Close Captioning Transcript from the Public Meeting on the Final Assessment of the Program for Enhanced Review Transparency and Communication in the Biosimilar User Fee Act

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>> Mark: Good morning! Can we go to

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the next slide, please. There we go, thank you. Good morning and welcome to the public meeting on the final

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assessment of the program for enhanced review transparency and communication in a bio similar user fee act.

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This is also referred to as CEPA. Next slide, please. I'm Mark and I am from the program evaluation and

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implementation staff at FDA center for drug evaluation and research or theatre. I'm facilitating. This was

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first passed in law in 2012, authorizing FDA to collect user fees to review the bio similar product

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applications. Under the second application, we committed to apply a new program, in bio similar

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application reviews and to have an independent contractor conduct an assessment of that program. The

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purpose of today's meeting for the assessment of the program for the 351K application for the program to fulfill

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part of that commitment. Next slide, please.

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Today's meeting has four main parts. First, the independent contractor will present their assessment. Second, a

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representative from FDA will present the agency's perspective on the assessment. Third, representatives

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from industry will present their perspectives on the assessment and finally, we'll provide time for

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questions and answers. We will not hold the public comment period. FDA invited everyone who registered for the

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meeting, prior to March 10th to submit a request for an oral statement but we did not receive any requests for an

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oral update. Next slide, please. During the meeting, you'll see the

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presenter's slide in the Zoom window. You can ask questions during the presentation by opening the Q and A

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box and type in your questions. Please indicate to whom you're addressing your question if you want it addressed

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during the meeting. These questions will be addressed during the Q and A period. All questions and comments

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will be a part of the public record. Next slide, please.

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We would also invite you to submit comments to the public docket which remains open to May 23rd, 2022. You

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can search for the docket number or final assessment for the program for enhance review transparency in

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communication in the bio similar fee act and www. Regulations.GOV and submit comments there. If you have

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technical difficults during the meeting, please type it in the Q and A box and someone will assist you. Next

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slide, please. With that, I am please today

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introduce our first presenter. Next slide. Valerie from the eastern research group will provide their

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assessment of the program. Take it away, Valerie.

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>> Valerie: Yes, thank you, Mark! Please go to the next slide, please. So my name again is Valerie and my

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pronouns are she, her, and I'm with eastern research group which is the independent contractor enlisted to

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conduct this evaluation or assessment at the program for enhanced review transparency and communication. So

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during this presentation, I'll give a little bit of an introduction to the assessment and then share some

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highlights of the results, answers to assessment questions and findings and recommendations. Next slide, please.

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Thank you. So in terms of introducing the assessment, I first wanted to describe the program in a little bit

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more detail. So the goals of the BSUFAII program is to improve efficiency and effectiveness of the

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reviews of 351 k BLA reviews for bio similars. Minimize the number of review cycles needed for approval.

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similars. Minimize the number of review cycles needed for approval. And promote transparency and enhance

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communication. So a major attribute of the program specific to, are similar to those in the parallel program for

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the prescription drug user program which was started in five and now continues to six. So the major

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attributes are having the review clock begin on a 60 day filing date. So the first 60 days after receipt are used

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to review the application to determine whether FDA will file the application and begin the review or refuse to

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file. Another attribute is a mid cycle

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communication which is touch point early to middle in the review to share the status of the application and

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review issues and so forth that have been identified to date. And then the late cycle meeting which addresses

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issues that continue to be outstanding and any new issues that have been identified in kind of related kinds of

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topics which we'll talk a little bit more. Next slide, please. So other attributes of the program include

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certain expectations at the BPD Type 4 meeting. So there's the expectation that FDA and the sponsor will reach

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agreement on the content of a complete application and also, reach agreement on whether the applicant will submit

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minor components on a delayed basis within 30 days after submission of the application. And if so, what those

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will be. The program also establishes the expectation that the applicants will submit a complete application on

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original submission unless there's been those agreements on the latest motion final components and that FDA will

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complete inspections within 10 months of application receipt. So if you can go to the next slide, please. Great,

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thank you. So as Mark indicated, FDA made some

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commitments in negotiations for specific to the program that is such a commitment and then this assessment of

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the program is a commitment that was created during that negotiation process. So the purpose of the program

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assessment is to identify relationships between program attributes such as the program as a whole and the attributes

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of the program that I just described. Review process attributes and attributes of the application such as

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therapeutic area or type of sponsor and so forth. So identifying relationships between those types of attributes and

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first cycle regulatory outcomes and time to first-cycle regulatory outcomes for approval or complete

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response. We also, as part of this assessment wanted to learn how applicants and FDA staff characterized

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communication and application reviews. When we started this assessment, we of course didn't know that the pandemic

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was going to come, not much further into the program. So because of the COVID-19 pandemic, we also examined

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the impacts of the pandemic on the implementation of the program so we'll talk about that during this session as

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well. Next slide, please. So in terms of

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our approach to the assessment, the first thing we did was to create a set of assessment questions that the

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assessment should answer based on the purpose of the assessment. We have been identified as a set of

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qualitative and quantitative metrics that we needed to collect data on in order to be able to answer those

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questions. We then developed protocols and instruments with which to collect the data that we need to quantify and

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develop answers for the metrics. And then collect data itself. So during the data collection process which is

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the bulk of the assessment, we observed meetings between FDA's staff and sponsor and applicant staff and just a

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note on terminology, we used word sponsor for companies and other entities that are sponsoring

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biosimilars development program and have not yet submitted an application for that similar. We use the term

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applicant once the company or other entity has submitted the application. So we observed meetings between FDA

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staff and sponsors and applicants. We reviewed a lot of documentation related to the application and after

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there was a first cycle action, we interviewed both applicant representatives and FDA review team

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members in order to understand their perspectives on communication and the review process and review

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transparency. We then analyzed the data in both qualitative and descriptive and quantitative matters and we

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developed some recommendations as part of an interim report that we produced in December of 2020. And the final

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report which we produced last month, February 2022. Next slide, please.

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So the final report for those who have seen it includes an executive summary and introduction to the

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assessment, our methods, results, assessment questions and answers, findings and recommendations and some

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appendixes. The report is available on the FDA's website, the URL is shown in tiny, tiny lettering but if you go to

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the assessment page on the FDA's website, you'll be able to find the final report. Next slide, please. So

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one the results section, we provide a bunch of results for the aspects of the review process and the program. So

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we provide results for the program overall, the BPD type 4 meetings, KWAUMT of 351 k applications, formal

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communication plans, day 74 letters, mid cycle communications. Late cycle meetings, advisory committee meetings,

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inspections, information requests and amendments and good review management principles and practices.

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Next slide, please. So now we're going to talk about some of the

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highlights of the review. You can see the faculty results in the report. So first, just to provide an overall

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picture. We present here what the cohorts were, the applications in the cohorts were for the program and the

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baseline which was one. So in the one, there was a total of 23 applications submitted that were filed and received

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a first cycle action. In the BSUFA2 program which is just the first four years of the program, and so the

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numbers are a little bit lower because we're looking at your years of the program and not a lot of time after

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the first four years to reach additional cycle actions. Versus all five years of the baseline plus

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several years in addition to look at any actions that took place during the five fiscal years of the BSUFA1. So 21

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applications were filed and received first cycle actions in the BSUFAII program. Of those, you can see that 14

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received approval, 6 received a complete response, and 1 received, one was withdrawn before -- after filing.

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So if you can go to the next slide, please. So we looked at a variety of attributes of the applications in the

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program and one of those were therapeutic areas of applications in the program and in the BSUFA 1

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baseline. In most cases, most applications had indications that fell into the rheumatology, dermatology,

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oncology, gastro enTROEology area. In the BSUFA, we had two with enDROE chronology and one with opthalmopathy

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indications and these percentages that you see here, some much more than 100 percent, because for any given bio

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similar, they are often indications that fall into multiple therapeutic areas. As you saw in the numbers,

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you'll note that the first cycle approval rate is higher in the BSUFA II program than in the one baseline.

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So this was 67 percent versus 39 percent in the first baseline. Next slide.

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So of the ones that got a response letter, the issues that were cited in

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the complete response letter for the reason for not receiving approval were largely in the product quality and

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quality microbiology areas as well as facilities. In BSUFA I, there was some that also signed immunogenicity and

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again, these sum to, these percentages sum to more than 100 percent because in any given complete response letter,

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typically cites more than one issue. More than one approval ability issue. Next slide, please.

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So we also looked at the time from receipt from 351KBLA to first cycle

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action. And as expected, the medium time to first cycle action was longer in the BSUFA II program because of the

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two month difference in the review clock. I mentioned earlier that the BSUFA II program establishes a 60 day

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filing period and the review clock starts at the 60 day mark so the difference in time from receipt to

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first cycle action are those two months, the 60 day period. Next slide, please.

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We also looked at goal extensions. In terms of goal extensions, in BSUFA

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I applicants were allowed to submit amendments and FDA could grant goal extensions in the last three months of

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the application review. In BSUFA II, FDA could grant goal at any point in the review process. Those goal were

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expected to be rare either based on a major amendment to the application or a situation in which the facilities

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were inadequately identified in the application and therefore, there was more time needed to adequately examine

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those facilities. So the purpose, the stated purpose or the intent in the BSUFA II program is to grant goal

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extensions when the extra three months that are provided by goal extension has a high likelihood of resulting in

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approval in the current review cycle that is that these are situations where, if there's a little bit more

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time, than there's time to complete the review of the major amendment or conducting inspections in time to have

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an approval in the first cycle of review. And indeed, that was the case. So what we saw is in the program goal

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extensions, major amendments were rare, just one. And that one was resulting in an approval and the baseline, there

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were three in those three resulted in approval as well. Next slide, please.

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So now I'm going to go through and talk about kind of the major MRIBTs of

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attributes of the BSUFA II program. The first one is the BPD type 4 meetings which are presubmission

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meetings that happen before the applicant submits the application and represents an opportunity for at that

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point, sponsors and FDA staff to talk about the intended application and what the content of a complete

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application might look like. Questions about content, format, organization, expectations and so forth. So many of

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the sponsors did request a BPD Type 4 meeting. About 75 percent did. Most of those meetings occurred at least two

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months before application submission which is kind of what the expectation is on average, it was about 6 months

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before application submission. And in interviews, we found that applicants, and again, we interviewed applicants

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and FDA review teams after the first cycle action approval or complete response and so in those interviews,

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applicants expressed they valued the opportunity to understand FDA's expectations for the application. And

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also, when applicants requested or sponsors at that point requested a BPD Type 4 meeting, the FDA provided

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responses before the meeting itself, that the sponsors found that FDA's preliminary comments before the

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meeting resulted in many of their questions. So they certainly expressed appreciation for the value of the

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preliminary comments. Next slide, please.

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We also looked at the quality of the application and we did it in a couple of ways. One is, we looked at the

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filing review documents for the applications to see if, to see what issues, technical or other issues were

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identified in the finding review documents. So based on the examination of the final review documents, all of

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the applications in the BSUFA II program were technically complete by the type of filing and of course, by

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the time of filing, that is an initial review just to see if the application is sufficiently complete and of

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sufficient quality to be able to conduct the review. It's not the complete review or detailed review so

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very often after an application is filed, FDA in their more detailed review, identify completeness or

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quality issues and needs to submit information requests or otherwise identified issues that were not

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apparent kind of in that initial review during the final review period.

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So after filing FDA primary reviewers, identified completeness and quality issues in 6 of 21 applications

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and those issues generally related to product quality, clinical or clinical pharmacology. Next slide, please. We

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also looked at formal communication plans and so the BSUFA II program provides an opportunity for applicants

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and FDA staff to create an alternate communications schedule during the review so that means that if they

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wanted to have a different time line for contacts, meetings, if they wanted to skip or change the timing of mid

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cycle communication, or anything of that nature, they could do so in a formal communication plan. Those

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formal communication plans are expected to be establish at the Type 4 meeting and BSUFA II, that option was not

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utilized so there was none in the program. Next slide, please. So we also looked at day 74 letters as the

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name suggested. FDA is expected to send a letter to

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the applicants by the 74th day after the receipt of the application and the letter is expected to identify any

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kind of initially identified potential review issues. That may have been identified at that point and also, to

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provide kind of a time line and so the Day 74 letters, did in fact, serve those purposes and what we see in the

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day 74 letters is that about 1/4th of those letters identified potential review issues and remember, this is

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still early in the review cycle and so FDA has not completed an in-depth review and so FDA then, after that

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point in time, will continue to conduct an in-depth review and identify other potential review issues. So of those

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potential review issues identified in day 74 letters, the majority had to do with probably quality and regulatory

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matters and also related to dedevice and statistics. Next slide, please. So the mid cycle communication again, is

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communication, usually by teleconference between applicants and FDA staff, review staff, kind of in

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the early mid cycle period. In interviews with applicants and FDA review staff at first cycle action was

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completed, we heard a lot of positive feedback about mid cycle communications. Applicants indicated

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they valued these mid cycle communications as a very important touch point to understand and receive

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a multi-disciplinary holistic view of FDA's kind of view of the application.

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They stated and also kind of early issues and so forth that have been

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identified. And this, they felt enhances the predictability of the review and also facilitates progress

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in review in terms of facilitating the ability to identify and understand and address any issues that have been

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found at that point. So we also heard that many FDA staff value the mid cycle communications for some more

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reasons. And that the mid cycle communication provides a predictable anchor point in the review which is

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useful for both the agency and applicants. Some FDA staff felt that the mid cycle communication is

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redundant to their existing communication channels so they felt that they would be communicating in

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similar ways or conveying similar information through their existing communication processes.

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So in the mid cycle communication, FDA identifies review issues that have

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been found to date. And what we saw in that is that, when mid cycle communications had, did identify

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product quality or facility issues, that it was associated with some what lower rate of first cycle approval and

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those that did not identify product quality or facilities issues were associated with the higher rate of

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first cycle group level. And that is consistent with our description of the complete response letters in which

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product quality and facilities are the major types of issues that are cited in those complete response letters. So

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FDA discussed review issues in 13 of 30MCC and most often were clinical and product quality issues. Next slide,

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please. So late cycle meetings, another

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meeting that is established in the BSUFA II program and they provide an opportunity to discuss the status of

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the application, significant issues, to ideally resolve those issues in order to be able to move forward with the

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review and hopefully, toward an approval. We found that the late cycle meetings were most often used to

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discuss information requests most marketing commitments and requirements, labeling and

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inspections. In some cases, FDA staff did not have significant issues to discuss in the late cycle meetings.

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And in those cases, they were primarily used for late cycle issues regarding PMCs and PMR labeling and so forth.

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Some FDA staff suggested there be an opt out option if there's no significant issues to discuss.

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Applicants felt that regardless of whether there were issues at the late

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cycle meetings, that they're still of value because it does provide an opportunity to discuss and facilitate

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forward movement with late cycle activities. Not surprisingly, late cycle meetings that have no

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substantial issues, were with a higher rate of approval. FDA discussed issues in substantive issues in 12 of 20 late

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cycle meetings and most often, they were product quality or quality microbiology issues. Next slide,

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please. So we also looked at advisory committees and BSUFA I, they held it for the first bio similar FDA. So with

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the BSUFA 1, FDA did hold a number of advisory committee meetings. So in BSUFA II, most of the biosimilars

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shared the same reference products as in BSUFA I so FDA did not hold advisory committee meetings for those.

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Exceptions are here and also, in these cases, FDA did not feel a need to hold advisory committee meetings.

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So in total in the BSUFA II this far, zero of 21 meetings. Next slide,

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please. Thank you! So we also looked at inspections and what we found is that, as I mentioned earlier, there

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was an expectation in BSUFA II that FDA complete inspections within 10 months of application receipt and in BSUFA

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II, FDA did complete 94 percent of the inspections within that time frame. In a minute, I'm going to talk about the

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impact of the pandemic because the major impact was on inspections.

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In this chart you see the distribution of inspection completion dates within the review cycle and what

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we see is that in BSUFA II, a majority of almost all of the inspections were in fact, completed in the 10 month

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time frame and that clusters around the 3 and a half to 7 month time frame. And in a couple of cases whether it's

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pandemic related delays of inspections and in cases of a goal extension, the inspections may have been completed

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later. And we see that in the baseline BSUFA I as well that relatively speaking, the inspections were

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conducted a little bit later in BSUFA I kind of relative to the review cycle because again, there's a two month

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difference in review cycle. Next slide, please. So again, when we look at the impacts of the COVID-19 pandemic on

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implementation of the BSUFA II program, and on the review process, the major impact was on inspections. And that's

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because historically, most inspections are conducted in person and OVENG during the COVID-19 pandemic, there

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during the COVID-19 pandemic, there were travel restrictions, resulted in delay of inspections for applications.

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So one thing I want to note is that

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this assessment covers applications that reach the point of a first cycle action. And so four applications that

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have not yet received a first cycle application, either because they were submitted kind of in perhaps, like the

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fourth year of the program and the goal date hasn't occurred yet, or because of pandemic related delays in

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inspections. Those applications are not covered in this assessment. And so what we'll see, proportionally more of

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the applications that receive first cycle actions after this assessment will have have had a pandemic related

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delays and inspections compared to those applications that are covered in this assessment. One thing that we

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noted is that the BSUFA II program inspections resulted in FDA Form 483 less often than baseline inspections,

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30 percent compared to 42 percent. So the 483 is a document that the FDA inspector will provide at the

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completion of an inspection when they identify a deficiency so in BSUFA II, proportionally, there were fewer

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deficiencies per application in form 483 in the BSUFA I program, BSUFA I reviews. So in interviews, applicants

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described the inspection process as direct and transparent and again, because we interviewed applicants

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where the application had received a first cycle action, there was some discussion of delays in inspections

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and you know, at that point, there was a lot of understanding that because of travel restrictions, FDA could not

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complete inspections in the same time line they would have hoped to or expected previously. During kind of

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the BSUFA II program, FDA did begin initiating alternative inspection processes that were document based

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where kind of a risk analysis indicated that type of process would be appropriate and safe so those were

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also considered helpful in direct and transparent during our interviews.

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Next slide, please. We also looked at information requests and amendments that were submitted throughout the

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review cycle of each application. What we found is that in the BSUFA II program, there were more information

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request and amendment items per application than in the BSUFA I baseline. Just to explain what we mean

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by items, FDA will submit information requests that often contain more than one item in the information request

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that they would like the applicant to respond to. And in turn, applicants will sometimes bundle their responses

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to information request items in amendments. There's not a one to one correspondence between information

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requests and amendments because applicants sometimes respond to items in either individually or in different

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kind of bundles than those that were presented in the information request. So what we see is the number of

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information requests in the BSUFA II program and the number of items in the BSUFA II program are higher in BSUFA

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II than in the BSUFA I baseline. And like wise, the number of

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amendment items per application is higher in the BSUFA II program but applicants can bundle the amendment

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items more in the BSUFA II program resulting in fewer amendments. In the BSUFA II program than in the baseline.

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Next slide, please. So here we showed the distribution of amendment items based on kind of the category of

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issues. And what we see is a large majority of amendments that fell into the product quality category and then

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small numbers of amendment items related to clinical pharmacology, facilities, statistics and so forth in

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other kinds of categories. Next slide, please. So now I'm going to go through the assessment questions and the

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answers we came up with based on our observations and the data we collected. Next slide, please.

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So the first two assessment questions were, what is the

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relationship between program attributes and 351K application first cycle regulatory outcome. And what is the

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relationship between program attributes and first cycle regulatory action time. So time from receipt to action.

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So as we indicated earlier, in the BSUFA II program, the first is higher than the baseline and in terms of

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timing, the first cycle reviews are longer in the BSUFA II program than in the BSUFA I baseline, again, because

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of the two month difference in the review clock. One thing that we typically like to look at is what is

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the overall approval rate over multiple cycles of review. So for applications that are approvaled in the first

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review cycle, one cycle to approval, and many times if an application receives a complete response, the

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applicant will then do more work and then submit a new application and undergo a second or third cycle of

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review. Sometimes that results in approval and sometimes not. So it's interesting to look at the overall

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time, the overall rate of approval and the overall time to approval in programs. And we could look at that

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overall rate and overall time to approval in BSUFA II because not enough time has elapsed in order for

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applicants to submit a second cycle application and for FDA to conduct second cycle reviews. So the theory is

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that if you have a higher rate of first cycle approvals, that might lead so a shorter overall time to approval

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because more of the applications are being approved in the first cycle which is a shorter time than having to

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resubmit and then undergo a second cycle review.

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So we might predict that it would be the case but BSUFA II but we can't actually look at that because of where

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we are with time. Next slide, please. So we also looked at the review process attributes. And review process

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attributes just have to do with various aspects of the review process whether those are informational request

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inspections or other parts of the review process. And because the numbers of applications were small in

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both BSUFA I and BSUFA II, they are just insufficient to answer this question about any relationships

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between review process attributes and first cycle regulatory outcome and first cycle regulatory time. So maybe

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over a number of BSUFA cycles, there will, eventually be an enough data but not at this time, next slide, please.

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So we also looked at the relationship between application attributes and 351K first cycle regulatory outcome

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and so application attributes have to do with the therapeutic area, the type of applicant that submitted the

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(k) first cycle regulatory outcome and so application attributes have to do with the therapeutic area, the type of

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applicant that submitted the application and so forth. So we found this is some what lower for those with

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hematologic and oncologiy. The numbers are low. Or if it's because of the high number in these therapeutic

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areas. So we mentioned that, but we certainly cannot say that is, staticically significant or a

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necessarily meaningful finding. We also observed as we indicated before, that first cycle approval rate is higher

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for applications with a major amendment. Again, that's consistent with the intent of granting the major

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amendment and a goal extension. And the first cycle approval rate is also higher for applications submitted by

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applicants who have previously submitted 351(k) BLAs and had those approved. And so, in one sense, this

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is kind of understandable because applicants with more experience are likely to kind of have a better

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understanding of FDA expectations for the application, have greater resources in terms of organizational

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expertise and facilities and so forth associated with what is needed to have an approvable application.

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On the other hand, that's not always true because sometimes

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applicants without prior experience with approved biosimilars can gain kind of that expertise through

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strategic hires, through consultants, through partnerships and so forth. So it is a trend but not one that is

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always the case. So we also looked at the relationship between application attributes and first cycle regulatory

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reaction time and not surprisingly, the time to first cycle action is higher for applications with a major

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amendment. Next slide, please. So in our interviews, we talked with both applicants and FDA review staff for

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applications that received a first cycle action. What we heard was largely positive. So from applicants,

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we heard that communication is excellent and constructive. That the mid cycle communication and late cycle

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meeting are valuable. That FDA review staff are responsive, constructive. There were a few applicants who did

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offer some suggestions and one of those was to ask FDA to provide updates on review act ivities after the late

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cycle meeting and to provide advance notice of information request and to aggregate information requests when

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possible and to notify applicants when, if and when, information requests and issues are resolved.

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On the FDA side, we also heard that the communication is excellent,

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constructive, collaborative, efficient, and effective. Similar things from both applicants and review staff on

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that front. Most also said that the mid cycle communication and late cycle meeting are useful and there were a

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few people who suggested that FDA be allowed to opt out of the late cycle communication or late cycle meeting if

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there's no review or substantive issues to discuss. Next slide, please.

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So we also asked about how applicants and review staff characterized application reviews so

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the previous slide was about communication. This slide is about reviews. So applicants on the whole

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thought that application reviews are transparent, redixitable and efficient. When they're part of a

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global team so they're needing to team members across time zones and continents. We did hear from some

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staff that it would be helpful to allow more time for primary reviews and also, to move inspections earlier do

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allow more time for reinspection if that's needed. Next slide, please.

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So now we'll talking about our findings and recommendations from the assessment. This is kind of a SIPT

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synthesized and consolidated look. Next slide, please.

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So the first finding is that overall, the BSUFA II program has been successful in enhancing review

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transparency and communication and so our recommendation here is that no action is needed. Next slide. The next

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finding is that overall, the new program milestone communications and mid cycle and late cycle has served as

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anchor points for review work and planning and for providing a forum for multi-disciplinary discussion

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application status and paths forward to resolve approval BLT issues and promptly if possible. Nothing needed

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here. Next slide, please. The third

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finding is that by requiring application completeness, the program has enhanced the ability of FDA to

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conduct first cycle reviews more efficiently and effectively and again, no action needed. So here, we talked

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about the impacts of the COVID-19 pandemic. So the finding hire is that except for some inspections and we'll

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allude to that a little bit later, but the program has continued to operate effectively during the COVID-19

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pandemic. And at this kind of overall level, no action is needed. Next slide, please. So now we look at

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specific topics within the BSUFA II program. So the first of those is that the BPD Type 4 meeting. So the finding

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is that in the BPD Type 4 meeting process, providing presubmission advice and templates for applications,

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content and organization helps sponsors prepare applications that meet FDA expectations. So the recommendation is

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to establish this as a good practice in the BPD Type 4 process. Next slide, please. So next, the late cycle

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meetings have generally been most valuable to applicants. When they were able to discuss additional topics of

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interest such as inspections, post market requirements and commitments and labeling. And so here, the

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recommendation is to consider soliciting discussion topics from the applicant and allocating time in the

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late cycle meeting agenda for applicant identified discussion topics and this is really going to vary from

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application to application because certainly when, at the late cycle meeting point, there's still sub

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stantive issues that need to be discussed and information requests, typically the time is taken on these

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issues. When there's fewer or none of those, then there is typically more time to discuss these late cycle

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activities. Next slide, please. All right, inspections.

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So what we heard from applicants is that on an application by application basis, FDA communication regarding

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inspections has generally been clear, allowing for good inspection coordination and contributing to

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overall review transparency and predictability. And again, here we see kind of the main impact of the

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pandemic so pandemic related travel restrictions, did lead to reduced predictability for inspection time

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lines and that was kind of a fact of life that everyone had to deal with due to travel restrictions. So to some

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extent, FDA was able to mitigate this challenge by instituting an alternative records process in cases

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where that was appropriate. But never the less, some actions have been deferred.

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We just note that at the time of this assessment, you know, FDA this

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gun doing the alternative record reviews and as time goes on, we expect that the impacts of the pandemic may

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diminish for one thing and also, that kind of alternate approaches to inspections may become more refined

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and more predictable just through experience and the ability to understand and define how and when

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these take place. Next slide, please. So with regard to information requests, we found that in some cases,

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the FDA target space were sometimes impact call for applicants and particularly those with a global

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presence, again, where they need to coordinate across the significant time zone differences. PCH.

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So in some cases, time zone

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differences were for one or two day response times so the recommendation here is where feasible, to promote IR

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response times of more than two days, or issue IRs earlier to allow for extended time in these situations.

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Next slide, please. So that concludes our summary of the assessment report. Again, you can find the complete

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results online. Thank you! >> Thank you for your assessment. Now,

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I'm pleased to introduce Sarah, director of FDA's therapeutic biologics and biosimilars. She will

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present her perspective on the assessment.

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>> Sarah: Thanks, Mark! Next slide, please. Next slide. So good morning and I would like to thank the eastern

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research group for their work in performing and presenting their assessment of the BSUFA II program for

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enhanced review. My job is to provide the FDA perspective and context on ERG's recommendations. F.

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. For those who are keeping track,

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there's 34 approved, with 21 being marketed including all those for oncology treatment and supportive

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care. Since we last met for the interim assessment, we have also seen the landmark approvals or three

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interchangable ones. The insulin YFGN, which is interchangable and this which is interchangable with humor RA. We

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have the first bio similar which is we anticipate coming to market later this year. Next slide, please.

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This chart displays the number and types of meeting requests. The number

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of bio similar product similar programs and reference products in the overall program over time. The total number of

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meeting requests is generally trended upward in time and does include some fluctuations but rebounded in 2021.

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The number of BPD program is represented by the green line for which there's publicly available data

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since 2016. The numbers here are also trending upward to near 100 in 2021.

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Similarly, the number of reference products for which there's a biosimilars program has trended up

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over time as represented to the blue line. Represented by the blue line, up to the number 45 as you can see there.

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Next slide. More directly related to the product topic, this chart shows the applications and -- the original

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number of BLA has fluctuated from 2 to 13 applications at a time as has the number of supplements. However, the

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number of manufacturing supplements is steadily increasing. The dark blue line represents new entities,

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therapeutic biological approvals in the new drug program which represent about 20 to 30 percent of all novel drug

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approvals. As you can see, they're in the same

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general 1 to 2 digit neighborhood as biosimilars approvals. Next slide. In that regard, the BSUFA program final

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assessment performed by ERG appears to be consistent with the findings of the final assessment as with the PDUFA

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program assessment, there's more first cycle approvals and fewer complete responses in the program cohort

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compared to the applications which were in the cohort prior to the implementation of the program. Next

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slide, please. As we discussed in the interim assessment, overarching findings are consistent with the PDUFA

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findings. Overall, the conclusions are that the program approach is working well and the additional communications

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enhance predictability of review and first cycle review efficiency. And additional findings specific to this

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final assessment suggests that during the pandemic, the program has continued to operate effectively with

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a possible exception of some inspections which were impacted by travel restrictions. As ERG noted, to

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some extent FDA was able to mitigate this challenge by instituting an alternative review process in cases

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where it's appropriate, never the some, some inspections and FDA actions were deferred and the context were really

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product and application specific and the requirement for a prelicensing inspection for facilities that have

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not yet inspected really did impact our flexibility in those areas.

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Next slide, please. The final specific findings and recommendations were the same for the interim

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assessment and the best practices that are recommended to be implemented more broadly or consistently. I won't

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repeat them here but suffice to say that we are going to be soliciting for specific communication best practices

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and we'll be planning to incorporate those in document updates as part of our BSUFA III change effort. Next

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slide, please. So in summary, the program for enhanced review transparency and communication appears

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to be working as expected in providing similar benefitings as its implementation of this. It does not

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indicate a need for informational process changes for applications within the program, with the possible

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exception of inspections which is a topic area on its own and not specific to the program per se. And is an area

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identified by specific evaluation III. As discussed specific recommendations for changes or major process based on

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best practices and our plan will be continue to seek out implement, document these process improvements to

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enhance transparency and communication towards the goal of facilitating efficient bio similar product

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development. So thanks for your time and your attention. I will turn the meeting back over to Mark now to

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introduce our industry speakers. >> Thank you, Sarah. Next, we'll hear

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from industry perspectives who will give their perspectives. Speaking first is David, senior vice president

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for sciences and regulatory affairs for the association of accessible medicine. David?

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>> David: Thank you, Mark! Good morning, everyone! THAURNG for this

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Thank you for this opportunity to speak today. My name is David and I'm senior vice president at the

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association for accessible meds or AAM. Today, I'm speaking on behalf of the biosimilars counsel. We appreciate the

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opportunity to participate in today's meeting of the final assessment of the program for enhanced review

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transparency and communications in the biosimilars user fee act. The counsel has reviewed the report issued by the

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eastern research group. For short overall, we agree with the findings of many of our members had an opportunity

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to contribute to the research described in this report. And we appreciate the program evaluation and ERG report

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where specified in the FDA's BSUFA II commit letter. We are pleased to see this supports the value of many of the

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improvements and communications and the enhancements we made in BSUFA II.

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BSUFA II had a twelve month review cycle with touch points during the BLA process compared to BSUFA I. While

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other enhancements introduced in BSUFA II and increased FDA experience may have contributed, we believe that the

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additional communication touch points introduced during the BLA reviews played a significant role in the

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higher rate of first approvals of documented within the ERG report. As ERG report suggested new program

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enhancements that are going to be introduced in BSUFA III and it will address mainly the communication

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deficiencies, ERG identified and the current BSUFA development and review process. Be F.

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For example, permits discussion of

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the bio similarity, without providing comparative, analytical summary data for BLA meetings will give applicants

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and FDA to align under the very out set of the program. This will present the waste of time of resources of

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applicants and the agency. The new type 2 meetings, allowing for rapid targeted feedback gives applicants

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additional avenues to communicate with FDA about discreet questions. We are pleased that under BSUFA IIIFDA, it

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will answer questions of clarifying nature of all meeting types. These enhancements will improve

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communication quality reducing the burden of FDA and leading to more first cycle approvals. While we hope

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that increased communications during BLA reviews will lead to more first cycle approvals, we also appreciate

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the increased communications which will allow applicants to better understand deficiencies if any are identified by

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the FDA. Clear and early understanding oaf

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ing of deficiencies will allow them to address them during the early cycle. While the points highlighted in the

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ERG report was the impact of inspection deficiencies, especially those related to COVID-19 inspection backlogs.

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Multiple applicants have found themselves in the position of receiving a facility only CRL instead

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of an approval because FDA was unable to conduct pre approval inspections. This created significant challenges

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because applicants with not determine when this can be addressed. FDA needs to find a way to communicate more

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transparency around pre approval inspections especially when the lack of inspections is a sole barrier to

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the approval of an authorize approvable application. We also observed that FDA offered reports and inspections review

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metrics for biosimilars along with those along with the new biological products. This makes it difficult to

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know how long FDA is using their additional tools like document review, mutual recognition, or remote

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interactive evaluations for the 351(k) applications versus the 351A applications. While ERG and FDA found

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no action is needed for inspections, we believe there are actions that could be taken even during the COVID-19

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pandemic and as it moves into an endemic situation.

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We would encourage you to see two parts of reporting to make it clear what is truly happening in the

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biosimilars program versus all BLAs. Finally, we encourage the agency to help its reviewers develop a better

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vocabulary around biosimilars. We have noticed that many reviewers come to a 351(k) application from a perspective

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of 351A, BLAs. Which are based entirely around the clinical program. As we all know, 351(k) applications have a very

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different scientific backbone, with a clinical program only serving a conforming process. This can create a

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challenge when FDA reviewers ask for additional data that is provided from a 351(k) because it's what they're

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used to seeing in the 351A BLA. With that, I look forward to continuing these conversations and workshops as

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we go forward. Thank you! >> Mark: Thank you, David! Next

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slide, please. Next we will hear from Dr. Camelia Thompson, senior director of science and regulatory team --

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sorry, I'm reading the wrong part of this. Oh, sorry about that, Camelia. Let's hand it over to you.

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>> Camelia: Good morning, everyone! I'm senior director in the science and

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regulatory team at the bio technology innovation organization BIO. BIO is the world's largest trade association

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representing bio technology companies, academic institutions, state bio technology centers, and related

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organizations across the United States and in more than 30 other nations. BIO member have small start ups with only

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one or only a few FDA approved products to some of the largest bio pharmaceutical companies in the world!

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We remain committed to ensuring the

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success of the emerging biosimilars market through our engagement and ongoing policy developments related to

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biosimilars. Including a recent participation in the technical negotiations for the reauthorization

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of biosimilars user fee act, reauthorization BSUFA. Bio supports the increase competition and potential

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savings in the prescription drug marketplace that biosimilars provide, coupled with appropriate protections

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for innovative biologics to ensure continued development of new and life saving treatments.

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I would like to thank FDA for the opportunity to provide comments on the

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final assessment of the program for enhancement review transparency and communication for original 351(k)

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biologics licensing applications in the biosimilars user fee act.

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The underlying premises is that increased and improved communication between FDA and the application

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sponsored during the review would improve efficiency and reduce the need for additional review cycles. We agree

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with the conclusion of the assessment that the BSUFA II program has created conditions that enhanced the ability

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of applicants and be FDA reviewers to work towards application of the review in the first cycle.

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Ensuring timely scientific dialogue throughout the review process is a

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type priority for BIO member companies and we're pleased that the final report, noted most applicants and FDA

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reviewers characterized communications as excellent, constructive and cooperative. Additionally, findings

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confirm that application reviews were transparent and predictable. These interviews highlight good practices

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for both FDA and industry. We acknowledge best practices for communications during biosimilars

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application review or the responsibility of both industry and FDA. The assessment findings will

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inform future engagement between sponsors and reviewers and help achieve the BSUFA III performance

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goals of ensuring effective communication and advancing modern approaches to bio similar development

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and review processes. I would also like to highlight that sponsors and FDA review staff interviewed for this

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study reported that communication remained strong during the pandemic. The final assessment noted that

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program communications, transparency, predictability, and review processes generally remain similar over the last

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several years to what they had been before the pandemic. The main is the predictability of inspections which

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have been disrupted by operational changes and travel restrictions.

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However, FDA acted to mitigate this challenge to the extent possible by initiating an alternative records

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review process where appropriate. We applaud the FDA that in light of this challenge, applicant FDA communication

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and review transparency appeared to remain strong. In closing, I want to thank you for the opportunity to give

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this presentation today on behalf of BIO and its member companies. Our organization looks forward to working

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with the FDA and other stakeholders to ensure a timely reauthorization of the BSUFA III that will further approve

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processes and maintain high standards of the review program. Thank you!

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>> Mark: Thank you, Camelia! Next slide, please. We now have Rachel associate general council of the law

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and policy that will speak on behalf of the biosimilars forum.

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>> Rachel: Good morning! I'm associate general council, policy and

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head of U.S. regulatory policy at TEVA. On behalf of the biosimilars forum and members, I'm pleased to participate in

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the final assessment on enhanced review transparency in BSUFA.

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The biosimilars forum which I will refer to as the forum for short, is a non profit trade association whose

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mission is to educate stakeholders on the value of biosimilars and to improve access to biosimilars in the

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United States. Our members represent the majority of companies with the most significant U.S. biosimilars

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development portfolios including bio Gen, bio sciences, Pfizer, Samsung bio -- my remarks today represent the

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views of our members, all of whom manufacture or market biosimilar products and many of whom participated

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in the interviews of the ERG that are the subject of the report we are discussing today.

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While BSUFA II built on the success of BSUFAII I, and had great changes,

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there are still many areas we can further enhance communications between the agency and the sponsor. Our

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comments today center on three key areas. Inspections, application level communication, and regulatory science.

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While some of these issues in these areas are addressed in the BSUFA III commitment letter, we think it's

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important to bring attention to specific topics not covered by the commitment letter. Overall, the ERG

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says that the biosimilars program is well resourced to give focused attention on each individual

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biosimilar application. Particularly in light of the small

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size of the program and the correspondingly small number of biosimilar BLAs. Well coordinated and

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robust communications should be entirely feasibility. This is a unique opportunity for FDA. If done right,

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FDA can set a new standard for how to best communication before, during, and after application review to ensure the

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best quality applications are submitted and that these critical products reach patients as efficiently as possible.

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First, we'll talking about inspections recommendations. The ERG

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report concludes that FDA communication regarding inspection has generally been clear, allowing for good

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inspection coordination and contributing to overall review transparency and predictability. The

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report suggests that no action is needed. The forum respectfully disagrees with this conclusion. As of

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December 31st, 2021, four biosimilar applications are still awaiting FDA action due to the COVID-19 and

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communications on how the agency will address these delays as well as the remaining backlog of inspections has

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been poor. Often, responses about inspection

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are cursory and lacking specific time frames to help an applicant understand where they stand in the queue. As an

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example, I'm going to read an excerpt from a deferral letter that FDA sends when an application cannot be

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completed due to an inspectional delay. FDA states an inspection of the facility is required before the

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application can be approved. FDA must assess the ability of that facility to conduct the listed manufacturing

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operations in compliance with CGMPs. Due to restrictions on travel, we may be unable to conduct the inspection on

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X facility prior to the user fee date. We will continue to monitor the public health situation as well as travel

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restrictions. We are actively working to define an approach for scheduling outstanding inspections once State of

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safe travel will resume and based on public health needs and other factors.

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This statement provides no useful information which could even be a

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rough estimate about when FDA may conduct an inspection and therefore, when a sponsor can expect to begin

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marketing the biosimilars. Indefinite holds creates significant planning issues and delays

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patient access to safe, effective and lower cost biosimilars. FDA can do better here. In addition, applicants

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find themselves in the position of receiving a facilities only deferral instead of an approval because FDA

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cannot conduct pre approval inspections. This creates significant communications challenges and

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companies are at a loss as to when they can expect a final evaluation of the approve ability. As I talked about

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before, not having predictability about when the approval is coming which is really the under pinning of BSUFA is

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very challenging for companies, especially when planning the launching of products. As we pass the two year

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mark of the pandemic, it's frustrating that the agency has meaningfully addressed how to tack the backlog.

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None of the recommendations or time lines in the ERG report promised

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matter if biosimilar approvals are held up indefinitely due to inspectional delays . The forum encourages FDA to

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use the tools at its disposal to communicate clearly with sponsors about inspections and address the

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biosimilars inspections backlog. These tools include evaluating requests from establishments to conduct remote

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interactive evaluations, for surveillance inspections or pre approval inspections. Using remote

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interaction for section 704 records request to clear efficient OAI facilities. Utilizing mutual

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agreements in lieu, expanding recommendation to allow reliance on the factual findings in inspection

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reports generated from a virtual inspection, conducted by a recognized health authority under existing MRAs

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or by a capable authority in which FDA has an established confidentiality agreement or providing a detailed plan

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of how FDA intends to address the inspections backlog including how delayed applications will be

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prioritized. To conclude this section of my

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remarks, FDA can enhance its communications around inspectional delays to the benefits of both the

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agency and sponsors. Now, I will turn to application level communication issues. As an ERG report shows, the

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number of IRs submitted under BSUFA II is markedly higher than BSUFA I and we expect this trend to continue in BSUFA

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III. Notably the vast majority under BSUFA two involve quality product issues which is the biggest topic

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under LCMs. Receiving IRs during the end of the review cycle places an additional burden on applicants to

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respond quickly during a critical window prior to approval. This burden could be alleviated by FDA provided

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quality related IRs as soon as practical, buildings upon IR questions and the sequential and logical order,

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notifying the applicant, if and when it considers IRs to be resolved and providing advance notice in the

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likelihood of an IR and bundling IRs when possible.

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This type of communications is particularly important in the post approval space. Currently, our

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industry is being asked to rely on a 25 year old guidance to determine when reporting categories is appropriate

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for changes to CMC information in a BLA. Despite significant advancements over the last several years, FDA

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should prioritize issuance of a new post approval manufacturing changes guidance given the increase focus on

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product quality issues. Additionally, the forum agrees with

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ERG's conclusion that target dates for IR responses are often impact call for applicants with a global presence.

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Often, they receive IRs late in the week which makes the short turn around time difficult to meet with colleagues

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working in different time zones and with different cultural views on working over weekends. It would be

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helpful if the agency could prioritize sending IRs early in the week or allow for an extended response time whenever

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possible. Finally, it would be helpful if FDA

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would define what it considers to be a non clinical IR. There were no non clinical IRs issued under BSUFA I who

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which raises the question what is being raised. Methods for demonstrating biosimilarity would

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assist. From a procedural effective, this would be beneficial. Foreign members have been receiving FDA

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feedback recently limiting the number of questions permitted in a briefing book to ten as well as capping the

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duration of type 2 meetings. In many instances though, one ninety minute meeting may be productive than two

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sixty minute meetings and a single meeting saves both the agency and sponsors.

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Because the biosimilars program is so small, the commitment letter offers

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more flexibility than those of other fee programs and FDA should be eager to exercise flexibility to accommodate

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sponsor requests and adequately communicate requirements to assure first cycle approvals.

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The last topic we want to emphasize today is regulatory science. The forum

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is very excited about the enhanced communication regarding interchange BLT and streamlining biosimilar

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requirements that the new program will offer. Leveraging the regulatory science program and conducting a

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scientific workshop, in development of interchangable biologics to have guidances will accelerate not only

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guidance development but also will contribute to sponsors developing higher qualities submissions for

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agency review. And the forum and its members

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especially look forward to more scientific dialogue about the possibility of further streamlining

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the path to market for biosimilars through enhanced regulatory science. We hope that the agency will use the

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BSUFA III regulatory science program as an opportunity to further show many of the scientific issues that biosimilars

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face in the science process. Thank you for the opportunity to providing comments today. We are looking forward

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to continuing the conversation at the workshop in April.

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>> Mark: Thank you, Rachel. Next slide, please. Including the industry perspectives, we'll hear from Jessica,

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senior director of science and regulatory advocacy at Pharma.

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>> Thank you! My name is Jessica and I'm a senior director of science and regulatory advocacy at the

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pharmaceutical research and manufacturers of Pharma. This is a trade association, that enable

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RMA. This is a trade association, that enable patients to live longer, healthier and more productive lives.

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Over the last twenty years, PhRMA member companies have, including the estimated 91 billion in 2020 alone. We

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have many leading pharmaceutical companies. We appreciate the opportunity to participate in today's

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public meeting. PhRMA has been a strong supporter

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of, and participant in BSUFA since the inception. This was enact indeed 2012 to help provide FDA with resources and

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staffing specifically to support the biosimilar approval pathway and promote greater consistency, certainty

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and predictability in the review of biosimilar products. To advance these objectives, PhRMA supported

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establishment of the program for enhancement review transparency and communication under BSUFA II.

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We look forward to working with the agency as the program continues to

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mature. And an efficient review process as submitted by the program, can help ensure timely patient access to safe

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and effective biosimilar and interchangeably biosimilar products. And in fulfillment of the BSUFA II

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commitments, we appreciate the final assessments and the corresponding meetings to publicly discuss the

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findings. We believe that both the FDA and

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sponsor's perspectives are critical to understanding the advantages of, and opportunities for improvement for the

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program. And therefore, appreciate findings for both perspectives in the interim and final assessments. The

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final assessment confirms the ERG's preliminary that the program has created conditions that enhance the

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ability of sponsors and FDA reviewers to work towards application approval in the first review cycle. As we also

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noted in the context of the interim assessment, Pharma believes it can help during 351(k) application review.

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Should consider, establishing the process of providing presubmission advice and templates for application

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content and organization as a good practice for the BPD Type 4 meeting, soliciting discussion topics from the

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sponsor and allocating time in the late cycle meeting agenda for sponsor. And when feasible, promoting response

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times of more than two days or issuing information requests earlier to allow for extended response times.

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PhRMA encourages FDA to consider and address the additional targeted

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feedback that FDA obtained from the sponsors interviews through the assessments regarding potential

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improvements. We understand the importance of providing early notice of issues, including providing the

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advance notice of the likelihood and bundling information requests as possible.

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As outlined in the interim and final assessments, communications can

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further be approved by notifying the sponsor if and when FDA considered information requests and substantive

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issues to be resolved. We would like to highlight some of the other report findings related to opportunities for

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increased communication. As also noted, we believe holding ad hoc conferences can improve overall transparency and

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communications. As highlighted in the report, it is also helpful to sponsors when the FDA provides updates on

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review activities after the late cycle meeting. The final assessment notes that pandemic travel restrictions have

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led to -- and that FDA was able to mitigate this challenge to a certain extent by instituting an alternative

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records review process in cases where that was appropriate. Importantly, the BSUFA III commitments to apply

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COVID-19 lessons learned beyond the public current health emergencies.

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Under BSUFA III, FDA will develop guidance on alternative tools to assess manufacturing facilities named

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in pending applications. Additional changes outside of the program, including those outlined in the BSUFA

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III commitment letter may also help to approve the efficient development and review of biosimilar and

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interchangeably biosimilar products. These include modifications to existing types, the BIA meeting,

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establishment of a new meeting type for rapid targeted feedback to enable timely interactions between sponsors

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and FDA during biosimilar development and review. And advancing development of interchangable biosimilar products

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through guidance and piloting a regulatory science program focused on advancing the development of the

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products and approving the efficiency of biosimilar product. In conclusion, we appreciate the agency's efforts to

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meet the program's goals outlined in BSUFA II and would like to thank FDA for bringing together stakeholders

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today to provide their perspectives. PhRMA will submit written comments to the public docket. F thank you for

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. Thank you for your time! >> Mark: Thank you, Jessica. We will

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now transition to the question and answer session and public comment period. I will read the questions that

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have been submitted and direct them to the appropriate panelist or panelist. Let's move to the next slide, please.

01:35:08.000 --> 01:35:22.000
We probably need to go to the next slide as well. Perfect!

01:35:22.000 --> 01:35:29.000
Back one. So the two questions are directed to ERG. Valerie, I direct it to you first, and then Sarah and then

01:35:29.000 --> 01:35:32.000
open it up to the next panel. Is there any reason why clinical questions are not coming in during day 74? Just

01:35:32.000 --> 01:35:42.000
because it begins after the CNC data review? Valerie?

01:35:42.000 --> 01:35:51.000
>> Valerie: Thank you! Yes. Thank you for the question. So our understanding that clinical reviews, these various

01:35:51.000 --> 01:35:59.000
types of reviews do happen in parallel, however, day 74 is pretty early in the review cycle and so often the clinical

01:35:59.000 --> 01:36:11.000
review, the primary clinical reviewers have not had time to conduct an in-depth review yet and so the

01:36:11.000 --> 01:36:17.000
clinical issues are likely to come up after the day 74 letter. I don't know if FDA would like to respond further.

01:36:17.000 --> 01:36:30.000
>> Sarah: Yes, sure. I will say that,

01:36:30.000 --> 01:36:38.000
I think folks are looking for specific things early on before filing. And those issues for clinical are looked

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at and basically have been well addressed generally, I think. I think when these other questions are coming

01:36:47.000 --> 01:37:05.000
up, it's really as Valerie noted, when folks are getting into the real sort of meat of the review and writing up

01:37:05.000 --> 01:37:08.000
the review and then people start thinking a bit deeper on various issues and other questions come up.

01:37:08.000 --> 01:37:20.000
Anything else, Mark? >> Mark: I was going to ask if you

01:37:20.000 --> 01:37:28.000
are done, Sarah. Does anyone else on the panel want to comment? Not? So the second question, I will read it

01:37:28.000 --> 01:37:37.000
and turn it to you Sarah. Did FDA perform any remote GCP or GMP inspections for biosimilars during the

01:37:37.000 --> 01:37:49.000
pandemic period? In future, will there be a use of such remote inspection approach for biosimilar programs?

01:37:49.000 --> 01:37:59.000
>> Sarah: Okay, as the biosimilar forum noted, we did try to use the

01:37:59.000 --> 01:38:06.000
remote and alternative inspection tool approach during the pandemic for biosimilar applications. You know, I

01:38:06.000 --> 01:38:17.000
think that folks raise a valid point about trying to expand the use of these things. And I think there are

01:38:17.000 --> 01:38:25.000
efforts within the agency now to try to work on this further and that's actually described as a BSUFA III

01:38:25.000 --> 01:38:36.000
commitment as well. So my hope is we'll have a consistent approach to alternatives to an on site facilities

01:38:36.000 --> 01:38:46.000
inspection, especially in the event of these kinds of public health emergencies and other kinds of

01:38:46.000 --> 01:38:57.000
emergencies. But the deployment of them during the pandemic was relatively limited and we had to meet the GMP

01:38:57.000 --> 01:39:08.000
regulations. So it did result in some delays.

01:39:08.000 --> 01:39:17.000
>> Mark: Thank you, Sarah. Is there any other panelist that would like to comment on that question? Not? We

01:39:17.000 --> 01:39:22.000
can go ahead and move to the next slide, please. Thank you to everyone who asked questions and thank you to

01:39:22.000 --> 01:39:31.000
the panelist for your responses. On the topic of public comments,

01:39:31.000 --> 01:39:41.000
FDA invited everyone to submit a request of an oral -- and we did not receive a request by the cut off date.

01:39:41.000 --> 01:39:48.000

Next slide, please. However the opportunity to submit written comments is open until May 23rd. Once again, to

01:39:48.000 --> 01:39:54.000
submit the written comment to the public docket, you can search the docket number at www. Regulations.GOV.

01:39:54.000 --> 01:40:00.000
After this meeting, FDA will send an e-mail to registered meeting participants with their link to the

01:40:00.000 --> 01:40:10.000
assessment report, a link to the meeting page where a video recording of this will be posted and a link to

01:40:10.000 --> 01:40:40.000
the site where you can submit public comments to the docket. Thank you again for participating in meeting.