THE UNITED STATES DEPARTMENT OF

HEALTH AND HUMAN SERVICES

Food and Drug Administration

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Reauthorization of the : Docket No.

Biosimilar User Fee Act : FDA-2015-N-3326

(BsUFA) :

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PUBLIC MEETING

DATE: Tuesday, November 2, 2021

TIME: 9:00 a.m.

BEFORE: Tasha Ray, Meeting Moderator

LOCATION: Webcast via Zoom

JOB No.: 4839269

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M E E T I N G

MS. RAY: Good morning. We'll go ahead and get started. Welcome to the U.S. Food and Drug Administration's public meeting on the reauthorization of the Biosimilar User Fee Act referred to as BsUFA. My name is Tasha Ray. I work in the office of Program and Strategic Analysis in FDA's Center for Drug Evaluation and Research, or CDER. I will serve as today's moderator. BsUFA is the legislation that authorizes FDA to collect user fees to support the process for the review of biosimilar biological products. The current authorization of the program, BsUFA II, expires in September 2022. Activities are therefore under way to reauthorize the program for fiscal years 2023 through 2027. Today's meeting is an important step in engaging with public stakeholders on the BsUFA program.

The purpose of today's meeting as outlined in the federal Food, Drug and Cosmetic Act is to gather input from the public on the proposed recommendations for the reauthorization of BsUFA. The full text of the proposed BsUFA III commitment letter can be found

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on the Agency's webpage. We have also opened a public docket for those who wish to submit written comments.

After the public meeting and the close of the public docket, we will revise the recommendations as appropriate and present our proposed recommendations to congressional committees. We will cover several topics in our meeting today.

We will begin with Dr. Patrizia Cavazzoni, Center Director of CDER, who will provide opening remarks. Andrew Kish, Director of CDER's Office of Program and Strategic Analysis, will follow with the background on BsUFA and the reauthorization process. We will then have a series of presentations from FDA covering a proposed BsUFA enhancement.

Following these presentations, we'll take a 20-minute break. And then we'll continue the meeting with remarks from industry association representatives who participated in the negotiation process. Finally, there will be a public comment session for those members of the public who submitted an online request to provide comments.

As we do have a full agenda, we ask that

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speakers please adhere to the list and timeframes in the agenda. I'll also let you know if you're running over. Given our virtual format, this meeting will not include questions from FDA to any of the speakers nor will FDA be able to take any questions during the meeting. Although you cannot see us in person, please know that my colleagues who are leading and participating in the reauthorization process are listening, and we very much value your important perspective.

Today's meeting is not the only chance to gather public input. The public docket mentioned previously is open until December 2nd, and we encourage the public to submit comments. We will periodically be sending out the docket link throughout today's meeting. A recording and transcript of this meeting will also be made available online.

A few last housekeeping items. If you experience technical issues during the webcast, please contact us through the Q&A box at the bottom of the screen, and we'll do our best to assist you. You can also email us at emily.ewing@fda.hhs.gov. We'll have

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a 20-minute break around 10:00 a.m. If schedule modifications are needed, we'll send a notification in the top. With that, we look forward to beginning this important conversation. I'll now turn it over to Dr. Cavazzoni for your opening remarks.

DR. CAVAZZONI: Good morning. I want to welcome everyone to today's public meeting to discuss the proposed enhancements to the BsUFA program. Providing a transparency in opportunity for public engagement are a vital piece of the BsUFA process. Last November, we requested public input on priorities for BsUFA negotiations. And over the course of negotiations, we posted meeting in its, to FDA's websites (indiscernible) the BsUFA discussions.

Today, we will present the proposed enhancements to you. We look forward to your feedback and consideration in this step of the reauthorization. The public meeting is one of the final steps in the reauthorization process. The proposed enhancements for the third authorization of BsUFA provide funding for continued maturation of, of the biosimilar repeat program. This funding will help the Agency address

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current and future needs. The BsUFA III agreement provides support for the establishment of new supplement categories, timelines, and performance goals along with other enhancements through the review process.

Additionally, the agreement includes a focused effort to support the development of interchangeable products. This effort includes stakeholder input on key priorities for interchangeable development. BsUFA III also, also introduces a new BsUFA regulatory science pilot program. The pilot program will support research to advance the development of interchangeable products and improve the efficiency of biosimilar product development. Public input will also be critical to reviewing project progress and identify, identifying future regulatory science research that are needed for biosimilars. Importantly, the agreement provides continued sound financial footing for the biosimilar program. BsUFA III will build on the financial enhancements introduced in BsUFA II including maturing the capacity planning function, which is critical to

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ensuring FDA has the ability to keep pace with sustained increases in workload.

I am pleased that even as our centers continue to work hard on our COVID-19 response, our staff have been able to come to an agreement that addresses some current critical needs while looking towards the future. Of course, the success of BsUFA is not the result of FDA's work alone. Your participation is a crucial element. So, please, don't forget to provide comments and feedback to the public docket after this meeting. We look forward to continuing to work closely with you and to support you as we fulfill our mission to deliver on the promise of science with data-driven results and rigorous scientific analysis to protect the health of the American public.

Thank you again for attending today's virtual meeting and special thanks to all of the speakers on today's program. We look forward to a productive meeting.

MS. RAY: Thank you very much, Dr. Cavazzoni. I would now like to invite Andrew Kish to provide

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background on the BsUFA program, where we were, are at in the reauthorization process and a quick overview of the proposed enhancements.

DR. KISH: Okay. Thank you. Good morning, everyone, and thank you for joining the meeting. All right. So I'll -- I'm going to give a brief background on biosimilars, particularly the, the UFAs, and then also, also a brief overview of the reauthorization process and where we are today. We can go to the next slide.

So a little bit on just the user fee construct for those who have joined the, the meeting back in November or any of the other UFA meetings. This probably looks familiar but just as as reminder. So what, what are user fees? So Congress instructs FDA to establish a user fee program for the process of the review of the biosimilar biological product applications, and fee funds are added to new, to non-fee appropriated funds. They are intended to increase the staffing resources, the speed, and enhance the review process. A key distinction with user fees is that they pay for services that directly benefit the

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payers. This is what distinguishes it from a tax.

So what do we discuss in these technical negotiations? They are around desired enhancements of the specific activities related to the process, the review process. So that can include what new or enhanced process the FDA or industry will seek during this five, five-year timeframe. We discuss what is technically feasible to do and what are the resources required to implement and sustain those enhancements. The important distinction is that we do not discuss policy content. You may see in the agreement that there is agreement around issuing guidances. However, there is no discussion in these technical negotiations what the FDA's position will be in those guidances. Discussions also include mechanics of the user fee program. So into the nut and bolt of how fees are collected, the types and products are covered by each fee, and as you're probably aware, everyone in the, in the audience, the medical product industry programs must be reauthorized every five years. Going to the next slide.

BsUFA is still a relatively new program --

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not our, not our newest, but close to it. It came about in the BPCIA Act of 2009 where FDA was directed to develop recommendations for a user fee program. Something that's interesting at that point in time -- I know I mentioned this in the, the kick-off meeting back in November -- is there -- at that time when we had the conflict BsUFA for a specific user fee agreement, there were no market applications for products on the market.

There wasn't an established drug development process where history related to biosimilar biological products in the U.S. at that time. So after consultation with regulated industry and public stakeholders, FDA did come up with a BsUFA I arrangement in agreement as transmitted to Congress, and it was passed (indiscernible). But BsUFA is at its 9th year and as a point of comparison, BsUFA is is at it's 28th. BsUFA, since it's creation, has facilitated the approval of 31 biosimilar biological products for the American public.

Really brief overview of BsUFA I and BsUFA II and the key highlights of what was in those

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agreements, BsUFA I, as previously mentioned, really was just creating a user fee program really when there wasn't much experience, or really any experience with the process. So at that point in time, industry and FDA and other stakeholders agreed let's, let's go forward with referencing PDUFA fee amounts at, at the start of BsUFA.

So we -- we referenced the fee amounts and the fee types and added a new fee type for products in the development phase in order to generate revenue, support FDA's review work during the, the development IND stage and to, to enable sponsors to have meetings with FDA early in development. BsUFA I also introduced predictable timelines and review process performance goals. Again, primarily modeled on the BsUFA construct.

So as we transition to BsUFA II, we had several years of experience with, with the, the new pathway at that time when we were discussing BsUFA II. We also had some insight into program costs now that the program was off the ground. So BsUFA II, we were able to establish an independent efficient user fee

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structure based on program costs. So we no longer reference PDUFA. We also implemented the review program to promote the efficiency and effectiveness for the first cycle review of biosimilar applications and submit the minimized number of recycles necessary for each biosimilar approval. It also added commitments to assess the program and clarify the regulatory pathway that hits that capacity. Moving to the next slide.

So where are we today? I -- as Tasha and Patrizia already mentioned, this is a critical step in the reauthorization process. This is language from, from the statute. You might be familiar with it. So we go through a, a full process and around consultation. And then we move into the second step there, which is public review of recommendations. And the highlighted section is where we are today, and that's publishing the recommendations to Federal Register providing the public 30 days, at least 30 days to provide written comments to that docket and to hold this meeting today to get your feedback. After this meeting, the next step is then to review all the

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feedback that we receive through the public docket making the assessments if anything in the package needs to change and then transmit the recommendations to Congress no later than January 15th next year.

On the next slide is the, a graphical and review if you're not a fan of reading statute, like myself. A sense of a timeline for the BsUFA III reauthorization. If we start with the public announcement, a class in October of last year, we held negotiations with industry from March to July. We were going through a clearance process through the administration, and we are at the public meeting today.

And as -- as mentioned previously, we transmit the package to Congress no later than January 15th. And then it is with Congress to reauthorize BsUFA III. And the current specific agreements, sun sets on September 30th, 2022. And just a little bit on the BsUFA III agreement overview of my colleagues from FDA will do a deeper dive on each section. Go to the next slide.

This is around 10 enhancement areas that

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we're going to highlight today that are new changes going into BsUFA III. One is around supplements, a meeting management, best practices in application review, URRA human factors' timelines, sections as Dr. Cavazzoni mentioned, interchangeable products and regulatory science, expense and finance, hiring retention, and information technology.

So I would now like to turn it over to my colleague, Sarah Yim, who is the Director of the Office of Therapeutic Biologics and Biosimilars, who is going to give you more information on some of these enhancements.

DR. YIM: Thanks, Andy. Next slide, please. So I'm going to summarize for you the proposed BsUFA III enhancements for the first four areas that Andy mentioned. Starting with supplements, the changes introduce new supplement categories and timelines to expedite the review of supplements. This 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. Also depending on the content of this submission, the new

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timelines are 3 months, 4 months, 6 months, or 10 months from the supplement receipt date. Next slide, please.

Category A Supplements are supplements seeking to update the labeling with regards to safety information that has been updated in the referenced product labeling. This category has an action goal date of within three months of receipt of the supplement. Category B Supplements are supplements seeking licensure for an additional indication, when the submission does not include new datasets with the exceptions listed in the parentheses here, and the supplement also does not seek a new route of administration, dosage form, dosage strength, formulation or presentation, and the supplement has an up, up-to-date agreed upon initial pediatric study plan. This category has an action goal date of within 4 months of receipt of the supplement. Next slide, please.

Category C Supplements are supplements seeking to remove an approved indication. This category also has an action date, action goal date of

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within 4 months of receipt of the supplement. Category D Supplements are those seeking licensure for an additional indication when the submission contains new datasets, except for the types of datasets described in Category E and F Supplements also if the supplement does not contain an up-to-date agreed upon IPS fee. This category has an action goal date of within 6 months of receipt of the supplement. Category E and F Supplements both have an action goal date of within 10 months of receipt. Category E supplements are those seeking licensure for an additional indication where the supplement contains efficacy datasets. And Category F Supplements are those seeking an initial determination of interchangeability. Next slide, please.

So this slide summarizes the performance goals for a regional applications and supplements. There is no change to the timelines or goals for original biosimilar biological product applications or resubmitted original applications. Although not noted on this slide, there is also no change to the timelines for manufacturing supplements. For A

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through D Category Supplements, the performance goals start at 70 percent in 2023, go to 80 percent in 2024, and then 90 percent for years 2025 through 2027. For Category E and F Supplements, the performance goals are 90 percent within 10 months of receipt for original supplements and 90 percent within 6 months of receipt for resubmitted supplements. Next slide, please.

Moving on to meeting management enhancements, the enhancements include modifying the operation, operationalization of BIA meetings so that preliminary comparative analytical data is no longer expected in order to meet with FDA. The biggest change is the introduction of a new biosimilar product development meeting type called Type 2a. This meeting is intended to focus on a narrow set of issues requiring input from no more than three disciplines or review divisions. In order to facilitate a reduced meeting scheduling or written response time down to 60 calendar days. This is compared to the historical Type 2 meetings under BsUFA II, which are now called Type 2b meetings and still have a meeting scheduling

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or a response time of 90 calendar days. BPD Type 4 meeting requests have been modified to allow for the background package to be submitted up to 14 days after FDA receipt of the meeting requests instead of the BPD standard expectation of having the background package submitted with the meeting request. Finally, consistent with PDUFA VII, there will be a new follow-up opportunity for sponsors to submit clarifying questions after meetings or written response only responses. And, of course, we're going to be updating meetings, guidances, maps, and SOPs accordingly. Next slide, please.

Building on the lessons learned during BsUFA II, FDA will update relevant guidances, maps, and SOPs to reflect best practices in communication during application review. Next slide, please.

And, finally, consistent with PDUFA VII, there will be final performance goals for the review of use-related risk analyses and human factor study protocols. FDA will also provide guidance on considerations related to combination products.

Now, I'll turn the podium over to Dr. Laurie

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Graham to discuss the next set of enhancements. Thank you.

DR. GRAHAM: Thanks, Sarah. So I'm going to start today by talking about a couple of commitments around facilities. So can we go to the next slide, please?

Okay. So these, these commitments around facilities are also part of PDUFA VII. So the first commitment has to do with communications around pre-license inspections. So consistent with current practice, FDA notifies sponsors of pre-license inspections when we need to, for example, see the drug substance or drug product that is the subject of the BLA in manufacturing during the inspection. However, we want to ensure predictability, predictability around these notifications. So our commitment there is shown in this first bullet that we will notify sponsors at least 60 days in advance and no later than the midcycle of a pre-license inspection for applications not including supplements where FDA needs to see the product being manufactured. And, of course, we reserve the right to conduct inspections at

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any time during the review cycle regardless of whether or not we have communicated the intent to inspect to the sponsor.

The next statement I want to talk about with regards to facilities is about the use of alternative tools. So during the COVID-19 public health emergency where FDA has been limited in the inspections that we can conduct due to travel restrictions, we have really enhanced our use of alternative tools to evaluate facilities. So we recognize there is a lot of interest in how FDA will continue to use these alternative tools once travel restrictions are lifted. Our intention then is to look at how we have used these tools during the pandemic, what's worked, what hasn't worked, what changes do we have to make, and then to sort of determine how best to use these tools moving forward after the public health emergency.

So our commitment there shown in the second bullet is to, to commit to a guidance that will talk about our thinking on the use of alternative tools to assess manufacturing facilities named in pending applications beyond the COVID-19 pandemic. So when

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I'm talking about alternative tools, I'm talking about things like requesting existing inspection reports from sort of trusted regulatory partners through mutual recognition agreements or 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. Next slide, please.

So now I want to switch gears, and I want to talk about that focused area in BsUFA III about interchangeable products. So as you've already heard, there is a focused effort to further advance the development of safe and effective interchangeable biosimilar biological products, and this focused effort is multi-pronged.

So the first part of it is the research component, which is really about leveraging the regulatory science program that my colleague in OPQ, Steve Kozlowski, is going to be talking about in a couple of minutes. Our intent is to leverage the

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regulatory science program to advance product development, assist in a regulatory decision making, and support guidance development.

The next prong in our focused effort is stakeholder engagement. So we really do want to have a dialogue with industry. We want to talk about sort of challenges and, and how we can further develop interchangeable products. So we have committed to holding a scientific workshop on the development of interchangeable biosimilar biological products to help sort of identify future needs. This can include future guidance needs, future research needs. But we intend to have this workshop on or before October 31st, 2025.

Within 12 months following the public workshop, we intend to draft a strategy document for public comment. This strategy document will outline the actions the Agency will take to facilitate the development of interchangeable biosimilar biological products. The strategy document can identify sort of activities and deliverables including updating or creating new guidances, maps, SOPPs, guidances, and

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other changes to FDA programs. The strategy document will also include proposed timeframes for the specific actions outlined in the document. Our intent then is within 9 months of the closing of the comment period, we will publish a final strategy document. Next slide, please.

And the next and final piece of our multi-pronged focused effort is on guidance. We have committed to producing four foundational guidance documents. The first has to do with describing considerations for developing presentations, container closure systems, and device constituent parts for proposed interchangeable biosimilar biological products. The second guidance is a guidance on labeling for interchangeable biosimilar biological products. The third guidance is on promotional labeling and advertising considerations for interchangeable biosimilar biological products.

And, finally, the fourth guidance is a CMC guidance on post-approval changes. And this guidance will describe the nature and type of information for different recorded categories of sponsorship provided

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to support post-approval manufacturing changes to support biosimilar and interchangeable biosimilar biological products. And I want to point out that in addition to sort of committing to certain dates by -- by which we have the draft guidances up, we have also committed that within 18 months after the close of the public comment period on the draft guidance, we will either publish a revised draft or a final guidance.

And now I'm going to turn it over to my colleague in OPQ, Steve Kozlowski.

DR. KOZLOWSKI: Thank you. So I'm going to talk about the regulatory science program, if we could advance the slide.

So in demonstrating biosimilarity, a manufacturer generates an area of data that compares the proposed product to the approved reference product. Similarly, in interchangeability, which we have heard again about the, the focused effort to enhance those, there are data and information that are needed to support that, some of which are currently included in guidance.

In both of these areas, there are potential

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opportunities to better leverage data and information. Both provide a similarity and interchangeability. FDA is committed to enhancing regulatory decision making and in facilitating the best science-based recommendation in these areas, which are foundational to bias in work development. In doing this, we are piloting two demonstration products.

The first is advancing the development of interchangeable products, which, again, ties to the focused effort on interchangeable products. And that will involve evaluating the data and information, specifically calling out real world evidence, needed to meet the standards in determining interchangeability. That effort can include looking at differences in presentations and container closure systems on, and how the impact of those changes would be evaluated and also methodologies to predict immunogenicity, which can also really facilitate development of these products. The second effort is in improving the overall efficiency of biosimilar product development. And that will involve considering latest scientific knowledge in advances

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and our collective experience with biosimilars, which is a large dataset now. And so specifics in that will be streamlining through considering advance technologies in both analytical and pharmacological assessment. And similar to demonstration products on interchangeability, predicting immunogenicity is a key factor in enabling development, and that will be evaluated in the context of both of these demonstration products. If we could move to the next slide.

So how will these be communicated on the outcome of these two regulatory demonstration products? So in terms of interaction with stakeholders, there will be a midpoint public meeting to look at the progress of these projects and to solicit input on future priorities. Preceding that engagement will be an interim report on where the projects are on. And there will also be a final summary report on the outcomes of the research project within the pilot.

Now there will be a distinct strategy document separate from the report on the research

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pilot outcome that will really take what we have learned from the program and use it in developing a comprehensive strategy document. That will be a year after the projects are completed. And that project will include potentially updated maps, guidances, or other steps to leverage the information that we have gained and also timeframes for these actions. Thank you. We can move to the next.

So Joshua Barton is now going to talk about some of the financial parts of this resource capacity planning. So thank you.

DR. BARTON: Okay. Good morning. Thank you, Steve. My name is Josh Barton. I'm the Director of our Resource Capacity Planning Staff in CDER, and this morning I'll be speaking to you the financial topics as well a hiring and IT within BsUFA III. These three areas are foundational to ensuring the continued success of the BsUFA program and providing the resources, expertise, and technology to implement the BsUFA III enhancements describes by my colleagues earlier today. Next slide, please.

The financial topics were focused on building

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the financial enhancements, building on the financial enhancements in BsUFA II to advance the sustainability of the program resources and to further enhance the operational agility of the program. Topics in the financial area include resource capacity planning, enhancing financial transparency, and updates to the fee setting process.

So starting first with capacity planning, resource capacity planning is a capability designed to use data and analysis to help reform resource needs. BsUFA II included commitments to establish the RCT, or resource capacity planning, or RCT capability to modernize our time recording approach and to establish a new methodology to address review workload needs called the capacity planning adjustment. BsUFA III negotiated commitments are largely focused on continuing to ensure the RCT capability. As we collect more data on resource needs and refine methodologies for forecast and review workload, the RCT capacity will continue, continually mature. In addition, we will be working to further integrate RCT analytics in the Agency's resource and operational

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decision-making processes.

Specific commitments in this area include the publication of an implementation plan, which will outline the continual improvement approach for the capacity-planning adjustment and how it will integrate resource capacity planning analytics in the Agency's resource and operational decision-making processes for within BsUFA III. We'll provide annual updates on progress to that implementation plan and, and document how the CPA funds are being used within the BsUFA program in the annual financial report.

There will also be a third-party evaluation of the resource capacity planning capability, which will be published in fiscal year 2025. And these commitments are also designed to be consistent with PDUFA, PDUFA VII to build on economies of scale across the programs. The next slide, please.

Around financial transparency, this is largely a continuation of existing commitments within BsUFA II, whereby we will publish a five-year financial plan and hold a public meeting to discuss the plan. And that financial plan will be updated

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each year with the corresponding public meeting each year. There are a couple of commitments to, specific commitments to include certain information in the 5, 5-year financial plan including reporting on personnel compensation and benefits costs that exceed the funds provided by the personnel costs and benefit portion of the inflation adjustment. This is related to the new strategic hiring and retention adjustment, which I will speak to you briefly in the next slide. We'll speak to how we -- within the five-year financial plan how we plan on managing costs related to personnel beyond BsUFA III. And we'll provide updates on progress towards implementing the plans to reduce the carryover balance as committed to in BsUFA II and as, as we'll outline in FY '22 financial report. The next slide will also have some additional details on that. Next slide.

In terms of modifications or updates to the fee adjustment, the fee-setting process, the fee-adjustment process each year, the BsUFA III agreement includes modifications to the capacity planning adjustment to clarify the scope of the inputs of use

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in the methodology. It includes a new strategic hiring and retention adjustment to provide funds to cover costs for retaining high, retaining and hiring highly qualified scientific and technical staff for the BsUFA program. And it includes enhancements to the operating reserve adjustment to, 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, is 10 weeks, or the equivalent of 10 weeks of operations. And the defined maximum is, is phased into 21 weeks. It's phased in over the first couple years of BsUFA III, as outlined in the slide. So 33 weeks in FY '23, the equivalent of 27 weeks in FY '24, and the equivalent of 21 weeks in FY '25 and, and subsequent years remaining at a maximum of 21 weeks. Next slide.

So that's, that's -- that concludes the, the financial topics, and I'll speak to the hiring as well. Hiring is critical to the, the continued success of the BsUFA program and the implementation of the enhancements discussed earlier in the meeting

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today is, of course, our ability to hire and retain the necessary scientific and technical expertise to deliver on the program. In recognition of this under BsUFA III, FDA will continue reporting the hiring goals on the FDA website.

And there will also be a targeted assessment of hiring and retention to be conducted by independent contract or with expertise in HR operations and to be overseen by the directors of CDER and CBER. This assessment will build on the findings of previous evaluations conducted under both PDUFA VI and BsUFA III and will focus on, on improvement -- focusing improvements on, on remaining challenges. The assessment will be published in 2025 and will be followed by a public meeting to discuss its findings and the Agency's plan to address any recommendations coming out of this report. And this also is designed to be consistent with the PDUFA VII agreement to build on (indiscernible) scale across the programs. Next slide.

But shifting gears to the IT-related goals. As you may be aware, the FDA has published its vision

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for a modernized technology and data environment in its, in its, via its T map and, and D map, the technology and modernization action plan and the data modernization action plan. These commitments are the next step establishing and executing on a data and technology modernization strategy that reflects the vision in those preceding plans providing strategic direction and for the future state of, of these data-driven initiatives.

It's intended to increase transparency and support FDA to progress in key areas of focus such as leverage and (indiscernible) technologies for regulatory activities and, and enabling enterprise approaches where feasible. FDA will share progress in any needed adjustments to the strategy annually. Part of the modernization effort is the transition and enhancement of the Electronic Submission Gateway, or ESD, shifting from an on-premise implementation to a cloud-based solution with an improved architecture that supports expanded data submission bandwidth and storage all while continuing to ensure its stable continued operations.

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This modernized cloud-based ESG will include an enterprise identify and access management solution. It will streamline the registration and access of ESG. FDA will continue to provide, provide ESG performance metrics as well as periodic progress updates on this transition. And, again, these, these commitments are designed to be consistent the with PDUFA VII commitments as well.

And with that, I have completed my three sections, and we'll hand this back to our moderators. Thank you.

MS. RAY: Thank you, Josh, and thank you to all of our presenters. This concludes our overview of the proposed enhancements. So we will now take a break. As we're running a bit early, the meeting will resume at 10:05. Our session following the break will be industry comments, and I'll ask that the speakers of that session to make sure you're back a few minutes early. Thank you.

AUTOMATED VOICE: Recording stopped.

(Off the record.)

(Back on the record.)

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MS. RAY: Welcome back from our break. And now let's move into the next session for industry comments. We invited three representatives who were actively throughout the negotiation process, and these four agreed to participate. They are Cory Wohlbach from the Association for Accessible Medicines, Camelia Thompson from the Biotechnology Innovation Organization, Lucy Vereshchagina from the Pharmaceutical Research and Manufacturers of American, and Meaghan Smith from the Biosimilars Forum. Each speaker will have a maximum of 10 minutes. Cory, you are first and may start us off when you're ready.

MR. WOHLBACH: All right. Good morning, everyone. Good afternoon. My name is Cory Wohlbach. I'm a Global Vice President for Biosimilar Regulatory Affairs at Teva Pharmaceuticals, and today I'm speaking on behalf of the Association for Accessible Medicines, biosimilar's counsel. I was a BsUFA III negotiator sitting with the counsel, and I appreciated the opportunity to provide the AM perspective on BsUFA III enhancements that are described in the commitment letter.

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As all of us attending this matter today can agree, biologic medicines represent one of the great medical breakthroughs, breakthroughs of our time treating cancer, rheumatoid arthritis, Crohn's Disease, and many other previously untreated, or poorly treated conditions. Biosimilars hold the promise of making important medicines more accessible to patients. Through science that carefully, intricately characterizes the underlying protein, biosimilar sponsors are able to develop products that have no clinically meaningful differences in safety, priority, or potency as compared to their corresponding originator biologics. Biosimilars are projected to save Americans tens of billions of dollars over the next decade but only if patients can access, access them.

Since 2010, FDA has approved 31 biosimilars, and the pipeline is growing because of, because of upcoming patent expirations and investments in R&D by biosimilar developments, developers. The programmatic enhancements industry and FDA negotiated in BsUFA III will support timelier patient access to biosimilars

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helping translate scientific advancements into affordable medicines for American patients. AM is proud to represent companies that play a leading role in this effort. BsUFA has been a successful user fee program.

It has helped increase the rate of first cycle approvals for biosimilars, and there is clear and predictable pathway to market with a substantial body of guidance for industry and well-developed meeting structure ensuring sponsors get early and meaningful feedback from the FDA on development programs. BsUFA III builds, builds on that foundation of the existing BsUFA program and will help bring more biosimilars to market more quickly by investing in regulatory science, further enhancing communication between FDA and sponsors, and improving supplement review times, among other changes.

AM is pleased that the BsUFA III program will include a regulatory science program. Investing in regulatory science will lead to improvements in how FDA assess, assess the safety, efficacy, and quality of biosimilars. The two newly created pilot programs

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will investigate opportunities to streamline biosimilar development and will review the cited requirements to meet the regulatory standard of interchangeability. Importantly, there is ample opportunity for increasing transparency and communication by way of public feedback regarding the regulatory science projects that FDA will undertake. Another significant improvement is to the meeting process, which will enable earlier interaction between biosimilar sponsors and FDA without the need for preliminary analytical data.

Additionally, a new BPD Type 2a meeting will help better inform product development by allowing FDA to meet with sponsors on a rapid timeline to discuss very specific questions about biosimilar development plan. These rapid, targeted meetings will ultimately save resources, minimize, minimizing the need for lengthier meeting requests. The negotiating enhancements also include a provision to allow biosimilar sponsors to request that FDA clarify any items following a meeting. Again, to minimize the need to conduct another meeting to increase

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efficiencies. These process improvements will go a long way toward bringing biosimilars to market faster and ensuring the biosimilar sponsors submit complete applications to FDA.

The BsUFA III agreement will also bring more predictability and efficiency to supplement reviews. Now that more biosimilars have been approved, there is a need to streamline the process by which supplements are approved. The new commitments address this need by establishing different review metrics for different types of supplement, supplemental BLAs.

Finally, FDA has recently approved the first two interchangeable biosimilars, a milestone achievement for the biosimilars community. Still, more work needs to be done to provide additional clarity when seeking this regulatory designation. That is why it is important that the BsUFA III agreement includes commitments for FDA to publish multiple guidance documents related to interchangeability on topics including labeling and post-approval manufacturing changes. We look forward to participating in the development of these

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guidances, guidance documents through the public comment process.

In conclusion, the negotiated BsUFA III agreement includes significant improvements to advance biosimilar development and, ultimately, to improve patient access to high quality, safe, and effective biosimilars. The AM Biosimilar Council strongly encourage the administration in Congress to support the negotiated agreement and to enact it as well. Thank you.

MS. RAY: Thank you, Cory. We'll now move to Camelia Thompson from the Biotechnology Innovation Organization.

DR. THOMPSON: Good morning, everyone. I am Camelia Thompson, Senior Director in the Science and Regulatory Team at the Biotechnology Innovation Organization. Bio is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers, and related organizations across the United States and in more than 30 other nations. Bio's members develop medical products and technologies to treat patients

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afflicted with serious diseases, to delay the onset of these diseases, or to prevent them in the first place.

Bio and their member companies strongly supported the establishment of a pathway for the approval of biosimilars because we recognize that market entry of safe and effective biosimilars may provide increased choices for patients and physicians. We remain committed to ensuring the success of the emerging biosimilars market through our engagement and ongoing policy developments related to biosimilars, including our recent participation in the technical negotiations for the reauthorization of BsUFA.

In regards to supplements, BsUFA III will establish new performance goals and timelines for review and action on original supplements to add or remove an indication based on the content of the supplement. For example, the supplement may include efficacy-related datasets. Will also establish new performance goals and timelines for review and action on original supplements seeking to update the labeling for a licensed biosimilar or interchangeable product with regards to applicable safety information that has

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been updated in the referenced product labeling. Industry's focus here was predictability, and these commitments will provide enhanced efficiency, consistency, and predictability for sponsors regarding specific review timelines, and, ultimately, enhance patient access to biosimilars.

In regards to labeling, in order to help ensure patient safety, it is important that manufacturers of biosimilar and interchangeable products have a timely, clear, and transparent process for adding important risk information to their labels when that risk information is the same risk information included in the label of the referenced product. BsUFA III will facilitate prompt updates to safety information by establishing a review timeline for safety labeling updates for the biosimilar with regards to safety that has been updated in the reference product labeling.

In regards to meeting management, the BsUFA III commitments enhance the current formal BPD meeting types to better guide industry during the early development phase to minimize numerous meeting

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requests to the FDA due to early and effective collaboration and more efficiently support ongoing development programs. The BIA meeting description will be modified to enable sponsors to attain early FDA advice on overall development design including, but not limited to, novel study designs or endpoints or specific statistical approaches.

This can enable sponsors to discuss the feasibility of 351(k) licensure for their product earlier in development. A new meeting type will focus on a narrow set of issues and is subject to a 60-day goal to allow for rapid, targeted feedback. This will speed the process of obtaining input on focused targeted questions. The clarification of FDA feedback and comments will ensure a sponsor's understanding of FDA feedback and comments made during an FDA sponsor meeting or in a WRO would support efficient product development.

In regards to best practices, best practices for communications during biosimilar application review are the responsibility of both industry and FDA. This initiative will continue to enhance timely

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interactive communication with sponsors during drug application review. FDA and industry will discuss best practices for communication during application review and potential mechanisms to operationalize these best practices. Industry will be able to gain insight from FDA on preparing for the most productive meetings gained in BsUFA III.

In regards to human factors protocols and use-related risk analysis for combination products, the demand for Agency review and feedback of proposed human factors studies and or user risk-related analyses exceeds current staffing. And in contrast to PDUFA, there are no specific review goals agreed up on under BsUFA. BsUFA III will establish predictable timeframes for when to expect Agency feedback for the review of URRA and human factors study protocols.

This will have a significant impact on program development and application submission for drug device combination products. BsUFA also provides funding for additional FTEs based on the new review timelines. Guidance is also forthcoming regarding how a URRA along with other information can be used to

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inform when the results from a human factors validation study may need to be submitted to a marketing application.

On behalf of Bio, we look forward to working with all of you. This concludes my remarks, and thank you for your time.

MS. RAY: Thank you, Camelia. We'll now move to Lucy Vereshchagina from Pharmaceutical Research and Manufacturers of America.

DR. VERESHCHAGINA: Thank you and good morning, everyone. I'm Lucy Vereshchagina, Vice President of Science and Regulatory Advocacy at the Pharmaceutical Research and Manufacturers of America, or PhRMA.

PhRMA is a trade association that represents America's leading innovative biopharmaceutical research companies, which are devoted to discovering and developing medicines that enable patients to live longer, healthier, and more productive lives. PhRMA's membership includes mainly leading biopharmaceutical companies actively developing biosimilar medicines, and we appreciate the opportunity to participate in

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today's public stakeholder meeting and would like to thank the FDA and our fellow negotiators for developing important and impactful BsUFA III performance goals (indiscernible).

As many speakers before me mentioned, biosimilars are playing an increasingly critical role in bringing new options to patients and increasing competition. As previously mentioned, there is 31 FDA approved biosimilar products currently, including two interchangeable biosimilars as well as nearly a hundred programs in the FDA's biosimilar program. And while the U.S. has not had the biosimilar market in place as long as the EU, the U.S. market has significantly walked over the (indiscernible).

And, in fact, the U.S. has approved more biosimilar products than the EU have in a comparable period of time. And this is largely due to the regularity predictability and efficiencies that have been provided by the FDA's successful implementation of the abbreviated approval pathway for biosimilars and the resources provided to BsUFA.

As a result of growing competition,

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annualized savings due to biosimilars reached $6.5 billion dollars in 2020 and potential savings estimated to exceed $100 billion dollars in the aggregate between 2020 and 2024. Many innovative medicines are now competing with multiple biosimilar versions with some brand biologics currently facing competition from four to five biosimilars. And in 2021, average sale prices of biosimilars were as much as 45 percent less than the originator's price of the initial biosimilars (indiscernible).

PhRMA has been a strong supporter of and participant in BsUFA since its inception in 2012. And through the target of improvements outlined in the BsUFA III performance goals whether BsUFA III will build on the success of the program and help increase timely access to safe and effective biosimilar and interchangeable biosimilar products for patients.

I will highlight (indiscernible) provisions in the performance goals so (inaudible) specifically BsUFA III will advance development of interchangeable biosimilar products by providing information and guidance to sponsors for development of biosimilar and

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interchangeable biosimilar products. BsUFA III will also inform us of strategic development of guidance, best practices, and procedures, specifically that they will issue guidance on topics conditional for the development of interchangeable biosimilar products, hold a scientific workshop, and develop a strategy document on the development of interchangeable products. And they will also file a, a regulatory science program, which clearly outlines demonstration projects and deliverables focused on advancing the development of interchangeable biosimilar products and improving the efficiency of biosimilar product development.

BsUFA III will also enhance manufacturing, inspection, (indiscernible) communications, and modernize facility assessment of (indiscernible), which is based on (indiscernible). Specifically, BsUFA III will promote timely FDA communication responses regarding manufacturing facility inspections and provide guidance on the use of (indiscernible) of tools to assess manufacturing facilities' names, named in pending applications.

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BsUFA III will also modernize (indiscernible) infrastructure and support adoption of (indiscernible) technologies and to modernize of this data and (indiscernible) capabilities in allowing (indiscernible) efforts, BsUFA III will support (indiscernible)-based modernization of the Electronic Submission Gateway with an improved architecture that supports expanding data submission, bandwidth, and storage.

BsUFA III will also enact, enhance accountability and transparency in (indiscernible) activities and with organization plans by establishing a strategy on data-driven regulatory initiatives.

BsUFA III will also enhance of this hiring, retention, and financial management and will build on the foundational works started in BsUFA II to modernize financial and staff resource management, accountability, and transparency, including clear hiring goals and progress reporting. The additional staff will help ensure that the new BsUFA III initiative are implementable and that the Agency has supportive resources in place.

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BsUFA III also includes other important commitments covered in details by Dr. Thompson before me and other speakers earlier today such as specific timelines for review of certain applications documents including those seeking to update safety labeling to effect changes to the referenced product labeling, identification to existing meeting types, and establishment of when your meeting type for rapid targeted feedback to enable timely corrections between sponsors and their biosimilar drug development and review.

In conclusion, BsUFA III will play a critical role in improving the predictable, timely, and efficient development and regulatory review of biosimilar and interchangeable biosimilar products. And PhRMA fully supports both the proposed BsUFA performance goals as well as the timely legislative reauthorization of BsUFA. PhRMA looks forward to working with FDA, Congress, patient, and medical provider groups, and other stakeholders to ensure timely authorization of this important program and to make sure that there are no disruption to their daily

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activities. Thank you, and thank you for your time.

MS. RAY: Thank you, Lucy. We'll now move to Meaghan Smith from the Biosimilar Forum.

MS. SMITH: Thanks so much. Good morning, everyone. I'm Meaghan Smith. I'm an Executive Director of the Biosimilars Forum. On behalf of our members, I am pleased to participate in today's public meeting on the reauthorization of the Biosimilar User Fee Act. The Forum is a nonprofit trade association whose mission is to educate stakeholders on the value of biosimilars and to improve access to biosimilars in the United States. We thank FDA for your collaboration and hard work in negotiating the BsUFA III commitment letter.

Biosimilars are a key contributor to healthcare savings in the U.S. Although biologic drugs represent only two percent of medicines prescribed to patients in the U.S., the cost of these drugs represent approximately 40 percent of total prescription drug spending. Biosimilars provide the necessary competition to allow Americans access to lower-cost biologic alternatives, and their timely

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licensure is critical to ensuring patient access to many life-saving or life-altering medications. The Biosimilars Forum believes that the improvements to the biosimilar review program under BsUFA III represents FDA's dedication to bringing biosimilars to the market as efficiently as possible.

We applaud FDA's willingness to engage sponsors early in the development process and provide targeted feedback. We are glad to see that the commitment letter codifies the timeliness the Agency had agreed to for labeling supplement reviews, improves upon those safety labeling supplements, and includes supplements to add an indication without additional data. These commitments will go a long way toward improving the efficiency of the biosimilar review process.

The Forum was and is very supportive of FDA's inclusion of a regulatory science program under BsUFA III. We very much agree with FDA that regulatory science is key to bringing more biosimilars to market and perhaps, eventually, streamlining the pathway to market for certain biosimilar applications. Better

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regulatory science will both, both stir the Agency's understanding of analytical similarity, which, in turn, may reduce the need for confirmatory clinical studies in certain cases thereby enabling biosimilars to be made available to patients sooner.

FDA's focus on interchangeability through the regulatory science program should help to bring much needed clarity and guidance just as more interchangeable products reach the market. We are excited the FDA licensed the first interchangeable products this year, and we anticipate that by the end of BsUFA III, FDA will have even more experience with the development and approval of interchangeable biological products.

While these changes are laudable, the Forum does want to call attention to the impact of the current inspectional backlog on FDA's ability to meet its BsUFA III commitments. The COVID-related inspectional backlog has disproportionately affected biosimilars. The percentage of on-time actions for original biosimilar product applications, including resubmissions, plunged from 100 percent during Q3 of

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FY 2020 to 75 percent during Q4 and further dropped to 67 percent during Q1 of FY 2021.

This trend for biosimilar applications is markedly worse than for other user fee programs and suggests that biosimilars have been more adversely affected by pandemic-related inspectional issues. For the BsUFA III commitment letter to be a success and for FDA to continue to meet its goals of first cycle licensure of biosimilar and interchangeable products, the inspectional backlog must be addressed.

As, as we head into BsUFA III, we look forward with the Agency to implement the commitment letter to the mutual benefit of biosimilar sponsors and FDA. We are excited by the fact that there is now a robust enough biosimilar industry with enough development experience to help BsUFA mature over the next five years. We are at a critical inflection point for the industry, and we believe that the commitments FDA has made to biosimilar review will be critically important to sustaining and submitting the biosimilar pathway for years to come.

Thank you for the opportunity to speak today.

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The Forum strongly supports FDA's ongoing efforts to advance a robust biosimilars program. We are happy to offer our members time and expertise towards ensuring the continued success of the BsUFA program. Thank you.

MS. RAY: Thank you, Meaghan. We'll now move into the final session of today's meeting, the Open Public Comment. This is another important mechanism to engage the public in a conversation. Please keep in mind that FDA will not be responding to your comments, but they will be transcribed and be part of the public record. To facilitate a transparent process, we encourage you to note any financial interests that you have that are related to your comment.

If you do not have such interests, you may state that for the record. And if you prefer not to provide this information, you can still provide your comment. We collect an online request for comment as part of the meeting registration process. We have 4 people signed up. Each speaker will have 10 minutes to speak. As I stated previously, I'll verbally

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announce when your time is nearly up and then again shortly after the 10-minute mark if necessary. We will hear today from Cate Lockhart from the Biologic and Biosimilars Collective Intelligence Consortium and Radia Hocini from El Kendi Pharmaceutical.

We also had signed up Geetanjali Saini from Abhilashi College of Pharmacy and Andrew Siegel from the Global Colon Cancer Association, but they were not able to log in today. When I call your name, please unmute yourself and begin your comment. If you are having technical issues, please let us know and we can move onto the next person and come back to you once they're resolved. First up, we have Kate Lockhart.

DR. LOCKHART: Good morning, and thank you to the FDA for the opportunity to provide public comment. My name is Cate Lockhart, and I am the Executive Director of the Biologics and Biosimilars Collective Intelligence Consortium, or BBCIC. My organization resides under the umbrella of AMCP, the Academy of Managed Care Pharmacy. BBCIC is the only nonprofit research consortium dedicated to evaluating the real-world safety and effectiveness of biologics, including

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biosimilars, through a transparent science-driven approach to using real world data.

Our mission is to generate reliable real-world evidence that examines the safety and effectiveness of biologics in order to, to improve public health. BBCIC is a public service initiative that draws on de-identified healthcare data covering over 90 million patient lives in the BBCIC distributed research network that leverages some of the infrastructure and tools developed by the FDA for their sentinel system.

As a true consortium, BBCIC includes participants from stakeholder groups across the healthcare system including pharmaceutical manufacturers, health plans or insurance companies, pharmacy benefit managers, patient advocates, clinician experts, and academic scientists who all come to the table with the shared goal of producing rigorous unbiased research to build the evidence base around biologics including biosimilars.

My comments address FDA's commitment to enhancing regulatory decision-making and facilitating

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science-based recommendations through the regulatory science pilot program and its two demonstrated projects. BBCIC supports FDA's commitment to investigate and evaluate the data and information, including real-world evidence, or RWE, to meet evidence standards for determining interchangeability. BBCIC also supports FDA's goal to improve the efficiency of biosimilar product development, especially through the enhancement of regulatory decision-making based on the latest scientific knowledge.

While BBCIC encourages FDA's continued adoption of RWE as part of the regulatory process, we also recommend FDA identify and utilize additional sources of RWE like those from BBCIC that focus explicitly on biologics to foster efficiency and consistency by more broadly leveraging the evidence base of RWE.

For instance, BBCIC routinely conducts longitudinal and utilization analyses for products with available biosimilars to describe real-world product use and treatment patterns, patient

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characteristics, and clinical outcomes. Currently, we are conducting a large-scale retrospective real-world comparative safety and effectiveness study of all GSF products, both filgrastim and pegfilgrastim referenced products, and biosimilars. This is an ambitious study. It's the first study of its kind and scale. We are also studying medication switching patterns and outcomes in patients with rheumatoid arthritis treated with immunomodulating therapies, including tumor necrosis factor inhibitors and janus kinase inhibitors. Additionally, we're driving the state of real-world research through ongoing methods and infrastructure development initiatives.

Finally, BBCIC believes the use of RWE also supports FDA's goal to promote transparency in regulatory decisions by expanding the use of well-designed real-world studies as supplemental information beyond randomized clinical -- randomized controlled trials to better capture the diversity of a real patient population. Real-world studies offer a means to efficiently evaluate questions that are pertinent to all healthcare stakeholders such as

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patient outcomes and other effects of real-world product switching or confirmatory studies for regulatory decisions.

In conclusion, I would like to thank today's attendees for their attention and to FDA for the opportunity to provide public comment and for their consideration of BBCIC's perspective. Thank you very much for your time.

MS. RAY: Thank you, Cate. We will now move onto Radia. Radia, if you could please unmute yourself and turn on your video, and you can begin your comment. You should see a mute or unmute button in the bottom right corner of your screen. We can hear you.

DR. HOCINI: (Indiscernible.)

AUTOMATED VOICE: Recording stopped.

AUTOMATED VOICE: Recording in progress.

MS. RAY: Thank you, Radia. It sounds like we're having some trouble hearing. So that will conclude our meeting. Thank you to all of the public commenters. Like I said, this concludes our public meeting on the proposed BsUFA reauthorization. FDA

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values all of the input that's been generated from today's discussion, and we look, look forward to receiving further comments to our public document. Anyone from the public is welcome to contribute through the public docket. The recording for this meeting and the transcript will also be posted to FDA's BsUFA III webpage.

(Whereupon, at 10:41 a.m., the proceeding was concluded.)

CERTIFICATE OF TRANSCRIBER

I, SARAH E. COBETTO, do hereby certify that this transcript was prepared from the digital audio recording of the foregoing proceeding, that said transcript is a true and accurate record of the proceedings to the best of my knowledge, skills, and ability; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this was taken; and, further, that I am not a relative or employee of any counsel or attorney employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.

Sarah E. Cobetto

SARAH E. COBETTO