Public Meeting on the Recommendations for GDUFA Reauthorization

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November 16, 2021

A Matter of Record
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FOOD AND DRUG ADMINISTRATION

Public Meeting on the Recommendations for
Generic Drug User Fee Amendments
(GDUFA) Reauthorization

Virtual Meeting

Tuesday, November 16, 2021
9:01 a.m. to 11:58 a.m.

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PROCEEDINGS

(9:01 a.m.)

Welcome – Carter Beach

MR. BEACH: Good morning. Thank you for joining us. I'm Carter Beach, Deputy Director of CDER's Office of Executive Programs, and I'll be leading you through the meeting today.

I'd like to thank the industry negotiators for a collaborative and productive 18 months, getting us to this point, from the initial public meeting back in the summer of 2020. I'd also like to thank those of you who joined us for the stakeholder meetings throughout the negotiations. Thank you in advance to those who will speak today and to those who will submit comments to the docket. We value all of the engagement and feedback.

We're here to present the proposed reauthorization package that we have developed along with industry representatives. Today's agenda will start with opening remarks from Jacqueline Corrigan-Curay, the Principal Deputy

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Director at CDER. She led the GDUFA reauthorization process for FDA. Jacqueline will explain how we got to this point and what happens next.

From there, we will highlight GDUFA II successes, then we will summarize the key proposed enhancements in the GDUFA III package. After that, we will hear from industry representatives and other stakeholders. There will be time for public comments and finally closing remarks from Sally Choe, Director of CDER's Office of Generic Drugs.

The schedule here is our best estimate for these sessions. As you can see, there are breaks sprinkled in. We will stick as closely to this as possible, but may shift breaks here and there, depending on the flow.

Throughout the meeting, you will be able to submit clarifying questions in the Q&A box at the bottom of the presentation screen. We will do our best to address them. If you have substantive comments, they should be submitted to the docket.

With that, here's Jacqueline Corrigan-Curay.

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Opening Remarks – Jacqueline Corrigan-Curay

DR. CORRIGAN-CURAY: Thank you, and good morning. It's a real pleasure to be here to present to you our proposed recommendations for the enhancement for GDUFA III, but I want to just start a little bit and talk about this is really just our third reauthorization, so we've been rapidly building the modern generic drug program.

Our first program was back in 2013, not that long ago, and it was industry's and FDA's first effort to design a modern generic drug program, the first implementation of goal dates for ANDA submissions and making progress on the review of the ANDA backlog.

We are now in GDUFA II, reaching towards the end of GDUFA II, and the improvements we made there include simplified goal date structures; providing shortened goal dates for priority submissions; the launching of the pre-ANDA program for complex products; and providing accountability and reporting enhancements. As we entered into these negotiations, our goal was really to take the best

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of what we've already built and build upon that, and continue those successes.

As Carter mentioned, we started back in July of 2020 with our initial public meeting and perhaps some of you who joined us then. And then we spent about a year really working with industry through these negotiations, as well as meeting with our stakeholders to get the package together that we'll review with you today.

We had formal ratification between FDA and the industry in September of 2021, and then went through our internal clearance process. We published the FRN, as you know, at the end of October, and we're here today at our final public meeting.

As you can see, the docket will not close for public comments until December 12th, so you'll have time to take back what you've heard during this meeting and submit comments to the docket. We'll carefully review those comments, and then our goal is to transmit a final package to Congress in January of 2022.

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We entered the negotiations, as I said, with building on what we've achieved through GDUFA II with the goal of maximizing the value of each review cycle, and by that we mean our goal is really to get as many approvals in earlier review cycles. From a broad picture -- and we mentioned this in our public meeting -- what we were trying to do was advance those earlier cycle approvals through enhanced communication and review processes.

We also want to enhance the development, assessment, and approval of complex generic products, which you'll hear about a little bit today, and then to assure a sound foundation for GDUFA III.

I think as you listen to the presentations today about the commitment letter, I think we've accomplished much of what we set out to do, and I think it's because these were really shared objectives by FDA, industry, and also our public stakeholders.

I'd just like to reiterate our thanks to our

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industry trade group negotiators from the Association for Accessible Medicines, the Pharma and Biopharma Outsourcing Association, and the Bulk Pharmaceuticals Task Force, who really worked with us to achieve what we have today.

So again, these slides will be available to you. We'll have the links. Please review the Federal Register if you haven't looked at it and the commitment letter, and of course to submit comments, you should go to the docket. We look forward to hearing from you, and then we'll review and analyze those public comments on the proposed recommendations, take those into consideration before we transmit a final proposed package to Congress in January of '22.

It's really my pleasure to introduce some of my fellow negotiators. This is really the brain trust of the GDUFA negotiators. You'll hear today from Alonza Cruse, who's our Director of Office of Pharmaceutical Quality Operations; as well as Ashley Boam, the Director of the Office of Policy and Pharmaceutical Quality; Maryll Toufanian, the

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Director of the Office of Generic Drug Policy; Edward "Ted" Sherwood, as many of you may know, the Director of the Office of Regulatory Operations; and Rob Lionberger, the Director of the Office of Research and Standards.

Before we kick off into reviewing each of the different sections of the commitment letter, we thought it'd be really helpful to first provide an update on where we are in GDUFA II, and just walk through some of those continued successes of the program that we're building on for GDUFA III.

With that, I'd like to hand it over to Maryll Toufanian to walk us through, and we thank you for your attention, and thanks for being here.

Presentation – Maryll Toufanian

MS. TOUFANIAN: Good morning. It's a pleasure to be here. Today, as Jacqueline indicated, I have the good fortune to update this community on our activities under GDUFA II. At our public meeting last July, we were able to provide information up to this fiscal year, and thought, in light of everything that has been accomplished this

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prior fiscal year, we could share an update with you.

An update on GDUFA II, starting with what has been the focus of so many of our actions and our lives for the past several years, and that is addressing COVID-19, what the generic drug program has done to ensure that critical COVID-19 treatments are available to the American public.

I'll note that we've had 69 COVID-related original ANDAs and over a thousand COVID-related supplements. What this is, is really not only an indication of the extraordinary effort that the folks at FDA have done -- again, continuing to work remotely -- for the entire fiscal year, but also an acknowledgement to industry and the efforts that the generic drug industry took in light of all of the challenges facing supply chain and production, really putting in an extraordinary effort to make sure that the American public have the medicines that they need during this public health emergency.

To facilitate those activities on behalf of the agency and our industry partners, we issued

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three guidances really targeted on addressing the drug development and ANDA review during the COVID-19 pandemic, and in order to ensure that as much information was available to the public, we had two public presentations on COVID-19 related development activities.

In addition to all of the extraordinary work going on to address the global pandemic, we had the rest of the work that is so critically important to do. This year, we continued what we started in GDUFA II, and that is making sure there's no application left behind.

One of the real successes of the GDUFA II program is that every single generic drug application that is in our pipeline is now under the user-fee paradigm, and that structure really lends to a successful review process not only for original applications, but the growing number of supplements that we receive as a result of the extraordinary efforts in GDUFA I and GDUFA II to clear out older applications and make sure those products continue to be updated through the

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supplement process.
In this year alone, we had over 670 approvals, over 150 tentative approvals, which as many or most of you know is FDA's signal that an application has met our scientific standards for approval but cannot be approved because a patent or exclusivity has yet run.
In addition, we had over 90 first-generic approvals, and that's the first generic to specific references to drug or RLD, really critical activity on the part of both the agency and industry to get those generics out for the first time; an extraordinary number, over 1850 complete response letters, those communications back to industry identifying deficiencies that an applicant needs to address before we can move to approval.
During the course of the assessment, we issued over 4700 information requests and discipline review letters. Those are communications from FDA to applicants over the course of an assessment cycle, where we're really trying to make sure that we identify, to the extent possible,

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deficiencies/omissions in an application to move to an action, hopefully an approval or tentative approval in that cycle. And as a cornerstone to all of our work is the review of the drug master files, which is a foundational element of the generic drug program, and our DMF team reviewed over 550 DMFs.
In addition, we hit a really important milestone this year, and that is over 100 cumulative competitive generic therapy approvals. This was a new approval incentive that was established in the reauthorization of GDUFA II under FDARA to encourage the development of productsfor which there's no generic competition, older products.
We really have been very heartened and are very committed to continuing the success of that program, and I'll note that a significant number of those products that were approved under the CGT pathway did take advantage of the 180-day exclusivity that comes after one applicant meets certain criteria set forth in the statute. So that

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pathway is a success and one that we're really excited about continuing to implement.
We had a significant number of notable generic drug approvals. I won't read this list, but I will encourage all to take a look. I think all of us in the healthcare field can understand the benefit of these products and their approval. So I would say when these slides are available, to take a closer look at some of these approvals, a number of which are complex generic approvals, which I'll be speaking about in a little bit. But it was an exciting year for us with these and other approvals coming to fruition.
This is what I referenced and I'm going to talk about in a little bit more detail. This is really all of the work FDA and our partners have been doing for many years, but in particular in GDUFA I, and then even the heightened pace of GDUFA II, and that is really identifying the innovative science, the innovative technologies, that are necessary to get approvals for complex products, products that are complex because of a complex

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dosage form, active ingredients, and route of administration.
The agreement from GDUFA II really put a significant amount of focus on those complex generics, and those came to fruition this year in the approvals that you see below, the first complex generic of glucagon, for patients, to treat severe hypoglycemia in patients with diabetes. This approval was possible because of FDA research on analytical methods for peptides and immunogenicity studies testing for peptides.
We had our first complex generic for a parenteral iron product that treats iron deficiency anemia. FDA's investment into characterization and advanced bioequivalent study designs was really essential to this approval. The complex generic loteprednol etabonate ophthalmic suspension really resulted in investments we have made into particle size characterization and eye models, supporting a more efficient in vitro bioequivalence methodology.
Providing a little bit more detail on what we refer to historically is the FDA's pre-ANDA

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program. But that's a little bit of a misnomer because there's so much that goes on that is of benefit to the good work that happens in the pre-ANDA space to move complex generics from development to assessment, and ultimately approval.

We found the pre-ANDA program, concentrating on the science and technology behind complex generics, reduces time from development to market; helps address complex scientific issues; creates a pathway for us to communicate with prospective applicants; helps applicants develop more complete submissions; and what is essential is clarifying regulatory expectation in a very transparent way.

Also exciting, the Center for Research on Complex Generics is up and running. In August of 2020, FDA awarded a five-year grant to the University of Maryland and the University of Michigan to establish this center, which aims to enhance research collaborations with the generic drug industry to further FDA's mission of increasing access to safe and effective generic products.

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The goal will be pursued through collaborative research, training, and exchange of resources between FDA and the generic industry and stakeholders. It's the first of its kind, a cutting-edge center. We hope to stimulate innovative dialogue, disseminate current understanding of complex products and practices, and generate new knowledge, all with the goal of ensuring safe and effective high-quality generic drug products are available as soon as possible.

We've had a number of workshops, I'll note very successful in the virtual space. We had in the Generic Drug Forum the Lifecycle of a Generic Drug in April of 2021, over 2,500 attendees from 77 countries. It was an opportunity for industry and academia to interact with FDA subject matter and receive information to help applicants submit and ultimately pursue approval of their generic drug products.

In addition, we had our Generic Drug Regulatory Science Initiatives Public Workshop, and this is a really important opportunity that we have

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to hear from industry, to hear from academia, and to hear from external stakeholders about what their thoughts are with respect to identifying novel or innovative scientific methods that could be applied to generic drug development in the future. We use this input to develop our priorities for the following year on an annual basis.

We also had a number of very focused workshops, and these are interactive workshops, to a large extent, that allow FDA to share scientific information about a specific subject, and for industry to participate in those dialogues and learn a great deal about what our expectations are with respect to specific elements of generic drug development and review.

We have, as a general matter as I described, really focused on enhancing research transparency and industry engagement. The pre-ANDA program, as I've described what its intent was, the goal has come to fruition -- an estimated 500 meeting requests for that pre-ANDA program -- and we met our goal dates for product-specific guidances for

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new chemical entities.

Product-specific guidances, as most of us are aware, are those recommendations on specific drug products with respect to bioequivalence and other elements of generic drug development for a specific product. Making that information transparent in the form of a product-specific guidance is essential to timely development of generic drug approval.

The good news is that we have been active not only in our basements, but also globally. We've been really proactive this year on a number of international fronts. The first highlight of our global engagement program is the Parallel Scientific Advice (PSA) pilot program that we have partnered with the European Medicines Agency, or EMA, on.

This pilot program was designed to provide parallel scientific advice to prospective generic drug applicants for FDA's abbreviated new drug applications and EMA's marketing authorization applications for hybrid products for complex

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generics.
The PSA pilot program allows FDA and EMA -- the assessors, the folks actually looking at the applications or the data around development related to specific products -- to concurrently exchange their views on scientific issues during the development phase of complex generics and share that information with putative potential applicants.
We also have been very active in the ICH generic drug discussion group, which assesses feasibility of harmonization and the impact of public health for several complex generic products, categories, creating a comprehensive map of topics to recommend for the development of future ICH guidelines.
I think ICH, as we all know, has been incredibly successful in facilitating drug development. I think over the past several years, and this year in particular, the targeted focus on potential areas of ICH for generic drug development is really exciting and a really critical

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opportunity that we look forward to continuing to embrace. We also have the ICH M13 expert working group, which developed guidelines on bioequivalence for immediate-release or oral dosage forms.
Excitingly, we launched the global generic drug cluster in June of this year. It's the first forum established for leading regulatory agencies across the world specifically for generic drug topics. We're active in two working groups for the International Pharmaceutical Regulator Programme, or IPRP, the IPRP bioequivalence for generic groups and the nanomedicines working groups.
All of this work, really, we think will come to great benefits to the American patients because, as we know, the generic drug market place and the development space is really a global endeavor, and this work will all seek to make that as efficient as possible for generic drug applicants in the U.S.
Now, what's essential in terms of our activities under GDUFA II is making sure that generic drug developers know our expectations to the greatest extent possible. To that end, we have

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issued a significant number of final guidances.
I won't go through each, but as you can see, focusing on several different elements of generic drug development and review, how to submit your application and what steps one takes to maximize the different elements of FDA's work in the development and review of generic drug products; more specific heavily scientific guidancesto describe our expectations on complex scientific matters; and as I indicated previously, we sort of nimbly finalized a guidance regarding elements of generic drug review and development under the COVID-19 pandemic paradigm.
We also continue to issue draft guidances, including what was a critically important and very exciting guidance for us to publish, and that was new bioequivalence studies with PK endpoints for an ANDA, really reflecting a significant amount of innovative development in bioequivalence space over the last several years, as well as additional drug draft guidances. And as you all know, we try to work as consistently and as efficiently as

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possible, and FDA MAPPs really gives an important tool to FDA assessors, FDA policy developers, and the industry. It gives transparency into how FDA does its job.
With that, I am very happy to turn the microphone over to three of my colleagues. As Jacqueline thoughtfully introduced, Ashley and Ted are going to be talking about maximizing each review cycle, and I'll pop back in as a special guest star on a specific topic.
So with that, I look forward to speaking with you again in a few minutes.
Presentation – Ashley Boam
MS. BOAM: Thank you, Maryll.
It's a pleasure to be here with you today. I'm excited to start us off in sharing some of the proposed commitments in the GDUFA III commitment letter, in this section, elements that would help to, as was mentioned, maximize each review cycle.
In terms of Presubmission Facility Correspondence (PFC), this was an element that was actually included in GDUFA II. It was intended to

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provide a pathway for a shorter review goal for priority applications by allowing certain information related to manufacturing facilities and bioequivalence studies to be submitted ahead of the ANDA application itself, which would then enable FDA to provide an assessment of the need for a preapproval inspection. Then together, that would allow FDA time to conduct an inspection, if needed, and still meet that shorter goal date of 8 months.

During the GDUFA III negotiations, we discussed with our industry colleagues approaches that might help increase industry's use of this provision to have more ANDAs eligible, then, for that 8-month priority goal date.

Notably, the changes that we have proposed are to narrow our focus in terms of the information to be submitted on the manufacturing information and the bioequivalence study information that are critical for FDA in terms of making that assessment of whether an inspection is needed to support approval and to outline how non-substantial changes can be made in between the submission of the PFC

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and the ANDA, as long as that information does not change our assessment regarding the need for an inspection.

We hope that these changes will lead to an increase in the number of ANDAs using this pathway and being eligible for that shorter review timeline.

At this point, I'll turn the microphone over to my colleague, Ted Sherwood.

Presentation – Edward Sherwood

MR. SHERWOOD: Great. Thank you.

Good morning, everyone. We are going to address a couple goal date extensions. We will start with major issues. In certain cases, applicants' responses to mid-cycle information requests or discipline review letters may trigger extensions of the first cycle.

These extensions will be based on the major amendment goals, and they will be applied from the date of amendment submission. FDA hopes that under this commitment, applicants will provide timely and thorough responses that allow for an increase in

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the number of first-cycle approvals.

Further, we are allowing for goal date extensions for minor issues. Again, applicants' responses to certain information requests and discipline review letters may trigger extensions of the current cycle. Unlike the goal extensions for major issues, this extension is available for any appropriate cycle.

In this case, the extensions will be based on the minor amendment goals and they will also be applied from the date of amendment submission. FDA hopes that under this commitment we can reduce the number of cycles necessary for approval.

With a purpose similar to the extensions provisions just discussed, the imminent approval process for bringing applications to approval or tentative approval under GDUFA II was strengthened in GDUFA III as imminent actions. The name change appears subtle, but it allows for improved communications with applicants in situations where the agency may be able to take tentative approval by the goal date, or the agency could wait a little

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while past the goal date to issue a full approval on the first approvable date.

It also strengthens the ability to resolve small issues that are still needed towards the end of a cycle through information requests and discipline review letters, without penalty of missing a goal date, to provide applicants the opportunity to gain approval or tentative approval within the current cycle.

The opportunities discussed in the last two slides will reduce the number of complete response letters issued, the number of cycles needed, and help reduce the total time to approval. This is a win for industry, FDA, and the patients.

Here, we will pivot towards Controlled Correspondence. We are largely maintaining the current process and goals. To minimize confusion with complex products, we are replacing the standard and complex controlled correspondence designations with Level 1 and Level 2.

The biggest change to the Controlled Correspondence program will be an expansion of the

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definition of an eligible Controlled Correspondence to allow questions from applicants in certain circumstances after an application has been submitted. This expansion is designed to improve communication between applicants and the agency about next steps necessary for an applicant, such as the design of new bioequivalence studies or implementation of post-approval changes.

Another change in GDUFA III will be that responses to requests to clarify ambiguities will increase from the current 14 calendar days to 21 calendar days to allow FDA to catch its breath and prepare a thoughtful explanation of its response on the Controlled Correspondence.

Now, I will turn this back over to Ashley for further updates.

MS. BOAM: Thanks, Ted. Actually, I think this slide is for Maryll.

Presentation – Maryll Toufanian

MS. TOUFANIAN: That's right.

An exciting element of the proposed commitment regards suitability petitions. These

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are the petitions, the existence of which was established in the statute. They permit prospective applicants a mechanism to request permission to submit an ANDA for a different route of administration, strength, dosage form, or a different active ingredient in a fixed-combination drug product from a reference-listed drug; and whether we can accept and approve such an ANDA that would not be pharmaceutically equivalent and therefore not be rated, but nonetheless could be submitted with much less data than would be required than, say, a full ANDA, and therefore creates a new product that might address public health need or a niche in the market that's not currently addressed.

Starting in 2024, there will be goal dates for new suitability petitions. In order to obtain a goal date, prospective applicants can withdraw a previous petition and resubmit. We note there are a number of suitability petitions currently pending with the FDA. We understand the desire to move this more quickly as a result of the goal date, so

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we identified and negotiated a mechanism by which a petitioner can withdraw a petition and resubmit in 2024 to get a goal date.

In general, we will commit to addressing suitability petitions in the order that they are received, but we'll prioritize certain suitability petitions that fit one of the categories delineated, including one that can mitigate or resolve the drug shortage or prevent future shortages; address a public health emergency or anticipated to do so under the same criteria as would apply to a former declaration of emergency; that would be for a new strength of a parenteral product that could aid in eliminating pharmaceutical waste or mitigating the number of vials needed for dose by addressing differences in patient weight, body size, or age; or are the subject of a special review program under the PEPFAR program.

So handing things back to Ashley, who you've just heard, and also Alonza Cruse, who Jacqueline introduced. He's our director and fellow negotiator

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of the Office of Pharmaceutical Quality Operations for ORA. Thank you.

Presentation – Ashley Boam

MS. BOAM: Thanks, Maryll.

The proposed GDUFA III commitment letter has several provisions related to manufacturing and facilities. As you heard Maryll speak about in her opening remarks, drug master files and, in particular, type 2 drug master files are a key part of the generic drug program. We have a couple of provisions in the proposed letter to help streamline their assessments.

We have found that DMFs can be a challenge for ANDA applicants because the response time from DMF holders and getting back to us related to questions that we raise can be longer -- for example, can be longer than 3 months -- which then can limit the ability for the DMFs to be adequate in a single review cycle, which then also can delay the ANDA's ability to be approved.

GDUFA III would provide opportunities for an earlier review of certain drug master files for

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priority ANDAs to allow for that early start with the hopes of having DMFs be considered adequate early enough so that the ANDA, if also adequate, could move forward to approval or tentative approval.

A second pain point that we discussed was that, in some cases, DMF holder would submit an amendment to their DMF that corresponds to a time that's late in the review cycle for the ANDA referencing that DMF. And because FDA then needs to assess that amendment to ensure that it doesn't have an impact on the ANDA, that can, in some cases, lead to a delay in our ability to move forward with an approval or tentative approval of the ANDA application.

FDA has agreed to communicate to industry that prior to a DMF holder submitting what in many cases is a non-substantive amendment to the DMF, they should coordinate that timing with an ANDA applicant who is referencing that DMF in order to avoid unnecessary delays and approval.

You heard my colleague, Ted Sherwood, talk

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about the controlled correspondence program. One of the major changes we proposedin GDUFA III is to expand the controlled correspondence program to include questions in the post-approval space. These questions typically focus on the manufacturing-related changes, so providing a mechanism for those questions to come in and receive a response with goal dates associated will help to facilitate development in the post-approval space.

When an original application is submitted, you may be familiar with the Form FDA 356h, which includes a lot of information about the product being submitted in the application. It also includes information about the manufacturing facilities to be used to make that product.

One of the questions that the applicant is asked to address on that form is whether all of the facilities are ready for inspection should an inspection be needed. We do have cases on occasion where a facility is marked as not ready for inspection at the time that the original ANDA is

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submitted, and this can lead to delays in our ability to approve or reach tentative approval for that application.

GDUFA III would allow for an ANDA with a facility marked as not ready for inspection to receive an extended goal date to allow additional time for the facility to become ready. And if that does happen during the initial period, FDA will then set a new goal date, either 8 or 10 months, as appropriate priority or standard from the date of that amendment.

If the application is not amended with all facilities being ready during that initial 15-month period, we will then extend the goal date by another 15 months, and then we'll proceed to take action during that overall 30-month period.

With this, I will turn it over to my colleague, Alonza Cruse from ORA.

Presentation – Alonza Cruse

MR. CRUSE: Good morning, and thank you, and thank you, Ashley. Good morning, all.

FDA has been working throughout to ensure

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that we are providing education and feedback on the status of our surveillance inspections. One of the further enhancements in GDUFA III, continuing something from GDUFA II, is providing that information to foreign regulators regarding our inspection processes to further support safe and effective pharmaceutical products by the US-based pharmaceutical industry.

FDA's inspection classifications database under GDUFA II was updated on a monthly basis. The new version of our inspection classification database provides more frequent updates every week, whereas the former database was updated only monthly. This dashboard will continue to show the results from final classifications being as no action indicated, voluntary action indicated, or official action indicated for each of the areas within the inspection.

As you know, FDA inspections play a vital role in the drug approval process, and it is with that, working to try and increase the rate at which the approvals can occur. If a facility is named in

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an application that has been found to be Official Action Indicated, generally that ANDA cannot be approved.

One of the enhancements of GDUFA III is to post a new post-warning letter meeting, which will provide an opportunity for the eligible facilities to meet with FDA after making progress on their corrective action plans in order to remediate some of those deficiencies. Along with this reinspection, it's commonly needed to show and to resolve any OAI status that a firm may have, and it allows for the application approval under GDUFA III should that remediation be proved successful. These include reinspection timelines for both domestic facilities, as well as our international facilities for inspections.

Clarifying Questions

MR. BEACH: Thank you, all. As you can see, we've reached our break a little bit early here. We have received a couple of questions in the chat. I will read one of them now, and, Ashley, I believe you have an answer to this one.

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"For priority ANDAs that is planned for submission on or after October 2, 2023, when is the earlier date by when a DMF holder submits a DMF to prompt an early review of the DMF?"

MS. BOAM: Thanks, Carter.

The provision of a commitment letter would allow for a DMF holderto submit a request for assessment of that DMF 6 months prior to the planned submission of the ANDA. There are a couple of other provisions to make sure that the ANDA would qualify for priority review, so I would refer you to that section of the letter. But the idea is that the request for assessment could come in 6 months prior to the planned ANDA submission. Thanks.

MR. BEACH: Thank you, Ashley.

We received one other question about access to the slides. We are going to request that they be posted following this meeting. Please allow a day or two for that to occur.

Let's call this 15-minute break until 10 a.m., so we will rejoin at 10 a.m. Thank you.

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(Whereupon, at 10:00 a.m., a recess was taken.)

MR. BEACH: We are at 10 o'clock. Welcome back. We will go to Rob Lionberger for proposed enhancements to the complex generics program.

Rob?

Presentation – Robert Lionberger

DR. LIONBERGER: Good morning, everyone. I'm happy to be here today to talk about the enhancements in GDUFA III that we've made for our complex generics.

We're only seeing part of the slides.

(Pause.)

DR. LIONBERGER: Great. We'll be on this slide, so thanks very much for fixing that.

I want to talk a little bit about complex generics. Just to remind you, in GDUFA III, the definition of complex generics will remain the same as it was in GDUFA II. It will cover locally-acting products that are not solutions, complex dosage forms, products with a complex device constituent part, and products with complex

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active ingredients; so no change to the definition.

I also want to remind people of the scale of complex generics relative to the non-complex products. If you look at currently active reference products in the Orange Book, about 25 percent of those are complex, but if you look at products that don't have approved generics yet, it's about 30 percent. But currently, only about 13 percent of our ANDA approvals are for complex generics.

So we envision if we're moving toward an environment where a complex product is equally likely to have a generic as a non-complex product, that you might have to double or triple the amount of effort for applying to the complex ANDAs in the submissions.

So there's still a gap between the complex products available and the ANDAs that are being approved for those products, and that leads to a lot of the focus of the GDUFA III enhancements on improving movement of the complex generics through the system.

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There are a bunch of aspects of GDUFA III that help in complex generics. It begins with our regulatory science program that continues to develop the scientific foundations for our review of complex generics and providing appropriate and timely scientific advice for their development.

The regulatory science program feeds into our product-specific guidances -- we'll talk a little bit about the improvements there for complex generics -- as well as we continue to maintain in GDUFA III the pre-ANDA product development meetings that have been very successful, where applicants can discuss the development programs for complex generics and potentially propose alternatives to product-specific guidances. We also, in the GDUFA III enhancements, will have some improvements to the product-specific guidance program, and transparency and communication around the product-specific guidances.

As applications are submitted to FDA and move through the reviewer assessment process, you'll see several enhancements in GDUFA III

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related to complex products. First, we have improvements to our presubmission meetings to improve their use and link them more closely to the ANDA review process.

We have enhanced options for the mid-cycle meetings for complex generics that will provide more interaction between FDA and the applicant in that process, and have a new post-CRL scientific meeting, that if you reach a point after you've gone through the first review cycle and there are still complex scientific issues that are resolved, you have the opportunity to engage with FDA on a similar level to the pre-ANDA product development meeting about complex scientific issues.

We think that all of these, when put together, will help move complex generics through the system more efficiently and more transparently.

I want to talk through, in a little bit more detail, some of the specific improvements in GDUFA III. As we start with the product-specific guidance, the GDUFA II goals on product-specific guidances remain. I want to remind you that these

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focus on non-complex, new molecular entities, essentially providing product-specific guidances two years after approval; a reminder that for most new molecular entities, the first filing date, legal filing date, is usually four years after the approval date. So this provides two years of development time for the products before submission.

Again, the GDUFA II goal around complex products remains that we will provide PSGs for all complex products as soon as possible. We still aspire to do that. But what we've added in GDUFA III are new goals for complex products new drug applications as they're being approved after the beginning of GDUFA III. So we committed in the letter to provide 50 percent of those PSGs for new complex products in 2 years and 75 percent in 3 years.

So the idea of this is to evolve to a system where there are PSGs available for all products, and as new productsget approved, then both for the non-complex and complex PSGs, the product-specific

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guidances appear relatively quickly; so they are there to frame development. If you have alternative approaches, you can use pre-ANDA meetings, and you have time to do that before you submit ANDAs.

This is part of moving toward that type of system. We intend to continue to work on the older complex products that don't yet have product-specific guidances, but also begin to phase in a system that provides the PSGs for the complex products as the new drug products are approved. This new commitment will provide the resources to do this and, again, increase the rate at which complex products and PSGs become available.

Just to remind people of the value for this, by having the product-specific guidance available, they provide clarity on the path toward an ANDA submission, but we want to make sure that the product-specific guidances themselves don't become barriers to innovation. Every product-specific guidance has alternative approaches that are allowed, so, again, it's not the intention of

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providing this clarity to restrict innovation.

The GDUFA II product development meetings explicitly mention this, that one valid topic for a pre-ANDA product development meeting is you want feedback on pursuing an alternative approach to a product-specific guidance. So that aspect already exists in GDUFA II and will continue in GDUFA III, that PSGs should not restrict innovative approaches, but provide clarity around current thinking.

But we've heard during our negotiations, also, that sometimes the PSG revisions do create uncertainty. So in GDUFA II, we began to provide a process where we provide public notice of upcoming PSG revisions, and we've expanded and integrated this into the GDUFA III commitment. As well, we'll talk about some of the other PSG enhancements to provide more feedback on the interaction between product-specific guidances and development programs.

One new feature of GDUFA III is what we call a product-specific guidance teleconference. This

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is a situation that can be involved if an applicant has begun an in vivo study that differs from a posted PSG recommendation.

If you've begun an in vivo study perhaps following an older product-specific guidance, or in cases where there was no product-specific guidance available, and FDA posted product-specific guidance that describes a different type of study, in this situation we recognize, and through the negotiation process heard from industry, that this can be a particular pain point, so we've developed a system to provide enhanced communications in this situation.

In this situation, you the applicant would be eligible for a new teleconference within 30 days of your request to discuss the impact of the PSG recommendation on your development program. So there are various possibilities of how different your study is from the recommended study, and this will allow a discussion of the specific facts of your situation in that light.

Then, if there is additional scientific

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follow-up needed after this initial triage of what the difference is and what the potential impact is, then there's an opportunity for additional scientific meetings related to this study. And again note, this is not just limited to complex products; it does cover all products. But this should improve transparency and help minimize concern about what happens once a PSG revision is posted, and provides a place to get clarity and assign further discussion around this.

As we move into the meeting process and closer to the ANDA submission, I just want to remind you that in GDUFA III, pre-ANDA product development meetings that are present in GDUFA II remain essentially unchanged, so we're not really going to talk about them today.

So we'll skip over them, but it doesn't mean they don't exist, it doesn't mean they're not important, and it doesn't mean they're not used significantly, but just that there is no new enhancement for the pre-ANDA product development meeting.

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The product development meetings are those that cover new approaches and provide scientific advice, but as you move closer to submission, what we noticed in GDUFA II is that the GDUFA II presubmission meetings were not used very significantly, and one of the possible reasons was a very long timeline for these meetings that didn't fit into efficient movement toward submission.

In GDUFA III, we proposed some revisions to the presubmission meeting. In these revision meetings, you can have the meetings within 60 days of the request. The meetings will focus on application orientation, preparing FDA to review your application, and describing to FDA what's unique.

You will get feedback from FDA staff at the meeting or advice on how to present the innovative approaches of your application more clearly in the submission. The eligibility for the presubmission meeting remains the same as the presubmission meeting for GDUFA II. If you have a pre-ANDA product development meeting, you have the option of

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having the presubmission meeting.

I would think that the value creation for the presubmission meeting is really to help move from the scientific advice that you've been getting prior to application submission -- through controlled correspondence, through meetings, to reading the product-specific guidances -- to the review team.

Internally, these presubmission meetings will allow FDA to form the ANDA review team when the meeting request comes in. This will enable internal knowledge transfer and help FDA prepare for unique or complex issues. If you flag to us here's something unique about this submission and FDA has more time to prepare for that, you're more likely to get a first-cycle approval than if you surprise us with a complex issue at the submission time.

Again, all of this is focused on providing a more efficient ANDA review for complex generics. But again, it will only be effective if industry uses this option. This is, again, a new feature.

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We hope that it will be useful. We intend to also learn from this as well. But it is a new option that will be available in GDUFA III.

As we move into the ANDA review process for complex generics, GDUFA III provides some enhancements to the current mid-cycle meeting. Again, the improvements, the eligibility for the mid-cycle meeting for complex products is the same as GDUFA II. It's complex products that's used the pre-ANDA meeting process; so not every complex product, only ones that use the pre-ANDA meeting process because we want to encourage those pre-application discussions for the complex products.

In the new system for the mid-cycle meetings, within 7 days of the last mid-cycle communication, an eligible applicant -- i.e., one who's had a pre-ANDA meeting for a complex product -- may request one of two mid-cycle meetings. In this request, you'll describe the specific deficiencies that you want to discuss.

The first option is the mid-cycle meeting.

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Similar to the current one, this meeting will be held within 30 days of the request, but at this meeting, the applicant may ask for the rationale for any deficiency identified in the mid-cycle or ask questions related to FDA's assessment of the data that was submitted in the ANDA; so essentially clarifications of the review; questions about data that's already been submitted.

Again, we feel that compared to the current mid-cycle meeting, this will increase interaction between FDA and industry at this meeting. So again, even though it's similar, it will have some improvements in the interactions as well.

Or there's an enhanced option. We call this the enhancement cycle meeting. This one allows applicants to ask questions about potential new data that they might submit in response to deficiencies. In order to do this, since its data that FDA has not seen yet, FDA will need more time to look at this and provide appropriate answers. This meeting will be held within 90 days of the last mid-cycle DRL.

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Unfortunately, to fit this meeting within our review cycle, we need to have a goal date extension if you enhance this meeting. So this doesn't fit within the 10-month cycle unless you have an extension.

So it's up to the applicant which approach they want to take. If they want to ask questions related to the data that was already submitted, the regular mid-cycle meeting is appropriate. If you want the enhancement cycle meeting with additional questions about new data or responses to deficiencies, there's a 60-day goal date inspection.

Again, these revisions will allow more interactions at the mid-cycle meeting. Both options provide more opportunities for applicants to develop questions. But they allow also the applicant to have some choice to optimize their review process, more effort in the current cycle, or will move quickly to a final decision in the cycle. This, again, gives more control to the applicant to help optimize the review process.

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After any complete response, we've added a new feature of GDUFA III for complex products. If you receive a complete response letter where,basically, you learn that you did the wrong study for whatever reason: proposed an alternative approach, it wasn't accepted; you were doing something different; something came up unexpectedly that you have to do some different type of study in your resubmission -- so this is not for a case where you did a study, it failed, and you have to repeat the study, and you're just repeating the same study because there's an execution error.

It's really the situation where you're doing a new study. You're changing the design of the study because your first study failed and you want to have feedback from FDA before you conduct that next study. In these cases, for the new study -- and it also can include a comparative human factors study and you want to discuss the potential design of that study, or a new approach to active ingredient sameness.

Again, if you're doing something new that

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wasn't done in the original submission, and you want scientific feedback before you submit that new type of study, you can use this post-CR scientific meeting.

Again, as was mentioned earlier, there's a new controlled correspondence process that allows you to ask written questions while you're in CR status. Again, that will give you a faster answer than this meeting, but if it's a more complex issue, like the types of things you might discuss in the current GDUFA II product development meeting, this meeting might be appropriate. You will get a grant/deny decision within 14 days, and the meeting within 90 days after the decision.

Again, the value we think will be created by this is the product development meetings have been very successful and widely used presubmission, but they can't be used under GDUFApost-submission. So now we're able to use them and provide this opportunity for interaction while you're in CR status if you've reached the same type of scientific impasse.

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These are, again, meetings we believe will help resolve complex scientific issues that are blocking the path to approval. So if you find at that first review cyclethe study that you submitted was not appropriate, you can get additional feedback on a new approach and hopefully come back toward approval faster.

To conclude, I just want to summarize the progression that's been happening through the GDUFA program for complex generics. In GDUFA I, we added a research program that continues to advance the science for complex generics. In GDUFA II, we added the pre-ANDA meeting program to improve scientific advice during product development. This has been widely used and very successful.

In GDUFA III, we've added enhancements post-submission to help move complex products toward approval; so again, a progression building the scientific foundations, more communication during product development, and now adding in GDUFA III more communication during product review and assessment.

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Thank you all, and we're moving on to our next topic.

Clarifying Questions

MR. BEACH: Thank you, Rob.

Rob, we have a couple questions here. Before we move on, I will read them. They're pretty similar questions, but I will read them together, and you can answer them how you see fit.

The first one is, "How will the applicant know that they have received their last mid-cycle communication? Is there a process in place for the request outside of the 7-day time request?"

DR. LIONBERGER: FDA's project managers will make it clear to you when the next last mid-cycle communication occurs if there's any ambiguity around it. Again, if you want this meeting, you must respond within 7 days, but FDA will make it clear that this is the appropriate mid-cycle communication to make that request on.

MR. BEACH: Okay. Thank you. I think that answers both of the questions.

We have a couple of other questions on

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different topics.
Ted, the first one is for you, and they're asking about the reports that you all put out and wondering how things are counted; where there might be an application in a tentative approval and another in full approval, are they counted twice, and then a variation on that same question, which you've seen.
MR. SHERWOOD: Certainly. Thank you.
High level, we are counting each agency action. It is possible for a tentative approval to be issued early in the year, then later in the year an approval is issued. In this case, each action is counted.
When we issue the tentative approval, we don't know for sure that an approval will be sought. Further, those actions require considerable agency resources. Also, it is possible for one strength of an application to be approved, while another strength may need to be tentatively approved at the same time. Again, each action will be counted.

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Thank you, Carter.
MR. BEACH: Thanks, Ted.
One for you, Ashley, a question about the PFC program. "Can you provide more detail with respect to the specific changes to the PFC requirements? Will the current PFC guidance be revised to reflect this critical information necessary for inspection?"
MS. BOAM: Thanks, Carter.
While I'd love to delve into the details, I'm not sure we are set up to do that today. So we won't get into the weeds of how that will be changed, but certainly we expect to communicate those changes to our industry colleagues and a mechanism that would allow for public comments also; so be looking for that. Thank you.
MR. BEACH: Thank you, Ashley.
We have another question about availability of the slides. Again, we will request that they get posted following this meeting. You may want to allow a day or two for that to actually occur.
There is a Q&A icon at the bottom of your

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presentation screen there. If you can ask the questions in that, it's better for us to track in there and make sure that we're answering them efficiently.
We have one other question here. "Would FDA also grant a post-CR meeting for pre-GDUFA III complex ANDAs that are still under review, and would FDA provide response to proposals from applicants on any studies/technical queries to address the CR questions?"
DR. LIONBERGER: We will clarify in guidance the exact rules for the legacy products. But in general, I think we anticipate that after GDUFA III starts, if you're in CR status and it's a complex product, that you'll be eligible for this meeting. And that's what we've done through GDUFA II as we implemented these transitions. You're not eligible for these meetings until -- you have to be in CR status after the start of GDUFA III.
In terms of the other question, I did talk a little bit about getting feedback on studies. So again, the commitment letter is very clear. This

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is not, oh, I'm repeating my study because I failed the study and I want some feedback on that. It's really, I'm doing a different study and I want feedback on that study design. That's what the meeting is for, a different type of study design.
Again, in GDUFA III, you also will have the option to use the post-CR Controlled Correspondence to ask general questions about the study that you're conducting. Say that you're repeating a failed bioequivalence study, and you have some question about that study; the Controlled Correspondence will get you a faster answer to that question.
So again, the post-CR scientific meeting is generally intended if you're doing some different type of study. So based on the CR you received, you had to change the approach that you're taking because the approach that you're taking wasn't adequate and you need feedback on the approach. That's what the scientific meetings are for.
If I have to repeat a study or I'm doing another study -- let's say you're doing another

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study and you're following our product-specific guidance, and you just want a clarification question on that. That's probably much more appropriate and a faster answer to the Controlled Correspondence process under GDUFA III.

MR. BEACH: Thank you, Rob, and one more for you.

"Will the proposed CR scientific meeting apply to complex ANDAs prior to GDUFA III?"

DR. LIONBERGER: Yes. We don't intend to limit this meeting to complex products filed after GDUFA III, but you must complete the review status. So once you go into CR status in GDUFA III, then you can request this meeting if you otherwise meet the criteria that were in there. So there's no limitation in the commitment letter to applications submitted under GDUFA III. So it covers all complex products that enter into the CR status.

MR. BEACH: Great. Thank you, Rob, and thank you for the questions.

We will now move over to Lisa Berry and Bethany Rue to talk about the financial structure

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for GDUFA III.

Presentation – Lisa Berry

MS. BERRY: Hi. I'm Lisa Berry from CDER's Office of Management, and I'm here with Bethany Rue from CDER's Office of Strategic Programs. We'll be talking about how the negotiated financial changes set a sound foundation for GDUFA III.

There are several key areas that we want to highlight. First, I'll be talking about modifications to the fee structure, additional resources to hire staff, and financial transparency; then Bethany will be talking about resource capacity planning and the two new target revenue adjustments, the annual capacity planning adjustment and the annual operating reserve adjustment; and then Bethany will wrap up the financial piece by showing how these two new adjustments are integrated into the annual fee-setting process.

Overall, the GDUFA III fee structure remains largely unchanged from GDUFA II. As in GDUFA II, GDUFA III has five fee types, the abbreviated new

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drug application or ANDA filing fee; the ANDA program free; the drug master file or DMF fee; the active pharmaceutical API facility fee; and the finished dosage form, FDF, facility fee.

Modifications were made to the allocation of fee revenues among those five fee types. The first one is the ANDA program fee increased from 35 percent of target revenue to 36 percent of target revenue. At the same time, the API facility fee decreased from 7 percent of target revenue to 6 percent of target revenue. The other allocations remain unchanged.

Overall, the FDF facility fee allocation remains at 20 percent. Within the FDF facility fee category, there are two types of facilities, the FDF and the contract manufacturing organization or CMO. In GDUFA III, there is a change to the CMO fee.

In GDUFA II, the CMO fee is one-third of the FDF fee. And in GDUFA III, the CMO fee is 24 percent of the FDF fee. For API and FDF facility fees, the foreign fee differential remains

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unchanged at $15,000, which is the same as GDUFA II.

As a result of the negotiations, 128 staff will be hired in fiscal year 2023 for the generic drug program and will support the program enhancements agreed to in GDUFA III that you've heard about earlier. FDA will provide progress updates in the hiring of these 128 staff that are to be hired as part of our commitment to financial transparency.

FDA confirmed its commitment to financial transparency and will continue to, one, publish a 5-year financial plan with updates each fiscal year and, two, hold a public meeting about the plan and other financial commitments. In addition, components of the capacity planning adjustment and the operating reserve adjustment that Bethany will be talking about will also be included in the GDUFA 5-year financial plan.

I will now turn it over to Bethany Rue, who will provide information on resource capacity planning, the capacity planning adjustment, and the

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operating reserve adjustment.

Presentation – Bethany Rue

MS. RUE: Thanks, Lisa.

As Lisa mentioned, I'll be walking through two new annual adjustments to the target revenue setting process that will begin during GDUFA III, the capacity planning adjustment and the operating reserve adjustment.

Beginning in GDUFA II, several foundational steps were taken to support the development of the first of these two adjustments, the CPA. During GDUFA II, FDA committed to build a resource capacity planning capability, which included implementation of modernized time reporting and development of a methodology to accurately assess changes in the resource needs of the generic drug program. This methodology is the methodology used for the capacity planning adjustments.

In GDUFA III, the agency plans to continue to develop this capability by publishing a plan outlining the capacity planning adjustment implementation and planned integration of resource

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capacity planning in the agency's resource and operational decision-making processes. This plan is scheduled to be published by March 2023. We will provide annual updates on the plan and progress made on the FDA website.

We will also conduct an independent third-party evaluation of the resource capacity planning capability and the capacity planning adjustment, and we will publish for public comment by the end of fiscal year 2025.

Now I'd like to provide some further details about the capacity planning adjustment. It is a methodology that would be used annually to adjust target revenue for the additional resource needs due to sustained increases in workload of the GDUFA program. The CPA adjusts for specific categories of direct review work, which are listed at the bottom of the slide.

The CPA would be capped at 3 percent of inflation-adjusted base revenue unless certain ANDA submission conditions are met. These include the total number of ANDAs submitted or the proportion

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of complex ANDAs submitted. The CPA will be implemented for GDUFA III starting for fiscal year 2024 fees. FDA would publish rationale for any CPA adjustments in the annual fee rate Federal Register notice for that fiscal year.

Now I'll provide some details on the operating reserve adjustments. The operating reserve adjustment will replace the final year adjustment in GDUFA III. Beginning in fiscal year 2024, the operating reserve adjustment would allow FDA to increase target revenue to maintain sufficient operating reserves of carryover user fees.

The operating reserve adjustment would be phased in and gives FDA the option to increase target revenue to maintain at least 8 weeks of reserve in fiscal year 2024, 9 weeks in fiscal year 2025, and 10 weeks for fiscal year 2026 and thereafter.

If estimated carryover balance at the end of the fiscal year for which fees are being set is projected to be in excess of 12 weeks of operating

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reserve, FDA would be required to decrease the target revenue for that fiscal year to reduce operating reserve to be not more than 12 weeks. FDA would provide the rationale for adjustments to the operating reserve in the annual fee rate Federal Register notice for that fiscal year.

The operating reserve adjustment is designed to not be included in the base revenue for subsequent years. This way the adjustment is made for one fiscal year without creating a long-term impact on revenue.

On this slide, we show an example of the target revenue setting process and where the capacity planning adjustment and operating reserve adjustment fit in. Each fiscal year, the base revenue is adjusted for inflation, then the capacity planning adjustment is added, followed by the operating reserve adjustment. Both of these are, if taken, to arrive at an annual target revenue.

For the subsequent fiscal year, the base revenue would be the inflation-adjusted base

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revenue amount plus the capacity planning adjustment from the previous fiscal year. Note that the operating reserve adjustment would not go into the subsequent fiscal year's base revenue.

This concludes my portion of the presentation, and now I will turn it back over to Carter Beach.

Clarifying Questions

MR. BEACH: Thank you, both.

Before we move to the next section of the agenda, we do have one more question for Ashley.

"Can you please clarify how the DMF review will work prior to ANDA submission under GDUFA III?"

MS. BOAM: Thank you, Carter. I'd be happy to.

There are additional details in the proposed commitment letter, and I would certainly refer you there. But briefly, the DMF holder would need to submit a request for this early DMF assessment. They would need to include at least one letter of authorization with a pre-assigned ANDA number for

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that planned ANDA submission; a reference to the corresponding reference-listed drug so we would know in what context we were starting the assessment of the DMF; and then obviously the information about having paid the DMF fee.

With that information in hand, we agree that the proposed ANDA submission that would then follow would qualify for priority, and again, I refer you to the commitment letter for some more of those details. Then we would begin the assessment of the DMF, and then begin interacting with the DMF holder as appropriate if there were outstanding questions.

I hope that provides a little more clarity. Thank you.

MR. BEACH: Thank you, Ashley.

We do have one other question. "Does FDA intend to limit the number of Controlled Correspondence for a product at two at a time, like it is currently done in GDUFA II?" Will that carry forward?

MR. SHERWOOD: Hi, Carter. This is Ted Sherwood. I can address that one. We are not

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changing that aspect of GDUFA II.

MR. BEACH: Okay. Thank you, Ted.

With that, we will move on to the industry perspective segment, and Lisa Parks from AAM will speak.

(No response.)

MR. BEACH: We have you there, Lisa?

(Pause.)

MS. PARKS: Can you hear me?

MR. BEACH: Yes. There you go.

MS. PARKS: Great. Thank you.

Presentation – Lisa Parks

MS. PARKS: Good morning, and thank you for the opportunity to speak today. I am Lisa Parks, Vice President of Sciences and Regulatory Affairs at the Association for Accessible Medicines. I am speaking today on behalf of industry negotiators and our respective member companies; so in other words, I drew the short stick.

Our three industry groups, the Association for Accessible Medicines, AAM; Bulk Pharmaceutical Task Force, BPTF; and Pharma and Biopharma

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Outsourcing Association, PBOA, are pleased to have developed with FDA the framework for a new 5-year authorization of the Generic Drug User FeeAmendments, GDUFA, for fiscal years 2023 through 2027.

As captured in the GDUFA III commitment letter, the negotiations covered very specific targeted areas to enhance the efficiencies of the abbreviated new drug application, ANDA, review process. The negotiated enhancements are designed to bring timelier access to more affordable generic medicines to America's patients by increasing transparency and communication between applicants and FDA during the presubmission, pending review, and post-approval phases of the lifecycle of an ANDA. We believe the added clarity to the agency's expectation, coupled with more engagement opportunities in the form of meetings, will advance timelier access.

Negotiating the third iteration of GDUFA involved refining and improving certain aspects of the program that were developed during GDUFA I and

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II, while also identifying key processes that would benefit from additional resources. The hallmark of this negotiation was to refine the existing processes and build upon the lessons learned to make the already strong foundation stronger.

I would like to take this time to briefly highlight several core areas of the agreement, starting with advancing approvals. As you have heard, FDA will continue assessment of an ANDA past the goal date if in FDA's judgment it may be possible to approve or tentatively approve an ANDA within 60 days after the goal date. FDA also committed to using information requests and discipline review letters to facilitate an approval or tentative approvalaction. In addition, FDA will also issue a MAPP on the process for reclassification of facility-based major complete response letter amendments on or before the agreed-upon date.

Last, under advancing approval, industry and FDA expanded the scope of Controlled Correspondences to include regulatory and/or

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scientific advice after issuance of a complete response letter or a tentative approval, or after ANDA approval, which were all considered General Correspondences prior to GDUFA III

Drug master files or DMFs; FDA will enhance communication on the timing for submission of solicited and unsolicited amendments to type 2 DMFs. The agency will also allow earlier submission of DMFs under certain conditions and will report in more detail on DMFs for which a user fee has been paid and for those that have undergone a completeness assessment.

Moving on to inspections, under GDUFA III, FDA will provide a pathway for reinspection of facilities with deficiencies identified during inspection to assess remediation and potentially close out official action-indicated warning letters in a more timely manner. FDA will also provide enhanced reporting of surveillance inspections, as well as including more detailed information in its inspections classification databaseto better reflect compliance status.

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For complex generics, as Rob outlined, to facilitate the swift development of complex generics, FDA has committed to issue product-specific guidances, or PSGs, for 50 percent of complex new drug applications within 2 years of the date of approval and 75 percent of such new drug applications within 3 years of approval while prioritizing PSGs for complex products that include NCE over those that do not.

The agency will also provide more opportunities for communication with applicants when a PSG is revised or a new PSG is issued after an ANDA applicant has already submitted an ANDA or commenced bioequivalence studies. The industry and FDA further developed various meeting types to accelerate the development and review of complex generic applications to ensure cost-effective alternative generic medicines are more timely accessible to patients.

Moving on to stability or suitability petitions, industry and FDA were able to create an effective system for the timely resolution of

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suitability petitions, adding agreed-upon metrics and providing additional resources for the agency to meet the negotiated commitments.

With respect to the financial stability of the generic drug program, industry worked with FDA to develop a robust funding model to provide the generic drug program with the revenue necessary to advance the approval of safe, effective generic medicines while addressing industry concerns about sustainability.

Unlike previous iterations of GDUFA, where FDA would estimate resource needs for the full 5 years and frontload all of those costs in year 1, adjusting for inflation fiscal year to fiscal year, GDUFA III will employ a capacity planning adjustment, or CPA, so there will be fewer upfront resources required and more flexibility from year to year to adjust the revenue base in order to accommodate FDA's projected resource needs.

FDA and industry negotiated percentages-based caps on the annual increases to the program costs, providing a degree of business certainty for

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the generic sector. The agreement also requires the agency to publish an implementation plan with annual updates, as well as conducting third-party evaluation of the CPA and their resource capacity planning function.

Use of real-time reporting and modernized time reporting will also aid in industry and agency's ability to keep the lines of communication open for financial transparency. Industry believes these enhancements to GDUFA will lead to a more effective program, while also taking into consideration the sustainability concerns of our industry and our suppliers and contract manufacturers.

We are confident that the commitments and resources in GDUFA III will benefit patients and we support the reauthorization of the program. We look forward to working with FDA to implement GDUFA III, and we will work with our industry members to ensure that the program brings maximum benefit to patients.

Before concluding, I would like to thank

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Jacqueline and the entire FDA negotiating team for the robust interaction and the continued collaborative discussions to achieve our shared mission to patient safety and access. We look forward to the ongoing dialogue. Thank you.

MR. BEACH: Thanks so much, Lisa.

We've got a number of comments asking about slides. Lisa did not have slides. So we're not frozen here; there just weren't slides to share here. And we have another question about slides being available for download. We will have them posted in the next day or two on the FDA website.

We will now move on to the stakeholder comments. Part of the statutorily mandated steps that we had to take throughout this reauthorization process was to have ongoing collaboration with stakeholders throughout the negotiations, so we held monthly stakeholder meetings. One of the consistent contributors there was Tonya Winders from the Allergy and Asthma Network, so she will now present.

Presentation – Tonya Winders

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MS. WINDERS: Thank you.

Again, Tonya Winders, President and CEO of Allergy and Asthma Network and the President of Global Allergy and Airways Patient Platform. It's my pleasure to be with you today. I appreciate the opportunity to speak.

Addressing health disparities has been our mission at Allergy and Asthma Network since 1985, and while many factors drive disparities, the high out-of-pocket costs of medications are a core issue, and increasing access to more affordable generic medicines remains one of the most effective ways to close the equity gap.

The Generic User Fee Act, GDUFA III, is currently being negotiated between U.S. Food and Drug Administration and the generic industry. This presents an important opportunity to improve access to complex generics, many of which treat asthma and allergies.

The goal of GDUFA is to speed FDA approval of new generic drugs, stimulate competition for branded drugs, and reduce drug pricing for

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consumers. We applaud FDA for the success the program has yielded to date, but there is more work that needs to be done specifically for complex generics; copies of complex medicines that are drug-device combinations or have complex formulations than conventional pills, many of which have taken years to win approval due to inefficiencies in the current process.

For example, our patient population relies on complex asthma inhalers and epinephrine auto-injectors as life-saving treatments, but a generic version of Advair, a popular asthma inhaler, was delayed in the approval process by three years, during which time the cost of the branded Advair increased by more than 50 percent.

The epinephrine auto-injector market is even a more alarming example. It took FDA 10 years to approve the first generic medicine, during which time the cost increased by nearly 600 percent. Rising medication costs has shed important light on the challenges of accessibility and affordability.

For millions of Americans, access to

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medications such as epinephrine auto-injectors or a quick-relief asthma inhaler can be a life or death matter. According to U.S. GAO, the average rate of first-cycle generic approvals is only 12 percent, a figure which is most certainly lower for complex generics. In fact, most applications take at least three review cycles before approved, with each review cycle adding 6to 10 months to the development timeline for a typical complex drug product.

Having to go through three review cycles to achieve FDA approval significantly delays patient access to much needed lower-cost complex generics. Delayed access to affordable meds only exacerbates the health and equity in our country. When it comes to Black Americans, study findings reveal they are already less likely to use controller medications for asthma or to carry an epinephrine auto-injector, and we know these care and treatment plans are not nice to have but are absolutely must-haves for our patient community.

It is important to understand that both

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asthma and allergies are conditions that require daily maintenance through medication to remain controlled. With the rising cost of branded products, coupled with the financial stress from the pandemic, we are at a critical inflection point in the U.S. where genericizing treatments must be a priority. Lower-cost treatment options will result in greater adherence and less rationing of care, in turn, creating a healthier population with less burden to the overall healthcare system.

As we look forward to turn the tide on public health, we should prioritize taking important steps to close gaps in health equity. Allergy and AsthmaNetwork is grateful to FDA for its ongoing efforts to increase access to lower-cost generic medications, and the time is now to work with FDA to elevate a collective patient voice so people of all backgrounds with chronic conditions like asthma and allergies can have access to safe, effective, and affordable complex treatment options. Thank you.

Public Comment Period

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MR. BEACH: Thanks so much, Tonya.

We are approximately an hour ahead of schedule here. We are prepared, I think, to move on to the public comments section, but I don't want to catch those presenters off guard. So if you're not ready to present, we can certainly come back after lunch, but first on our list here is Molly Ventrelli.

MS. VENTRELLI: Thanks, Carter. Can you hear me?

MR. BEACH: Yes Sorry to put you on the spot.

MS. VENTRELLI: Oh, not at all; not at all. It's fine.

Good morning, and thank you for the opportunity to give me a few minutes to speak this morning. I'm Molly Ventrelli. I'm the Senior Vice President of Regulatory Affairs at Fresenius Kabi, and one of the industry negotiators on behalf of AAM for GDUFA III.

First, just very quickly, I want to take this opportunity to thank Jackie and all of the FDA

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staff, as well as Lisa and Dave from AAM for their leadership and commitment through this negotiating process that was about a year long. There was a lot of effort that was put in by all of the teams that were involved, and I really appreciated the collaborative spirit that persisted even when we were talking about more difficult topics.

Negotiations by nature mean that it's a compromise at some points to get to the best possible path forward for everybody, and I think that that was certainly the case with GDUFA III. So to echo Lisa's comments and some from the FDA presenters this morning, I really believe the enhancements and progress that were made in GDUFA III will lead to a much more effective program overall that benefits patients, which is ultimately both FDA and industry's goal.

I'm going to talk a little bit this morning on a few key points around advancing approvals in suitability petitions, and it may be a little repetitious with what you've heard already from Ted, and Maryll, and Ashley, and Rob, but I think

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these points specifically bear a little repeating for everybody so that you take note.

GDUFA III brings a lot of enhancements around the current process on ANDA review and advancing approvals. There are a couple of points, again, that I want to make specifically in that area, and one is the imminent action pathway. That can be used to resolve some minor issues that are preventing approval, but in GDUFA II might have necessitated a complete response letter and another cycle.

This will allow an action within 60 days of the goal date, while still meeting the intentions of the metrics in terms of approval timing, but should increase first-cycle approvals and hopefully reduce the time and effort for both agency and industry.

FDA has also developed an approach to mid-cycle discipline review letters. If an applicant responds completely to a DRL by the given date, the agency will review that response within the first cycle and not defer it to a later cycle.

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It also gives the agency the ability to extend goal dates -- and I think Ted talked about this a little bit -- in order to complete a review of major responses. Again, it may extend a goal date, but it's eliminating another review cycle, which is ultimately the goal and will save us time in that.

In the event a CRL is issued, FDA has added additional pathways for applicants so that we can get some clarity or talk about some of these scientific issues. I think Rob had mentioned the post-CRL scientific meeting.

As an applicant, once you get a CRL, you can request a post-CRL meeting to just gain some clarity around a specific issue, and that's really the only option right now in GDUFA II that we have, but they've added some other ways to get some feedback on the CRL letter. You can submit a Controlled Correspondence or, as I said, for those more technical or scientific discussions, you can request a post-CRL meeting.

Again, these options are going to make it easier and will assist the applicant in providing a

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complete and adequate response to the CRL and hopefully reducing those review cycles.

Lastly, the last point under advancing approvals I want to make, in GDUFA III, the issue of late-cycle RLD labeling changes is also addressed. This has been a real source of frustration for both the agency and the industry for many years. In GDUFA III, FDA's going to concentrate the labeling review into the second half of the review cycle, and that will allow -- hopefully, what we're hoping for is a single labeling review.

This later review, coupled with the ability to use the imminent action pathway, will give the agency and the industry some flexibility and hopefully the ability to make some late-stage labeling changes when these late RLD changes happen, without actually negatively impacting approval timing in many situations.

I'd also like to talk a little bit about suitability petitions, and I know Maryll put up some slides for you guys, so I'm sure you'll see

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that, and it's also outlined in the letter.

Suitability petitions have for many years been an area that's been a bottleneck for the generic industry, and these petitions generally provide for new strengths or versions of a product that actually has some value to either the healthcare industry or the provider, and also the patients. GDUFA III is going to address this and will improve the agency's ability to assess and take action on these petitions.

Specifically starting in 2024, FDA is going to assess the petitions for completeness within 21 days, and then will assign a 6-month goal date. FDA has tiered the percent completion by year in order to be able to ramp up to get the necessary resources to take care of that. This 6-month goal is not going to be applied retroactively to any petitions filed before 2024, so if you have a petition that was filed before 2024, you can withdraw it and resubmit it in order to obtain a goal date after 2024.

As part of the implementation, FDA's going

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to look at some ways to determine if there's still interest in the backlog of pending petitions that exist today. We're hoping that also potentially getting a goal date may drive some of the withdrawal or resubmission of some of those petitions, but we would like to see a way to get that backlog down.

If there's a large number of petitions filed in a year, FDA will prioritize them based on drug shortage, public health emergency, PEPFAR, and by adding focus on these petitions, it's going to provide some additional options for patients and increase competition in the market.

In summary, again, thank you for giving me a few minutes today on GDUFA III. I hope it wasn't too repetitive for you, but we really feel that GDUFA III is going to bring some significant improvement over our current process in both efficiency and predictability, and then ultimately will deliver that value to the healthcare providers and patients.

Fresenius Kabi supports the reauthorization

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of GDUFA III, and I really look forward to continuing to work with FDA on implementation. So thank you very much for your time today.

MR. BEACH: Thanks, Molly, and thank you for your collaboration throughout the process.

Just one quick housekeeping item before we move along; Kiran, if you're ready, we'll move on to you, and then following Kiran, we will take a 20-minute abbreviated break and then go through the rest of the program.

Kiran Krishnan, it's all yours.

MR. KRISHNAN: Thank you very much, Carter.

Good morning, and thank you again for the opportunity to speak this morning. My name is Kiran Krishnan. I'm the Senior Vice President for Global Regulatory Affairs at Apotex Corp. I'm speaking today on behalf of Apotex Corp. I was one of the industry participants representing AAM in the GDUFA III negotiating team.

I'm here to provide perspective on two topics that have been agreed upon by the stakeholders and the FDA as enhancements in

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GDUFA III. You've heard a lot this morning from the FDA speakers, and a lot of what I'm going to tell you today is going to be repetitive, but it is important, as Molly mentioned, to emphasize the work that's been done and what would come out of this. It's important for the industry to take note of it.

I will be speaking specifically on the enhancements to the drug master file, otherwise known as DMF reviews and inspections. As Lisa mentioned in her statement, the negotiated enhancements are designed to bring timelier access to more affordable generic medicines to American patients by increasing transparency and communication between the applicant and FDA during the presubmission, pending review, and post-approval phases of the lifecycle of an ANDA.

I'll start with the DMF review enhancements agreed upon in GDUFA III. The agency and industry, as Jacqueline Corrigan mentioned this morning, have a collective goal of increasing the number of first-cycle actions that can lead to an approval or

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a tentative approval. One area of continued concern is the timing of the review of the DMF in relation to the timing of the review of the ANDA. You've already seen some questions asked for the FDA panelists this morning.

Today, the DMF, as all of you are aware, undergoes substantial review once the ANDA is submitted. This, as you can appreciate, creates an inherent challenge in terms of timelines for both the agency and the industry, considering we have a 10-month goal date.

The GDUFA III enhancements directly address these concerns by creating a mechanism for review of the DMF 6 months prior to the submission of ANDA referencing the DMF. It is envisioned that under this new paradigm, the review of the DMF, prior to the submission of the ANDA, will allow for the DMF holder and the FDA to work on issues prior to the ANDA submission.

Truly, this jumpstart of the DMF review not only gives the DMF holder the time to respond to the deficiencies, but also provides the agency

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adequate time to review the DMF response, and thereby allowing for more coordinated and efficient review of the ANDA. It is envisioned that this extra time will allow the DMF review to be completed and possibly be deemed adequate, allowing the applicant to work with the agency to resolve the ANDA comments during the review cycle.

This enhancement will allow for a greater chance to increase the first-cycle approvals. In order to balance the negotiated enhancements with program costs, we had to place the brackets around the type of DMFs that could be submitted in the 6 months in advance of the ANDA. The type of DMFs that can be submitted 6 months prior are the DMF that support the review of an original ANDA, an ANDA amendment containing a CR letter, and an ANDA amendment seeking approval for an ANDA that was previously tentatively approved.

Now, the commitment letter, as you've heard this morning as well from Ashley, describes the specific conditions under which the DMF can be submitted 6 months prior to the submission of the

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ANDA or the amendment.

The agency just did not stop for newer applications or applications pending review. They took it one step further and have agreed to allow this, where a DMF holder can also submit a request for assessment of a DMF 6 months prior to the submission of a prior approval supplement to add a new or an alternate API source. Now, this is limited mainly to drug-shortage products and to products to address the public health emergency.

These enhancements for the DMF review we certainly believe will go a long way in helping both the industry and the agency, and we thank the agency for taking these pragmatic measures to create a pathway to enable more one-cycle approvals.

The next aspect of GDUFA III that I want to highlight is on the transparency as it relates to the inspections. Now, in GDUFA II, as you all remember, the Office of Compliance, Office of Regulatory Affairs, and the Office of Pharmaceutical Quality did a stellar job and

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successfully implemented the 90-day decision letter.

Now, to further enhance the transparency and to offer increased predictability, as you heard from Alonza this morning, the agency agreed to have a time-bound process for conducting post-warning letter meetings and also conducting reinspections of both domestic and foreign facilities on a time-bound manner, based on a tiered goal for the various fiscal years, pursuant to certain requirements to be met by the site or the applicant requesting the meeting.

Now, this is very unique to the GDUFA program and provides the facilities that become non-compliant a formal pathway to seek agency's feedback on the adequacy of the remediation and its corrective action plans. More importantly, this is envisioned to prevent firms from prematurely requesting reinspection, which will enable the agency to better allocate its resources to remain focused on meeting its commitments.

The meeting pathway is optional for the

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facility to take advantage of. The facilities that have responded to a warning letter and submitted the remediation and corrective action plan can request a meeting 6 months after the warning letter has been issued. In certain circumstances, the applicant can ask for a meeting prior to 6 months, and the agency can grant or deny the meeting at its discretion.

These meetings will be granted or denied within 30 days of requests using a tiered goal for various GDUFA years to manage the workload. The agency will grant these meetings subject to its review of the firm's corrective and preventative action plan and the firm's progress with the remediation strategy.

In the event the meeting request is denied, the agency has also agreed to provide high-level feedback in terms of what is expected or to provide insight into the areas where the agency feels the firms need to provide further information, or to evaluate further, before it submits a subsequent meeting. I do believe that this is a very positive

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step, and I thank the agency for considering and including this as part of the commitment letter language.

It is envisioned that these meetings will help the firms gain additional clarity and insight to its course of action and any adjustment it needs to make to meet the agency's expectation. This process is expected to provide the facilities that need clarity to allow them to fully remediate the agency's concern. And again, as I mentioned, it avoids firms prematurely asking for reinspection.

Furthermore, the agency is also committed to setting a time-bound process to act on the request for for-cause reinspections, and they've agreed to schedule these for-cause reinspections in a time-bound manner. The agency will respond to a request for reinspection within 30 days. If a decision is to grant the reinspection, such inspection will be scheduled within 4 months for domestic facilities and 8 months for foreign facilities, based on a tiered goal for each of the fiscal years in GDUFA III.

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I would like to take this opportunity to thank Dr. Jacqueline Corrigan, the FDA leadership team from CDER, from ORA, and the Office of Generic Drugs for working with the industry negotiating team to develop these enhancements. These enhancements will go a long way in creating transparency and increasing predictability for the industry.

We are confident that the commitments and the resources in GDUFA III will improve access to important generic medications for patients, and therefore, Apotex Corp supports the reauthorization of the GDUFA III program. We look forward to working with the FDA to implement the commitments in GDUFA III. Thank you again.

MR. BEACH: Thanks so much, Kiran.

We are going to take a 20-minute break right now. We'll say 11:30 back here, and we will continue with the public comment section, and next up will be Diana Zuckerman. Thank you.

(Whereupon, at 11:09 a.m., a recess was taken.)

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MR. BEACH: Welcome back, everyone. We will continue now with the public comment session.

Diana Zuckerman, it's all yours.

DR. ZUCKERMAN: Thank you. Can you hear me?

MR. BEACH: We can.

DR. ZUCKERMAN: Okay. Great. Can you put up my first slide, please?

I'm Dr. Diana Zuckerman, President of the National Center for Health Research, and I appreciate the opportunity to speak today. My perspective is based on my 30 years of working on issues pertaining to the safety and effectiveness of medical products.

I have postdoctoral training in epidemiology and public health and was a faculty member and researcher at Vassar, Yale, and Harvard before moving to Washington to work as a congressional investigator on FDA issues in the U.S. Congress. I also worked at HHS and the White House.

Our Center is a non-profit think tank that scrutinizes the safety and effectiveness of medical products, and we don't accept funding from

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companies that make those products. On a side note, I'm one of FDA's biggest fans because I fully appreciate the agency's importance.

As a founding board member of the Alliance for a Stronger FDA, I work with non-profits and industry to increase appropriations for the FDA, and I'm going to talk for just one more minute before getting to the rest of my slides.

Our center supports the GDUFA efforts to ensure getting safe and effective generic drugs to market as quickly as possible. We understand that FDA needs user fees to achieve that goal, but today I want to focus on the safety and effectiveness issues in the GDUFA III commitment letter.

As you know, all the different user fee negotiations are behind closed doors with public health, consumer, and patient groups excluded. During the pandemic, it's become even more obvious that public trust is eroded when the public feels it isn't getting all the information it needs to make informed decisions, and today's GDUFA meetings and presentations have been focused on what

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industry wants and needs, and what they're willing to pay for, and not on what patients and consumers want and need. Only one stakeholder comment was a patient group, although other groups would have appreciated the opportunity to speak during that time slot.

Our health care is the most expensive in the world. The U.S. spends more than $3000 more per person on health care than the second highest country, which is Switzerland. Without generic drugs, the cost of U.S. health care would be even higher, so trust in generic drugs is absolutely essential to help make health care affordable.

For that reason, we encourage the FDA to talk more about what you are doing to ensure that generic drugs are truly identical to brand names in all the ways that matter to patients.

What are the metrics in the commitment letter? I pointed out just a few -- by the numbers that were included in the commitment letter -- of the things that seemed to be focused more on safety to us. The number 6 was the number of inspections

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conducted by domestic or foreign establishment location and inspection type and facility type, and number 7 was the median time from beginning of inspection to Form FDA 483 issuance. These are obviously very important to industry as well, but at least they seem to be a metric that says to us that these inspections are taking place in a way that's important.

Number 8 was the median time from Form FDA 483 issuance to the warning letter, et cetera, et cetera. You can all read; I don't need to read this to you, and number 9, the median time from the date of the warning letter, the import alert, or regulatory meeting to resolution.

Again, these are metrics of importance to industry and, obviously, to the FDA, but also can be very important to patients and consumers to feel that these inspections matter and that decisions are being made based on the information they are carefully gathering at these inspections.

The last two that I'm going to mention, the last two metrics, number 12, which is the number of

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citizen petitions to determine whether a listed drug has been voluntarily withdrawn from sale for reasons of safety or effectiveness, pending a substantive response for more than 270 days from the date of receipt.

The citizen petitions, obviously, are sort of a dual-edged sword because, on the one hand, you wouldn't need citizen petitions if things were moving as smoothly as one would like. But then again, the fact that there are citizen petitions means that the FDA needs to respond to them in a timely manner, but not just in a timely manner, but also in a meaningful way, so I encourage that to be reworded as well; then number 18, the percentage of facility reinspections carried out within 4 or 8 months after the letter to the facility, indicating FDA's intent to reinspect.

So again, this is important to all stakeholders, but certainly carrying out reinspections shows that the FDA is on top of things and that these inspections, which we think are very, very important, are being done in a

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timely manner.

In conclusion, I want to say that we would have liked to see in the commitment letter some other metrics that are more specific to ensuring patients, consumers, and the public health community that these user fees are being used in a way that doesn't just speed the process along, doesn't just make life easier for industry -- that was very important -- but also ensures that the products being approved by the FDA are exactly as they've been described to us. That's what the public needs to continue to have trust in generic drugs, and as I said, that is so essential for our healthcare system. Thanks very much.

MR. BEACH: Thank you, Diana.

Brian McCormick?

MR. McCORMICK: Good morning. Thanks, Carter.

My name is Brian McCormick. I am Vice President and Chief Regulatory Counsel for Teva Pharmaceuticals. I'm also Teva's head of Global Regulatory Policy. I had the privilege of serving

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as an AAM member company representative for the GDUFA III negotiations.

I want to start by thanking FDA for its collaboration in negotiatinga well-thought-out and robust commitment letter that will serve the agency and industry well in the coming years. While GDUFA II has been a great success, there are aspects of the generic drug program that need more attention moving forward.

Through the hours we spent at the negotiating table, we arrived at an agreement that builds upon the successes of GDUFA II and looks ahead to the types of applications that FDA will be assessing over the next five years. As GDUFA III is adopted and implemented, I believe we will see a more predictable, transparent, and scientifically driven system to support the development and approval of generic drugs.

I'll focus my brief remarks today on those aspects of the GDUFA III commitment letter that Teva believes will most improve the development and approval of complex generic products. As many

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others have noted, the commitment letter offers a number of new and enhanced meetings that will provide FDA and industry with more opportunities to discuss the novel scientific issues that arise before and after the submission of ANDAs for complex products.

For example, one significant issue that industry hopes to address under GDUFA III is the risk to generic entry created by the issuance or revision of product-specific guidances applicable to pending or tentatively approved ANDAs.

The PSG program is one of the great successes of GDUFA to date, but when a PSG is issued or revised, and the approval standards change for an applicant midstream, it's difficult to overstate the obstacles this creates, especially for complex products.

The additional time and expense required to meet the new standards can undermine the entire business case for an applicant to bring a product to market, and currently there is no opportunity to discuss with FDA how to mitigate or address the

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changes in a way that would allow the application to move forward.

Regulatory science must continue to advance, and FDA should continue to develop new and revised PSGs, but it must do so carefully with an understanding of potential unintended consequences. The improvements to the PSG program made under GDUFA III will help to address these challenges.

FDA has committed to making the PSG revision process more predictable and transparent for industry. The agency's commitment to post on its website when it intends to update a PSG will allow industry to better plan for potential changes and build them into the regulatory strategy when possible.

We also appreciate that FDA will make clearer how it intends to prioritize PSGs and how industry can contribute to that prioritization. The agency has also committed to publishing PSGs for new chemical entities and complex products within predictable time frames after NDAapproval.

Most importantly, under GDUFA III, industry

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will have the opportunity to meet quickly with FDA when the agency issues or revises a PSG applicable to an applicant's product once in vivo work has begun. The applicant and FDA will be able to discuss the PSG, the impact on the development program, and how to address gaps.

If this initial teleconference is not enough, the dialogue can continue through Controlled Correspondence or at another meeting to discuss the scientific rationale for an approach different from the one described in the new or revised PSG. While these PSG meetings are not a guarantee that an ANDA will be approved in the current or even the next assessment cycle, they represent a significant step forward.

Two other meeting types for complex products have been enhanced under GDUFA III, which we believe will go a long way toward improving the assessment process and bring you more generics to market in fewer cycles. These are the enhanced mid-cycle meeting and the post-CRL scientific meeting.

While GDUFA II offers meetings at both of

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these points in the assessment cycle, the meetings tend to be perfunctory and do not offer meaningful opportunities to discuss scientific issues with FDA. In Teva's view, the ability to have a meaningful dialogue with FDA at both of these points could be a gamechanger for complex products.

Under GDUFA II, the mid-cycle meeting is merely a chance for FDA to update an applicant on the status of its application. No additional questions are asked and industry cannot discuss with FDA how to address deficiencies during the current assessment cycle.

Under GDUFA III, industry will have the option to discuss with FDA how to address deficiencies identified in the mid-cycle discipline review letters. This will allow an applicant to respond to FDA during the current cycle through an amendment or, at worst, more quickly begin developing the data needed to gain approval on the next cycle. Either way, this is a more efficient process than having to wait for a complete response letter.

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The same goes for the post-CRL scientific meeting. Many post-CRL meetings under GDUFA II are frustrating. They're restricted to clarifying questions with applicants' proposed questions often rejected by FDA, and do not offer an opportunity to discuss data or an applicant's strategy to address the issues raised in the CRL.

Under GDUFA III, industry will have the option to discuss with FDA the new data needed to secure approval on the next assessment cycle. Moreover, the timing of this meeting will not be limited. An applicant can request a meeting at any time in this post-CRL development process. This will lead to fewer cycles and faster approvals because industry will be able to respond to CRLs with the information that FDA needs, taking the guesswork out of the development process.

Finally, I wanted to take a moment to underscore the value of one meeting that will not be changing from GDUFA II to GDUFA III, the product development. The development process for complex products is long and challenging. Being able to

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meet with FDA early and throughout the process is crucial, and the product development meeting offers a key forum to discusssubstantive scientific issues.

These interactions lead to improved ANDA quality and fewer assessment cycles. Especially in the absence of a PSG for a complex product, getting the agency's guidance prior to submission makes all the difference.

In closing, Teva unequivocally supports the GDUFA III commitment letter. We were proud to participate in the GDUFA III negotiations with our industry and trade association colleagues, and we're looking forward to continuing our dialogue with the agency to bring more generics to market faster.

We believe that complex generic products, in particular, play an important role in lowering healthcare costs and making room in the healthcare system for the innovative and more expensive therapies that come to market each year.Thank you very much.

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MR. BEACH: Thanks so much, Brian. We appreciate your participation in the negotiations.

Next, Raghuram Pannala?

DR. PANNALA: Hello, everybody.

MR. BEACH: We'll have your slides up in a moment.

DR. PANNALA: Can everybody hear me?

MR. BEACH: Yes.

DR. PANNALA: Hello, everybody. Good morning. I'm Raghuram Pannala, working for ScieGen Pharmaceuticals. I've been working in the industry from the time of [indiscernible] filings, GDUFA I and II. Today I'm going to present our company's thoughts and my thoughts.

This is the disclaimer. ScieGen Pharmaceuticals appreciates all the great work by the agency on GDUFA in the pandemic time. The thoughts presented are only for suggestions and for the betterment of the program.

For the sake of convenience of this talk, I'll make the three categories. The initial filing on life cycle management may be covered by the

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filing fees. The scientific enhancements and complex generics may be covered by the program fees. Audits, emerging technologies, and continuous manufacturing may be covered by the facility fees.

Communicating internally on the forms in the ANDA review status is quite a task. If GDUFA can adapt the model of e-commerce, firms can check the current status of ANDA online, and it will be helpful if we can know about an upcoming event and predictable day on approval for launch preparations.

This is shaping out to be more critical in the new normal due to ongoing supply chain issues, which may live with us for some time. With CASA and AA [ph] tools in place,this may be an achievable task. A graphic presented below is a snapshot of how it may look like.

Our firm has received some first-cycle approvals and [indiscernible] approvals. We appreciate all the great work by the agency. The below case study [indiscernible] is a development

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opportunity. In this case, the initial goal date was 2018 December, and the approval of August 2019.

The delay may be reduced with 3 months if ScieGen Pharmaceuticals agreed with dissolution specs during the first deficiencies we got. Also, the 6 months would have been avoided if the DMF deficiencies would have been issued through all the ANDA filings in advance . Also, the DMF deficiencies would have been reviewed in context with the drug product. This is scope [indiscernible] development on this part, so that is the reason we present it.

Coming under the initial review process, that is from filing to approval, some points for consideration. Major review points on drug product and DMF, which may delay approval and be communicated in faster year, which will help the ANDA holder in attempting resolution. The facilities part may not be possible in our attempts, but it will be helpful. Mid-cycle review status updates are not guaranteed in GDUFA II, but it will be very helpful if mid-cycle status, along

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with discipline status, is updated automatically to all the ANDA filings.

In some [indiscernible] training sessions, major deficiencies are presented. It will be helpful for firms to develop the quality of filing if top 10 deficiencies are published periodically. Some of the other regulatory agencies are following this model.

Administrative form updates by FDA emails, like GDUFA emails, and [indiscernible] emails will be helpful. Some of these are from the [indiscernible] updates. The recent DMF 3938 form is appreciated. There may be some delays due to the PET and regulatory clearances. These delays may be avoided before just the end of the GDUFA goal date.

The text in gray is supporting data on ancillary points. [Indiscernible] management. FDA is advocating and increasing emerging technologies, which is very helpful. Some time and funds are also needed together to the aging facilities' upkeep and switching to new technologies. This

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will be a great help to small and medium-size organizations.

As cited here, the examples from changes to NDA and ANDA guidance, dated 2004, as we all know, with different levels of understanding on technologies and the equipment being used, the changes may be reclassified, increasing firms to embrace new technologies, which may save time, money, and ensure more compliance, and come back to the world of technologies.

Speaking on the DMF review, dealing with DMF changes allow DMF holders to file independently whenever possible, and the changes will help ANDA holders a lot. The guidance, [indiscernible], DMF changes guidance, [indiscernible] CBE supplements and accepting some changes from DMF holders in annual reports. Allowing facilities to be communicated to ANDA holders in 30 or 60 days on the day of filing will help ANDA holders to speak to the DMF holder and resolve the issues. We are very much thankful for the recent Form 3938 [indiscernible] the DMF.

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Scientific enhancements [indiscernible], training programs are within our [indiscernible], and case studies presented are really appreciated. It will be really helpful and useful if model documents are released just like the QbD nitrosamine risk assessment and a few models have as requested. ICH quartile and established conditions is being advocated by FDA. Once we'll try to attempt if there is a model filing document developed.

Coming to facilities and inspections, thanks to all the developments mentioned in the GDUFA III commitment letter on the facilities and also on the role of CPA. A few comments on the current scenario.In the facility inspection database, when they are searching for some of thefirm's inspectional status, they're not updated, so maybe updating as I was told monthly or 15 days will be very helpful. Before filing, we can check the inspectional status of the firm which we are dealing with.

OAI firms [ph] inspection to be finished and

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helping to decide on pending ANDAs and supplements. There may be some more transparency brought into the selection of firms for the inspection. The tools firms will use for inspection are the guidance documents. The inspectional guidance has released in the last [indiscernible]. Firms are relying more on the 483 issued to others. This is something like preparing for an exam on someone else's papers.

So maybe the agency should look at the inspectional guidance documents some time before, and revising and bringing the current scenarios into them.

I'm very much thankful for the FDA and management for allowing me to present my thoughts, and colleagues for sharing their thoughts during the presentation. I'm very much happy to present my thoughts to GDUFA III reauthorization process. ScieGen Pharmaceuticals supports GDUFA III reauthorization and looks forward to work with the agency as per the expectations and statute. Thank you.

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Clarifying Questions

MR. BEACH: Thank you so much. We appreciate the input.

We have some time here for questions and answers. I have one here for Lisa Berry.

"What is the fee for type 3 DMF?"

MS. BERRY: The DMF fees are only for type 2 DMFs, and there is no fee for a type 3 DMF.

MR. BEACH: Thank you, Lisa.

Again, there's a Q&A icon at the bottom of the presentation screen here. If you have any questions, please enter them there.

We will continue to keep an eye on that as we [inaudible – audio gap] here. But in the meantime, we want to have closing remarks from Sally Choe from OGD.

Sally?

Closing Remarks – Sally Choe

DR. CHOE: I'm Sally Choe, Director of FDA's Office of Generic Drugs. It has been extremely valuable hearing from everyone today as we prepare to proceed with our work to implement GDUFA III.

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As we wrap up today's productive and insightful meeting, I want to give a special thank you to everyone who has made it possible to get to this stage. In particular, a sincere thank you to the FDA staff and industry members who worked over the past year to develop the set of recommendations we have discussed today.

Thanks to your dedication, hard work, and long hours, we have a solid proposed commitment letter that was the foundation of our robust public discussion today. Thank you also to the patients, consumer groups, and all stakeholders who engaged in the process of negotiations and provided insights and input as well. And lastly, thank you to everyone who joined us today and provided feedback that we will most certainly take into account as we move forward.

Because of the work done up to this point and input we've received, FDA is well equipped to build on the success of GDUFA II and take our generic program into the next era with GDUFA III. This includes the GDUFA III goals of achieving

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earlier approvals through enhanced communication and assessment processes; enhancing the development, assessment, and approval of complex generic products; and assuring a sound financial foundation for GDUFA III.

FDA is committed to meeting the performance goals outlined in the proposed commitment letter. Our next job, before GDUFA III implementation starts, is to consider the public views we heard today, as well as comments submitted to the docket, and make any necessary changes to the commitment letter needed.

We will then transmit the GDUFA III recommendations to Congress no later than the statutory date of January 15, 2022. We are confident Congress will agree this proposal is a positive step for FDA, industry, and public health. We look forward to providing updates to FDA staff and the public about how GDUFA III will be carried out and how that will assist us in fulfilling our mission of ensuring Americans have access to safe, effective, high-quality, and more affordable

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medicines. Thank you againfor your time today.

Thank you, Carter.

Clarifying Questions

MR. BEACH: Thanks so much, Sally.

We do have one question here in the chat.

"Can you explain more how regulatory science research feeds into PSGs?"

Rob Lionberger, do we have you here?

DR. LIONBERGER: Yes. Most of our product-specific guidances, especially for the complex products where there's some novel aspect of it, there is some regulatory science work that has to be done before we can identify the appropriate work.

Sometimes this is done through our collaborations with FDA labs, where we need to measure certain things to determine that they can measured. Some instances are a little more advanced, that we want to develop techniques to measure something that maybe hasn't been measured before that's necessary for approaches to bioequivalence. Sometimes this is done through

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external research collaborations with experts outside of FDA as well.

Some of the product-specific guidances really do require that level of effort in order to provide a pathway in the product-specific guidance that we know will be effective and leading toward a generic drug product.

Adjournment

MR. BEACH: Thanks, Rob.

I appreciate everyone's flexibility as we shifted the agenda here a little bit. I hope on balance, you appreciate the earlier end time. At the moment, we don't have any open questions, so we will close out here.

Thank you for your attendance and participation. We really value the engagement and input. We look forward to your comments in the Federal Register and going through those and addressing them.

As mentioned, we will deliver the proposed GDUFA III package to Congress in January, and then we'll work toward a smooth transition from GDUFA II

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to GDUFA III.

Have a nice day. Thanks again.

(Whereupon, at 11:58 a.m., the meeting was adjourned.

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