and scientific and regulatory requirements for which the sponsor seeks agreement (e.g., are the clinical endpoints adequate to assess



whether there are clinically meaningful differences between the proposed biosimilar biological product and the reference product).

- b. Within 45 days of Agency receipt of the protocol and specific questions, the Agency will provide a written response to the sponsor that includes a succinct assessment of the protocol and answers to the questions posed by the sponsor. If the Agency does not agree that the protocol design, execution plans, and data analyses are adequate to achieve the goals of the sponsor, the reasons for the disagreement will be explained in the response.
  - c. Protocols that qualify for this program include any necessary clinical study or studies to prove biosimilarity and/or interchangeability (e.g., protocols for pharmacokinetics and pharmacodynamics studies, protocols for comparative clinical studies that will form the primary basis for demonstrating that there are no clinically meaningful differences between the proposed biosimilar biological product and the reference product, and protocols for clinical studies intended to support a demonstration of interchangeability). For such protocols to qualify for this comprehensive protocol assessment, the sponsor must have had a BPD Type 2b or 3 Meeting, as defined in section I.I, below, with the review division so that the division is aware of the developmental context in which the protocol is being reviewed and the questions being answered.
  - d. If a protocol is reviewed under the process outlined above, and agreement with the Agency is reached on design, execution, and analyses, and if the results of the trial conducted under the protocol substantiate the hypothesis of the protocol, the Agency agrees that the data from the protocol can be used as part of the primary basis for approval of the product. The fundamental agreement here is that having agreed to the design, execution, and analyses proposed in protocols reviewed under this process, the Agency will not later alter its perspective on the issues of design, execution, or analyses unless public health concerns unrecognized at the time of protocol assessment under this process are evident.
2. **Performance goal:** 90% of special protocols assessments and agreement requests completed and returned to sponsor within 45 days.
  3. **Reporting:** The Agency will track and report the number of original special protocol assessments and resubmissions per original special protocol assessment.

## H. MEETING MANAGEMENT GOALS

Formal BsUFA meetings between sponsors and FDA consist of Biosimilar Initial Advisory and BPD Type 1-4 meetings. These meetings are further described below.

- A Biosimilar Initial Advisory Meeting is an initial assessment limited to a general discussion regarding whether licensure under section 351(k) of the Public Health Service Act may be feasible for a particular product, and, if so, general advice on

the expected content of the development program. Such term does not include any meeting that involves substantive review of summary data or full study reports. Only one BIA meeting may be granted per program. While preliminary comparative analytical data from at least one lot of the proposed biosimilar or interchangeable product compared to the U.S.-licensed reference product is not required for the meeting request, sufficient information should be provided with the meeting request to enable FDA to make such a preliminary determination related to potential licensure under section 351(k) and to provide meaningful advice. This should include, as appropriate:

- Identification of reference product.
  - The indications intended to be sought for licensure.
  - A comparative analytical similarity plan, including preliminary identification of the Critical Quality Attributes and planned characterization methods.
  - If a sponsor seeks to utilize a non-US-licensed comparator during development, the proposed bridging strategy for US-licensed reference product and that comparator should be provided.
  - A conceptual plan for non-clinical studies or rationale and justification of why such studies may not be needed.
  - A conceptual description of the planned clinical pharmacokinetics and/or pharmacodynamic study(ies), including proposed endpoints.
  - If the sponsor plans to conduct a comparative clinical safety and efficacy study, a conceptual plan should be provided. This would include the patient population and proposed endpoints.
  - Any guidance already received from other health authorities on product development.
  - Identification to the FDA of the regulatory status in other jurisdictions.
- A BPD Type 1 Meeting is a meeting which is necessary for an otherwise stalled drug development program to proceed (e.g. meeting to discuss clinical holds, dispute resolution meeting), a special protocol assessment meeting, or a meeting to address an important safety issue.
  - A BPD Type 2a Meeting is a meeting focused on a narrow set of issues (e.g., often one, but not more than two issues and associated questions), requiring input from no more than 3 disciplines or review divisions. In order to request a Type 2a meeting, sponsors must first have had a BIA or other BPD meeting with the Agency. Requests could include:

- Defined CMC post-approval commitments (e.g., related to analytical methods) discussing the approach in advance of conducting the study to ensure the approach is in line with the Agency's expectations.
  - Immunogenicity testing strategy following prior FDA recommendations/feedback.
  - Feedback on revised study design when revisions are based on prior FDA feedback.
- A BPD Type 2b Meeting is a meeting to discuss a specific issue (e.g., proposed study design or endpoints) or questions where FDA will provide advice regarding an ongoing biosimilar biological product development program. This meeting may include substantive review of summary data, but does not include review of full study reports.
  - A BPD Type 3 Meeting is an in depth data review and advice meeting regarding an ongoing biosimilar biological product development program. This meeting includes substantive review of full study reports, FDA advice regarding the similarity between the proposed biosimilar biological product and the reference product, and FDA advice regarding additional studies, including design and analysis.
  - A BPD Type 4 Meeting is a pre-submission meeting to discuss the format and content of a complete application for an original biosimilar biological product application under the Program or supplement submitted under 351(k) of the PHS Act. The purpose of this meeting is to discuss the format and content of the planned submission and other items, including identification of those studies that the sponsor is relying on to support a demonstration of biosimilarity or interchangeability, discussion of any potential review issues identified based on the information provided, identification of the status of ongoing or needed studies to adequately address the Pediatric Research Equity Act (PREA), acquainting FDA reviewers with the general information to be submitted in the marketing application (including technical information), and discussion of the best approach to the presentation and formatting of data in the marketing application.

## **1. Response to Meeting Requests**

- a. **Procedure:** FDA will notify the sponsor in writing of the date, time, and place for the meeting, as well as expected Center participants following receipt of a formal meeting request and background package. Table 1 below indicates the timeframes for FDA's response to a meeting request.

**Table 1:**

<b>Meeting Type</b>	<b>Response Time (calendar days)</b>
Biosimilar Initial Advisory	21
BPD Type 1	14
BPD Type 2a, 2b, 3 and 4	21

- i. For Biosimilar Initial Advisory and BPD Type 2a or 2b meetings, the sponsor may request a written response to its questions, rather than a face-to-face meeting<sup>2</sup> or teleconference. If a written response is deemed appropriate, FDA will notify the sponsor of the date it intends to send the written response. This date will be consistent with the timeframes specified in Table 2 below for the specific meeting type.
  - ii. For the BPD Type 2a meeting, while the sponsor may request a face-to-face meeting, the Agency may determine that a written response to the sponsor’s questions would be the most appropriate means for providing feedback and advice to the sponsor. When it is determined that the meeting request can be appropriately addressed through a written response, FDA will notify the sponsor of the date it intends to send the written response in the Agency’s response to the meeting request. This date will be consistent with the timeframe for a Type 2a meeting. If the sponsor believes a face-to-face Type 2a meeting is valuable and warranted, then the sponsor may provide a rationale in a follow-up correspondence explaining why a face-to-face meeting is valuable and warranted, and FDA will reconsider this request. If FDA agrees to grant the face-to-face format, the Agency will strive to schedule the meeting to occur within 60 days of FDA’s receipt of the meeting request.
- b. Performance Goal: FDA will respond to meeting requests and provide notification within the response times noted in Table 1 for 90 percent of each meeting type.

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<sup>2</sup> A “face-to-face” meeting includes both in-person meetings and virtual meetings on IT platforms that allow for both audio and visual communication.

**2. Scheduling Meetings**

- a. Procedure: FDA will schedule the meeting on the next available date at which all applicable Center personnel are available to attend, consistent with the component’s other business; however, the meeting should be scheduled consistent with the type of meeting requested in Table 2. Table 2 below indicates the timeframes for FDA to schedule the meeting following receipt of a formal meeting request and background package, or in the case of a written response for Biosimilar Initial Advisory and BPD Type 2a and 2b meetings, the timeframes for the Agency to send the written response. If the requested date for any meeting type is greater than the specified timeframe, the meeting date should be within 14 calendar days of the requested date.

**Table 2:**

<b>Meeting Type</b>	<b>Meeting Scheduling or Written Response Time</b>
Biosimilar Initial Advisory	75 calendar days from receipt of meeting request and background package
BPD Type 2a	60 calendar days from receipt of meeting request and background package
BPD Type 2b	90 calendar days from receipt of meeting request and background package
	<b>Meeting Scheduling Time</b>
BPD Type 1	30 calendar days from receipt of meeting request and background package
BPD Type 3	120 calendar days from receipt of meeting request and background package
BPD Type 4	60 calendar days from receipt of meeting request*

\*Note the background package for BPD Type 4 meetings must be received no later than 14 calendar days after FDA receipt of the meeting request.

b. Performance goal:

**Table 3:**

<b>Meeting Type</b>	<b>Goal</b>
BPD Type 2a	FY 2023: 50% of meetings are held or written responses are sent within the timeframe FY 2024: 60% of meetings are held or written responses are sent within the timeframe FY 2025: 70% of meetings are held or written responses are sent within the timeframe FY 2026: 80% of meetings are held or written responses are sent within the timeframe FY 2027: 90% of meetings are held or written responses are sent within the timeframe
Biosimilar Initial Advisory and BPD Type 2b	90% of meetings are held or written responses are sent within the timeframe
BPD Type 1, 3, and 4	90% of meetings are held within the timeframe for each meeting type

**3. Preliminary Responses**

- a. Procedure: 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 or teleconference meeting date for BPD Type 2b and Type 3 meetings.

- b. Performance goal:

**Table 4:**

<b>Meeting Type</b>	
BPD Types 2b and 3	90% of preliminary responses to questions are issued by FDA no later than five calendar days before the meeting date

**4. Meeting Minutes**

- a. Procedure: The Agency will prepare minutes which will be available to the sponsor 30 calendar days after the meeting. The minutes will clearly outline the important agreements, disagreements, issues for further discussion, and action items from the meeting in bulleted form and need not be in great detail. Meeting minutes are not necessary if the Agency transmits a written response for Biosimilar Initial Advisory, BPD Type 2a, or 2b meetings.
- b. Performance Goal: 90% of minutes are issued within 30 calendar days of the date of the meeting.

**5. Conditions:** For a meeting to qualify for these performance goals:

- a. A written request and supporting documentation (i.e., the background package) must be submitted to the appropriate review division or office. The background package must be submitted at the same time as the written request for Biosimilar Initial Advisory, BPD Type 1, 2a, 2b and 3 meetings. For BPD Type 4 meetings, the background package must be received no later than 14 calendar days after FDA receipt of the written request.
- b. The request must provide:
  - i. A brief statement of the purpose of the meeting, the sponsor’s proposal for the type of meeting, and the sponsor’s proposal for a face-to-face meeting, teleconference, or for a written response (Biosimilar Initial Advisory and BPD Type 2a and 2b meetings only);
  - ii. A listing of the specific objectives/outcomes the sponsor expects from the meeting;
  - iii. A proposed agenda, including estimated times needed for each agenda item;

- iv. A list of questions, grouped by discipline (For each question there should be a brief explanation of the context and purpose of the question);
  - v. A listing of planned external attendees; and
  - vi. A listing of requested participants/disciplines representative(s) from the Center with an explanation for the request as appropriate.
  - vii. Suggested dates and times (e.g., morning or afternoon) for the meeting that are within or beyond the appropriate time frame of the meeting type being requested.
- c. The Agency concurs that the meeting will serve a useful purpose (i.e., it is not premature or clearly unnecessary). However, requests for BPD Type 2b, 3, and 4 Meetings will be honored except in the most unusual circumstances.

The Center may determine that a different type of meeting (i.e., Biosimilar Initial Advisory, or BPD Type 1-4) is more appropriate and it may grant a meeting of a different type than requested, which may require the payment of a biosimilar biological product development fee as described in section 744H of the Federal Food, Drug, and Cosmetic Act before the meeting will be provided. If a biosimilar biological product development fee is required under section 744H, and the sponsor does not pay the fee within the time frame required under section 744H, the meeting will be cancelled. If the sponsor pays the biosimilar biological product development fee after the meeting has been cancelled due to non-payment, the time frame described in section I.I.1.a will be calculated from the date on which FDA received the payment, not the date on which the sponsor originally submitted the meeting request.

Sponsors are encouraged to consult available FDA guidance to obtain further information on recommended meeting procedures.

## **6. Guidance, Clarity, and Transparency**

- a. Guidance: By September 30, 2023, FDA will issue a revised draft of the existing draft guidance on “Formal Meetings Between the FDA and Sponsors or Applicants of BsUFA Products” with information pertaining to BIA, Type 2a, and Type 4 meetings, as well as the follow-up opportunity described below. In addition, FDA will update relevant MAPPs and SOPPs.
- b. Follow-up opportunity: For all meeting types, to ensure the sponsor’s understanding of FDA feedback from meeting discussions or a WRO, sponsors may submit clarifying questions to the agency. Only questions of a clarifying nature will be permitted, i.e., to confirm something in minutes or a WRO issued by FDA, rather than raising new issues or new proposals. FDA will develop criteria and parameters for permissible requests, and FDA may exercise discretion about whether requests are in-scope. The clarifying



questions should be sent in writing as a “Request for Clarification” to the FDA within 20 calendar days following receipt of meeting minutes or a WRO. For questions that meet the criteria, FDA will issue a response in writing within 20 calendar days of receipt of the clarifying questions. FDA’s response will reference the original meeting minutes or WRO.

- c. Transparency: On or before March 31<sup>st</sup>, 2025, FDA will publish on its public webpage certain metrics regarding the new Type 2a meeting and sponsor requests for face-to-face meetings for year 1 and year 2 of BsUFA III.

## **II. ENHANCING BIOSIMILAR AND INTERCHANGEABLE BIOLOGICAL PRODUCT DEVELOPMENT AND REGULATORY SCIENCE**

To facilitate the timely development of biosimilar and interchangeable biological products and their availability to patients, FDA will focus on enhancing communications during application review, including inspection communications, and advancing the development of combination and interchangeable products. FDA will also pilot a regulatory science program focused on enhancing regulatory decision-making and facilitating science-based recommendations in areas foundational to biosimilar and interchangeable biological development.

### **A. PROMOTING BEST PRACTICES IN COMMUNICATION BETWEEN FDA AND SPONSORS DURING APPLICATION REVIEW**

The utilization of best practices in communication during application review are the responsibility of both industry and FDA. Efforts from both industry and FDA are needed in order to continue advancement, improvement, and updating of best practices.

To continue to enhance communication with sponsors during biosimilar application review in BsUFA III, FDA will update relevant guidances, MAPPs and SOPPs, as appropriate, on or before December 31<sup>st</sup>, 2023 regarding best practices in communication. FDA will utilize input from the BsUFA II final assessment of the Program, FDA experiences, and discussion from a meeting with industry on best practices in FY 2022 to update the above documents, as appropriate.

### **B. INSPECTIONS AND ALTERNATIVE TOOLS TO EVALUATE FACILITIES**

#### **1. Enhancing Inspection Communication for Applications, not Including Supplements**

FDA and industry believe enhanced communication between review teams and industry on certain pre-license inspections can facilitate an efficient application review process.

When FDA determines for an application, not including supplements, that it is necessary to conduct a pre-license inspection at a time when the product identified in the application is being manufactured, FDA's goal is to communicate its intent to inspect a manufacturing facility at least 60 days in advance of the pre-license inspection and no later than mid-cycle. FDA reserves the right to conduct manufacturing facility inspections at any time during the review cycle, whether or not FDA has communicated to the facility the intent to inspect.

## **2. Alternative Tools to Assess Manufacturing Facilities Named in Pending Applications**

During the COVID-19 public health emergency, the FDA expanded its use of alternate tools for assessing facilities named in applications, including exercising its authority to request records and other information in advance of or in lieu of an inspection, granted per section 704(a)(4) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 374(a)). Where appropriate, the Agency also increased the use of information, including inspection reports, shared by trusted foreign regulatory partners through mutual recognition agreements and other confidentiality agreements. As FDA continues to gain experience and lessons learned from the use of these tools, FDA will communicate its thinking on the use of such methods beyond the pandemic.

On or before September 30, 2023, FDA will issue draft guidance on the use of alternative tools to assess manufacturing facilities named in pending applications (e.g., 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). The guidance will incorporate best practices, including those in existing published documents, from the use of such tools during the COVID-19 pandemic. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It then will work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.

## **C. ADVANCING THE DEVELOPMENT OF BIOSIMILAR BIOLOGICAL-DEVICE COMBINATION PRODUCTS REGULATED BY CDER AND CBER**

### **1. Use-Related Risk Analysis (URRA)**

Sponsors employ URRA to identify the need for risk mitigation strategies and to design a human factors (HF) validation study. Based on a URRA, a sponsor may propose that a HF validation study is not needed to be submitted to support the

safe and effective use of a biosimilar biologic-device combination product. FDA will establish the following procedures for review of URRAs for combination products:

- a. The sponsor should submit a request for review of their URRA to their IND. The submission should include specific questions, justification that a HF validation study is not needed to be submitted including any supporting information, and scientific and regulatory requirements for which the sponsor seeks agreement.
- b. Within 60 days of Agency receipt of the URRA and specific questions, the Agency will provide a written response to the sponsor that includes a succinct assessment of the URRA and answers to the questions posed by the sponsor. If the Agency does not agree that either the URRA or the sponsor's justification are adequate to support the absence of a HF validation study, the reasons for the disagreement will be explained in the response.
- c. URRA submission: performance goals for FDA will be phased in, starting FY 2024 as follows:
  - i. By FY 2024, review and notify sponsor of agreement or non-agreement with comments for 50% of filed submissions, within 60 days of receipt of submission.
  - ii. By FY 2025, review and notify sponsor of agreement or non-agreement with comments for 70% of filed submissions, within 60 days of receipt of submission.
  - iii. By FY 2026, review and notify sponsor of agreement or non-agreement with comments for 90% of filed submissions, within 60 days of receipt of submission.
  - iv. By FY 2027, review and notify sponsor of agreement or non-agreement with comments for 90% of filed submissions, within 60 days of receipt of submission.
- d. On or before the end of FY 2024, FDA will publish new draft or revised guidance for review staff and industry describing considerations related to biosimilar biologic-device combination products on the topics noted below.

Guidance will convey FDA's current thinking regarding how a URRA along with other information can be used to inform when the results from an HF validation study may need to be submitted to a marketing application. The guidance will provide a comprehensive, systematic and stepwise approach with examples, when applicable, to illustrate how to make this determination.

- e. Sponsors may still elect to submit a URRA with a HF validation protocol and will only be subject to timelines in Section II.C.2., For Human Factor Validation Study Protocols.

## **2. Human Factor Validation Study Protocols**

Human factors studies are conducted to evaluate the user interface of a biosimilar biologic-device combination product to eliminate or mitigate use-related hazards that may affect the safe and effective use of the combination product. Over the past decade, more combination products have been developed to deliver therapeutics via different routes of administration (e.g., parenteral, inhalation) with complex engineering designs. HF validation protocols are reviewed during the IND stage with the goal towards developing a final finished combination product that supports the marketing application. To achieve this objective, FDA will establish the following procedures for review of HF validation study protocols:

- a. The sponsor should submit a human factors protocol to the IND with specific questions, including scientific and regulatory requirements for which the sponsor seeks agreement (e.g., are the study participant groups appropriate to represent intended users, is the study endpoint adequate, are the critical tasks that should be evaluated appropriately identified).
- b. Within 60 days of Agency receipt of the protocol and specific questions, the Agency will provide a written response to the sponsor that includes a succinct assessment of the protocol and answers to the questions posed by the sponsor. If the Agency does not agree that the protocol design, execution plans, and data analyses are adequate to achieve the goals of the sponsor, the reasons for the disagreement will be explained in the response.

Performance goals for FDA will be as follows:

- c. Beginning in FY 2023, review and provide sponsor with written comments for 90% of human factors validation protocol submissions within 60 days of receipt of protocol submission.

## **D. ADVANCING DEVELOPMENT OF INTERCHANGEABLE BIOSIMILAR BIOLOGICAL PRODUCTS**

FDA is committed to a focused effort to further advance the development of safe and effective interchangeable biosimilar biological products. The effort will address current needs, prospectively identify future needs and incorporate the following components:

- 1. **Research:** FDA will leverage the BsUFA III Regulatory Science Program to advance product development, assist regulatory decision-making, and support guidance development for interchangeable biosimilar products.

**2. Foundational guidance development:** FDA will develop foundational guidances for the development of interchangeable biosimilar biological products:

- a. On or before September 30, 2025, FDA will publish a draft guidance describing considerations for developing presentations, container closure systems and device constituent parts for proposed interchangeable biosimilar biological products. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It will then work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.
- b. On or before September 30, 2023, FDA will publish draft guidance on labeling for interchangeable biosimilar biological products. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It will then work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.
- c. On or before September 30, 2024, FDA will publish a draft guidance on promotional labeling and advertising considerations for interchangeable biosimilar biological products. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It will then work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.
- d. On or before September 30, 2024, FDA will publish a draft 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. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It then will work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.

3. **Stakeholder Engagement:** FDA will hold a scientific workshop on the development of interchangeable products to help identify future needs (e.g., guidance, research) on or before October 31, 2025. Within 12 months following the public workshop, FDA will issue a draft strategy document for public comment that outlines the specific actions the agency will take to facilitate the development of interchangeable biosimilar biological products. The strategy document may identify activities and deliverables including updating or creating new procedures, MAPPs, SOPPs, guidances, and other changes to FDA’s scientific and other programs related to the topics discussed in the workshop. The strategy document will also include proposed timeframes for the specific actions outlined in the document. FDA will consider public input and will publish a final strategy document within 9 months after the close of the public comment period on the draft strategy document.

## **E. REGULATORY SCIENCE TO ENHANCE THE DEVELOPMENT OF BIOSIMILAR AND INTERCHANGEABLE BIOLOGICAL PRODUCTS**

FDA is committed to enhancing regulatory decision-making and facilitating science-based recommendations in areas foundational to biosimilar development. Starting in FY 2023, FDA will pilot a regulatory science program broadly applicable to facilitating biosimilar and interchangeable biological product development. Project goals should not be specific to a product or product class<sup>3</sup>. The pilot program will focus on two demonstration projects: (1) advancing the development of interchangeable products, and (2) improving the efficiency of biosimilar product development.

### **1. Advancing Development of Interchangeable Products**

This demonstration project will be focused on progressing research to advance the development of interchangeable products. Specifically, this demonstration project will:

- a. 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, including:
  - i. Investigate and evaluate informative, scientifically appropriate methodologies to assess the potential impact of differences between proposed interchangeable biosimilar and reference product presentations and container closure systems.
  - ii. Investigate and evaluate informative, scientifically appropriate methodologies to predict immunogenicity by advancing the knowledge of analytical (including physical, chemical and biological function

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<sup>3</sup> See Guidance for Industry: Questions and Answers on Biosimilar Development and the BPCI Act, December 2018 Biosimilars, Revision 1, Q&A II.2.

assays), pharmacological and clinical correlations as relates to interchangeability.

## **2. Improving the Efficiency of Biosimilar Product Development**

This demonstration project will be focused on progressing 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. Specifically, this demonstration project will:

- a. Review and evaluate opportunities for streamlining and targeting biosimilar product development in consideration of scientific advancements in analytical (including physical, chemical and biological function assays), and pharmacological assessments and experience with prior biosimilar product development and marketed biosimilar products.
  - b. Investigate and evaluate informative, scientifically appropriate methodologies to predict immunogenicity by advancing the knowledge of analytical (including physical, chemical and biological function assays), pharmacological and clinical correlations as it relates to biosimilarity.
- 3. Stakeholder Engagement:** On or before October 31, 2025, FDA will hold a public meeting to review the progress of the demonstration projects and solicit input on future priorities. An interim report will be posted on FDA's website in advance of the public meeting. On or before September 30, 2027, a final summary report of outcomes from the pilot program will be posted on FDA's website.
- 4. Deliverables:** Within 12 months of the completion of the demonstration projects, FDA will use the learnings from the demonstration projects to publish a comprehensive strategy document outlining specific actions the agency will take to facilitate the development of biosimilar and interchangeable biological products. The comprehensive strategy document may include updating or creating new procedures, MAPPs, SOPPs, and guidances and will also include proposed timeframes for the specific actions outlined in the document. The comprehensive strategy document will be distinct from the final summary report of the pilot program.

### **III. CONTINUED ENHANCEMENT OF USER FEE RESOURCE MANAGEMENT**

FDA is committed to ensuring the sustainability of BsUFA program resources and to enhancing the operational agility of the BsUFA program. FDA will build on the financial enhancements included in BsUFA II and continue activities in BsUFA III to ensure optimal use of user fee resources and the alignment of staff to workload through the continued maturation and assessment of the Agency's resource capacity planning

capability. FDA will also continue activities to promote transparency of the use of financial resources in support of the BsUFA program.

## **A. RESOURCE CAPACITY PLANNING**

FDA will continue activities to mature the Agency's resource capacity planning function, including utilization of modernized time reporting, to support enhanced management of BsUFA resources in BsUFA III and help ensure alignment of user fee resources to staff workload.

### **1. Resource Capacity Planning Implementation**

- a. On or before the end of the 2nd quarter of FY 2023, FDA will publish an implementation plan that will describe how resource capacity planning and time reporting will continue to be implemented during BsUFA III. This implementation plan will address topics relevant to the maturation of resource capacity planning, including, but not limited to, detailing FDA's approach to:
  - i. The continued implementation of the Agency's resource capacity planning capability, including:
    - 1) The continual improvement of the Capacity Planning Adjustment (CPA); and
    - 2) The continual improvement of time reporting and its utilization in the CPA.
  - ii. The integration of resource capacity planning analyses in the Agency's resource and operational decision-making processes.
- b. FDA will provide annual updates on the FDA website on the Agency's progress relative to activities detailed in this implementation plan on or before the end of the 2nd quarter of each subsequent fiscal year.
- c. FDA will document in the annual BsUFA Financial Report how the CPA fee revenues are being utilized.

### **2. Resource Capacity Planning Assessment**

On or before the end of FY 2025, an independent contractor will complete and publish an evaluation of the resource capacity planning capability. This will include an assessment of the following topics:

- a. The ability of the CPA to forecast resource needs for the BsUFA program, including an assessment of the scope of the workload drivers in the CPA and their ability to represent the overall workload of the BsUFA program;



- b. Opportunities for the enhancement of time reporting toward informing resource needs; and
- c. The integration and utilization of resource capacity planning information within resource and operational decision-making processes of the BsUFA program.

The contractor will provide options and recommendations in the evaluation regarding the continued enhancement of the above topics as warranted. The evaluation findings and any related recommendations will be discussed at the FY 2026 BsUFA 5-year financial plan public meeting. After review of the findings and recommendations of the evaluation, FDA will, as appropriate, continue improving the resource capacity planning capability and the CPA.

## **B. FINANCIAL TRANSPARENCY**

1. FDA will publish a BsUFA 5-year financial plan on or before the end of the 2nd quarter of FY 2023. The plan shall recognize that the retention of the strategic hiring and retention adjustment required by section 744H(b)(1)(C) of the FD&C Act is subject to renegotiation under a subsequent reauthorization of BsUFA. FDA will publish updates to the 5-year plan on or before the end of the 2nd quarter of each subsequent fiscal year. The annual updates will include the following topics:
  - a. The changes in the personnel compensation and benefit costs for the process for the review of biosimilar biological product applications that exceed the amounts provided by the personnel compensation and benefit costs portion of the inflation adjustment; and
  - b. FDA's plan for managing costs related to strategic hiring and retention after the adjustment required by section 744H(b)(1)(C) of the FD&C Act expires at the end of fiscal year 2027, given this adjustment is not intended to be reauthorized in a subsequent reauthorization of BsUFA.
2. FDA will convene a public meeting on or before the end of the 3rd quarter of each fiscal year to discuss the BsUFA 5-year financial plan and the Agency's progress in implementing resource capacity planning, including the continual improvement of the CPA and time reporting, and the integration of resource capacity planning in resource and operational decision-making processes.

## **C. MANAGEMENT OF CARRYOVER BALANCE**

FDA is committed to reducing the carryover balance to no greater than 21 weeks of the target revenue by the end of FY 2025.

In the annual updates to the BsUFA five-year financial plan, FDA will 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.

#### IV. IMPROVING FDA HIRING AND RETENTION OF REVIEW STAFF

Enhancements to the biosimilar biological product review program require that FDA hire and retain sufficient numbers and types of technical and scientific experts to efficiently conduct reviews of 351(k) applications. During BsUFA III, the FDA will commit to do the following:

##### A. SET CLEAR GOALS FOR BIOSIMILAR BIOLOGICAL PRODUCT REVIEW PROGRAM HIRING

1. The BsUFA III agreement provides FDA additional user fee funding to hire additional staff for the biosimilar biological product review program in BsUFA III. FDA will set clear goals to hire the new staff outlined in Table 1.

**Table 1**

	FY 2023	FY 2024	FY 2025	FY 2026	FY 2027
CDER	14	1	0	0	0

2. FDA will report on progress against the hiring goal for BsUFA III on a quarterly basis posting updates to the FDA BsUFA Performance webpage.

##### B. COMPREHENSIVE AND CONTINUOUS ASSESSMENT OF HIRING AND RETENTION

The Directors of CDER and CBER will utilize a qualified, independent contractor with expertise in assessing HR operations to conduct a targeted assessment of the hiring and retention of staff for the biosimilar biological product review program. The BsUFA III assessment will be conducted under the same contract and by the same independent contractor that will conduct the assessment related to hiring and retention of staff for the human drug review program in PDUFA VII. The contractor will assess the factors that contribute to HR successes and challenges, including factors outside of FDA's control. The assessment will build upon the findings of previous evaluations conducted under BsUFA II and PDUFA VI with a focus on the changes and adjustments that have improved FDA's hiring and retention outcomes and which challenges remain. In addition to evaluating the outcomes of various hiring changes, the assessment will include metrics related to recruiting and retention in the biosimilar biological product review program, including, but not limited to, specific targeted scientific disciplines, attrition, and utilization of pay authorities. The report will include the contractor's findings and recommendations on further enhancements to hiring and retention of staff for the biosimilar biological product review program, if warranted.

The assessment will be published on FDA’s website on or before June 30th, 2025 for public comment. FDA will also hold a public meeting on or before September 30th, 2025 to discuss the report, its findings, and the Agency’s specific plans to address the report recommendations.

## **V. INFORMATION TECHNOLOGY GOALS**

Under BsUFA III, FDA will:

### **A. DEVELOP DATA AND TECHNOLOGY MODERNIZATION STRATEGY**

FDA will progress a Data and Technology Modernization Strategy (“Strategy”) that provides FDA’s strategic direction for current and future state data-driven regulatory initiatives.

1. No later than Q4 FY 2023, FDA will establish a Data and Technology Modernization Strategy that reflects the vision in FDA’s Technology and Data Modernization Action Plans, including:
  - a. outlining key areas of focus and approach including leveraging cloud technologies to support Applicant-FDA regulatory interaction;
  - b. articulating enterprise-wide approaches for both technology and data governance; and
  - c. aligning strategic initiatives in support of BsUFA review goals, drawing a line of sight between initiatives and the enterprise strategy (i.e. the agency-wide strategy also supporting components outside BsUFA).
2. The Strategy will be shared and annually updated to reflect progress and any needed adjustments. Milestones and metrics for BsUFA initiatives will be included in the updates.

### **B. MONITOR AND MODERNIZE ELECTRONIC SUBMISSION GATEWAY (ESG)**

FDA will continue to ensure the usability and improvement of the ESG.

1. Annually, FDA will provide on the ESG website historic and current metrics on ESG performance in relation to published targets, characterizations and volume of submissions, and standards adoption and conformance.

FDA will advance the ESG cloud-based modernization with an improved architecture that supports greatly expanding data submission bandwidth and storage, while continuing to ensure its stable operation.

2. Annually, FDA will provide on the ESG website historic and current metrics on ESG performance in relation to published targets, characterizations and volume of submissions, and standards adoption and conformance.
3. By the end of FY 2025, FDA will complete ESG transition to the cloud, including set-up and integration of an enterprise Identity and Access Management solution that will streamline applicant access to FDA resources.
4. Annually, FDA will share progress against the implementation project plan.
5. FDA will engage industry to provide feedback and/or participate in pilot testing in advance of implementing significant changes that impact industry's interaction with the enterprise-wide systems.

## **VI. DEFINITIONS AND EXPLANATION OF TERMS**

- A. The term “review and act on” means the issuance of a complete action letter after the complete review of a filed complete application. The action letter, if it is not an approval, will set forth in detail the specific deficiencies and, where appropriate, the actions necessary to place the application in condition for approval.
- B. A resubmitted original application is a complete response to an action letter addressing all identified deficiencies.