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OFFICE OF THE COMMISSIONER

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PUBLIC HEARING ON POLICY DEVELOPMENT --
REQUEST FOR COMMENTS
PART 15 PUBLIC HEARING

Wednesday, September 17, 2014

College Park Marriott Hotel and Conference Center
3501 University Boulevard, East
Hyattsville, MD 20783

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A G E N D A

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PROCEEDINGS

MR. FLANAGAN: So apologies. We don't have a podium up here facing you, so I'm going to stay seated as I make opening remarks. Apologies for the discourtesy.

Good morning. Welcome. And thank you very much for coming. The agenda says that I have 10 minutes of remarks, but I really don't. There is only one thing I want to talk about.

My name is Keith Flanagan. I am the Transition Lead for Policy in CDER's Office of Generic Drugs. There is a lot we would like to talk about, but the purpose of today's hearing is for us to listen and to learn from you. We have tried to be very conscientious and very meticulous about GDUFA implementation, but FDA isn't always 100 percent perfect about everything all the time. You have information, insights, and ideas that we need to do the best job that we can.

GDUFA creates a once-in-a-program-lifetime opportunity to build some policy infrastructure, and we want to make sure that we

do a great job, and we need your help to do that.

So with that in mind, again thanks for investing the time in preparing remarks. Thanks for coming all the way out here, and we earnestly welcome your comments. Thank you.

MS. NGUYEN: Good morning, everyone. My name is Martha Nguyen, and I am a Senior Policy Advisor in the Office of Generic Drug Policy. I am the presiding officer for the first panel today, and I would like to welcome you to this Part 15 hearing on policy development related to GDUFA implementation.

Before we begin, I would like to go over some logistics. First, please turn off any mobile devices because they might interfere with the audio in this room, but I am going to now give you conflicting information because I am also going to give you the Wi-Fi password for this hotel space, but you can write that down and use it during the breaks. The network is "Guest Net," and the user name and password are both "FDA," and those are case sensitive, so uppercase "FDA" for username

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and password.
Also, we ask that all attendees sign in at the registration desk so that we can track the number of attendees and follow up with you afterwards if there is anything else we think would be useful to share by e-mail.
The agenda includes two 15-minute breaks and a 1-hour lunch break. We'll try to end the hearing at 5:00, and if we finish before that, we'll end before.
For any media present, the press officer for today is Jordana O'Grady (ph). She is waving her hand in the back there. She will be the contact for any media in the room today.
So here are a few rules and procedures to keep the hearing moving as efficiently as possible. Each registered speaker will have 15 minutes to present. There are timekeeping lights on the podium that will let you know when your 15 minutes are up, but please also be mindful of your time allotment.
There is a little remote on the podium,

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and once the slides are on the screen, you will advance your own slides by pressing the right arrow.
After each presentation, the panel members will have 10 minutes to ask questions about the presentation.
No participant may interrupt the presentation of any other participant, and only FDA panel members may ask questions during or after the presentation.
If a speaker's presentation takes less than 15 minutes, we will move right into the questions from the panel members and then on to the next presentation.
If presentations from the registered speakers wrap up ahead of schedule, we will allow additional commenters to speak for up to 5 minutes each in open comment sessions after the first and second panels.
If you signed up to speak at the registration desk this morning, please look for your name on the list of commenters, which we will

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project onto the screen at the start of the open comment sessions.
Please approach the microphone in the order shown on the list. We will allow as many commenters as time permits. And a recording of this meeting will be transcribed, so please remember to use the microphone when speaking. The transcript will be accessible through Regulations.gov and on FDA's GDUFA website in about 30 days.
I think there was some miscommunication about whether this hearing would be webcast, and it's my understanding that FDA is not webcasting the hearing today.
So, as Keith mentioned, the purpose of today's public hearing is to seek input on GDUFA implementation from a broad range of stakeholders.
In the first panel, we are seeking comments on the five draft guidance documents that we have issued to date to facilitate implementation of GDUFA. We would especially like to hear if there are GDUFA implementation issues

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related to the draft guidances that have not been addressed; if there are other GDUFA implementation topics that need development of guidance; and, finally, if there are any generic drug development issues unrelated to GDUFA implementation that need the development of guidance. We will consider all information from this public hearing, including the public docket, when developing our future policy priorities. So any comments that aren't presented today can be submitted through Regulations.gov using the docket number for this hearing, which is FDA-2014-N-1168.
We have two distinguished panels of FDA experts to listen to the presentations today.
Kathleen (Cook) Uhl, Acting Director of the Office of Generic Drugs, will preside over the second panel, and we'll ask her to introduce herself when she arrives, but before the first panel members introduce themselves, I want to thank them, our presenters, and all of you in the audience for participating in this hearing today. We value your input, are grateful for your active

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engagement, and look forward to a very productive rest of the day.

Thank you.

Keith? Just introduce yourself.

MR. FLANAGAN: Again, I'm Keith Flanagan. I'm the Transition Lead for Policy in CDER's Office of Generic Drugs.

MS. KIM: I'm Nam Kim. I'm the Director of the Division of Regulatory Policy III in the Office of Regulatory Policy in CDER.

MR. YOUNG: I'm Johnny Young. I am the Acting Division Director for the Division of Filing Review in the Operations Office.

MS. GIAQUINTO: And I'm Elizabeth Giaquinto. I'm a Regulatory Counsel in the Office of Generic Drug Policy, Division of Policy Development.

MS. NGUYEN: So we'll now have our first presenter.

Priscilla?

MS. ZAWISLAK: Thank you, and thanks to FDA for allowing us to speak today. I'm here on

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behalf of the International Pharmaceutical Excipients Council, IPEC-Americas.

And the scope of what we would like to comment on today are some critical issues related to two of the draft guidances where active ingredients are included. One of them is the ANDA submissions refuse to receive standards, and the other is on the content and format of the ANDAs.

With respect to just general comments, there is confusion in the industry on FDA's policy on inactive ingredients, which needs to be clarified and communicated consistently in publications and guidance documents. The draft guidances that we've seen do not reflect historical practices both in industry and FDA in reviewing inactive ingredients, and the failure to clarify inactive ingredient issues prior to finalizing guidance documents is going to impact the GDUFA primary tenets of predictability and timeliness in the review process.

Further, FDA's increased emphasis on using the controlled correspondence prior to

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filing is resulting in increased delays in filing, and in the generics pharmaceutical industry they're not able to make high quality submissions and reduce the number of review cycles unless these inactive ingredient issues are adequately addressed.

With respect to the Refuse-to-receive Standards draft guidance, one of the biggest concerns that IPEC has had is on the acceptance of the family approach, and by that, we mean that materials that are compositionally similar and expected to have some toxicity, the same toxicity, profile, are considered excipient families. For example, they might differ in physical attributes, such as viscosity, but they are the same chemical entity, so the tox profile is similar.

Further, toxicology studies are typically conducted on representative material based on similarity across an entire family, not every grade within the family. There may be 10, 20, 50 grades within a product family, and these all have the same tox profile. This approach has

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been used for decades in the food and chemical industry. FDA CFSAN has typically used this approach for food additives, and the excipients are generally made in many cases in the same plants, the same process, as food additives. FDA CDER and OGD has also used this approach in the past until about 2011. So it's unclear to IPEC why OGD now thinks that this approach is not acceptable because this approach has been used for a very long time.

Also, with respect to the acceptance of the family approach, most of the inactive ingredients that are in drugs today have been safely used for over 50 years in a variety of uses, not just in pharmaceuticals but also as food additives and cosmetic ingredients. The expectation that data will be generated on each grade of the excipient is just not realistic. A lot of the data has been generated over the years, and to do new studies would be a major issue for a lot of companies.

There is also no evidence that using the

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family approach creates any significant patient safety risk. This also contradicts the IPEC-Americas work with FDA's OGD excipients working group on justifying the level of inactive ingredients by citing the level for a related excipient within the same family.

And then, finally, on the content format of the ANDA's draft guidance, this guidance refers to information included in the RTR to ensure submission of high quality ANDAs, but there are many issues in the RTR that should be clarified and resolved in regard to the inactive ingredients. This guidance also reiterates that information in the RTR should be followed without addressing the significant issues raised by IPEC and others. So due to our concerns over the comments previously provided which have not been acted on, IPEC-Americas will also be submitting more further detailed comments in writing after the hearing.

Thank you.

MS. NGUYEN: Thank you.

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Questions from the panel?

MR. FLANAGAN: So I understand policy concerns you raised concerning IID issues?

MS. ZAWISLAK: Mm-hmm.

MR. FLANAGAN: What has the experience of your members been with respect to the inactive ingredients database, and how could the functionality of that be improved to be more useful to you?

MS. ZAWISLAK: We've had an IPEC FDA OGD working group now for a couple of years, and we had provided some background information on some of the issues that caused our industry. I think we've made a lot of good progress. We have a draft question and answer document that is now going through I believe the Office of Policy to be issued that will address some of the more basic questions with a Phase II document, hopefully to follow that. But especially since the RTR draft guidance was published last year for comment, the number of issues that we, as excipient seller/manufacturers, are getting from our

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customers who are filing ANDAs has increased exponentially because there is so much confusion and the conflicting information that we're getting with regards to policy has been a lot of questions around that, and even some of the things that our working group has tentatively agreed on as to what we can communicate to industry, we're still now getting a lot of questions particularly after yesterday's publication, the final guidance, and we anticipate even more. So the policy issues have been a major impact on our organization.

MS. NGUYEN: Other questions from the panel?

(No audible response.)

MS. NGUYEN: Thank you.

Up next we have Steven Pressman.

MR. PRESSMAN: Thank you very much for having me here today. I appreciate the opportunity to speak. The area that I want to address today are the GDUFA fees, facility fees, associated with small business where the areas of certain businesses, I don't know that it was

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considered in a detailed matter of the impact that the fees have on small business. As far as the dollar volumes that these business do, the amount of ANDA business or generic drug business that these companies do, and in the area of companies that are just getting into the business and don't have any products on the market at such time, and without any negative references, but really at the mercy of whenever they get approval, they're just going to keep paying these annual fees.

So again in my discussions that I've had with the FDA over the past year or year and a half or so in regards to these fees were that there was representation from the industry when they came up with the guidance or when the guidance was thought of and created and that it has been put into law and therefore it cannot be changed. However, we just were notified in the past couple of weeks that the fees are now being increased. So it's quite surprising that the fees can be increased without any impact on the law, but there is no way to decrease them or to look at them to see about

reduction or reasserting how they need to be assessed against the different businesses.

Now, these fees may be a minor impact to some of the multibillion dollar businesses out there, but to a small business that's, let's say, under the $100 million range, it's a big impact, especially on some of these drugs we're waiting 2 to 3 years to get approvals. The dollars, the annual fees, add up when there are no other drugs in the marketplace that are currently being marketed.

And what this is doing, based on my discussions with other companies in the industry, it's discouraging competition and creating a barrier to entry, which I know the FDA is not looking to create a barrier to entry, but this is the impact that it's having. Perhaps one way to look at it would be if a company is under a certain threshold in generic drug volume out there, maybe the fees don't kick in until they hit a certain number of annual revenue.

So what's happening now are the major

companies just keep gaining market share and eliminating any competition from coming in, and it's increasing prices in the market place to the American public.

Also the issue of drug shortage comes into play with this type of situation, and again, as I said, drug price inflation.

So we now have 2 years of data on hand to see how the fees have been applied and the impact it's had on the Agency.

Sorry. I was thinking someone else was doing this, that's my mistake. So we can go back.

So, again, so as I said, the fees have been increased since their implementation. The impact to these larger companies out there is minor or no impact at all. And no offense to anyone in this room, but if I was a multibillion dollar company, I might want the fees to be $10 million a year so I will never have any competition coming against me.

And, again, as said, discouraging competition due to barrier of entry, creating an

oligopoly, innovation is being hampered, elimination of consumer generic drug choices, there are drug shortages, and the inflation of drug prices because the competition is being eliminated, and I know that that was not the purpose of implementing these fees, it was to get things through the process more quickly.

So the fees need to be looked at in more detail now that we have 2 years of data on hand. Company size should be a consideration. There are many other government agencies that use the size or dollar revenue of businesses to determine how the fees are going to be collected and how they are going to be utilized, and that will create a level playing field in the marketplace, and again, the ultimate recipient of this is going to be the American consumers who are paying for the drugs.

So, again, financial strength needs to be taken into consideration, and that seems to be the main theme here, and again what also needs to be looked at is, does a company have any ANDAs that have been approved with drugs in the market?

Because there is a big difference if it's going to take 3 years to get a drug approved and you're going to pay $750,000 in GDUFA fees, which may not have been even considered before the drug development process started versus just paying on an annual basis going forward.

And again the area that we referenced in the Federal Register.

Any questions?

MR. FLANAGAN: Yes. Thank you very much. The last slide proposes that if there were changes made in this space, that the financial strength of the company should be taken into consideration. Did you have any thoughts regarding how to do that? Would small companies self-certify as to their financial strength?

MR. PRESSMAN: Well, if, for an example -- and I'll just throw out round numbers for easiness sake -- let's say a company is only doing -- has no approvals per se. I don't think there should be any facility fee until they receive an approval because we're at the mercy, for lack of a

better term, of the FDA of whenever the FDA gives the approval, if they ever give the approval. So what is the purpose of paying an annual facility fee if we're not producing any drugs out of that facility and selling them to the public?

And as far as again any thoughts on how to certify, we all file tax returns. That's probably the simplest way of looking at it. There has to be some honor and integrity in the business world, and if, let's say, are you doing more than $10 million a year in generic drug business? No? Okay, maybe that needs to be the number. If you're doing less than $10 million, maybe you don't pay a facility fee, maybe you only pay one-tenth of a facility fee. Perhaps if you're doing a billion dollars of business and this could result in more income for the GDUFA program versus less income, if there was a sliding scale, maybe a company doing a billion dollars a year in generic drug business needs to be paying $2 million a year in fees versus only $250,000 in fees.

So it needs to be sat down obviously and

the discussion needs to take place in a more detailed manner than just in a 15-minute conversation, but I've gone and met with Congressman Waxman about this. He was actually shocked when I explained these things to him. I said, did anyone even think for one second to take into consideration how this is going to impact small business and again ultimately the American public that all you're doing is pushing out companies, you're not encouraging competition, you're stifling it? And he immediately said you're 100 percent right. It's now been into law, we don't know how to change it, but again if the fees are able to be changed upward, I know the fees can be changed downward.

So, again, I'm open to come out and meet with anybody at the FDA and have discussions. We just got a letter recently where -- and this was an argument that I had, we had ANDAs on file at our company before the fees were put into place, and we were told, oh, you're stopped right now. The process is stopped for you at the FDA until

you pay these fees. We said, well, they didn't exist before we made our submissions. We just got a letter now that we paid the fees, the clock was now rolled back for us to when we originally did the submissions, which is how it should have been. In other words, we should not have been told, "Oh, you haven't paid your fees." Well, the fees didn't exist when we submitted. I see a puzzled look on your face, so that's why I'm explaining. The fees weren't in place when we made the submissions, so why would we be now delayed a year when it was a policy that didn't exist before? And it's not a crime, but my analogy was, well, you can't be convicted of a crime that wasn't a crime when you did it and now you made it a law and, oh, by the way, you did this a year ago.

MR. FLANAGAN: Thank you. Thanks for clarifying it. Thanks for traveling all the way out here.

MR. PRESSMAN: My pleasure. Thank you.

MS. NGUYEN: Up next we have David Gaugh.

MR. GAUGH: Thank you. And thanks to the FDA and the panel for holding this open public hearing. We greatly appreciate it, and this is a very important topic for the generic drug industry.

So let me just give a little bit of background. So GPhA represents the manufacturers and distributors of generic pharmaceutical products; manufacturers and distributors of the bulk active chemical industry; and suppliers of other goods and services for the industry. Our manufacturers produce 90 percent of all pharmaceuticals dispensed in the United States, and their products are used in more than 3 billion prescriptions every year. And the generic products represent greater than -- and this slide says 84 percent, but we just have some new data out that that number has now jumped up to 86 percent of all prescriptions dispensed in the United States.

I show this slide just to show a representation of who we are and how much we

affect from a different company's standpoint. And GPhA has two different member organizations or categories I should say, not different organizations. One is a member, full member, which is this representation. These are 29 of these member companies. We also have 42 associate member companies that we represent. So upwards of 70 companies.

And I would also like to point out that this is an important enough issue to us today that we have 21 of those companies here in representation and 52 members of those companies. So very important topics for us and you'll have several later today at the open mic session providing some input and some clarity to some of this information that you provided us.

So first off, I do want you to know that GPhA and its member companies are very committed to GDUFA. We were at the table when GDUFA was negotiated, and, no, not everything got negotiated perfectly necessarily in GDUFA1, but there will be a GDUFA2 we would anticipate, and so we'll have

some clarity from some of the speakers we hear today and that we've heard at other times on what we can do to get to GDUFA2, but it is very important to us. It helps speed the process and enhancement of the approvals, and so we must equip the FDA to be able to do that. We know that and that's why the industry stepped up to $300 million a year roughly, or 1.5 billion over the course of the 5 years to provide those resources for the FDA to be able to do the things that they need to do to get to our ANDA and ANDA approvals in a more efficient and timely manner. But with that said, we do need to be working together to ensure that the millions of Americans and patients around the world continue to receive the timely access to safe, effective, and affordable drugs.

And I would like to point out just as a reminder that GDUFA has three key public health aims:

safety, access, and transparency. So I think those are words that we all know very well, but I don't want us to forget that those are three

very important tenets of GDUFA.

And as I go through some of these slides, they are going to be pretty high level slides, and the reason for that is that we're going to be providing much more granular detail as we get to comments into the open docket over the next several weeks, so we're pulling those together with our member companies.

As part of this slide deck -- and I'm not going to go through all of it because I only have 15 minutes, but it is a 25-slide deck, and there is some significant detail in what we're calling the appendix to the deck, so I'll refer to that a little bit. I'm not going to go through it now, but I do put that out for you to be able to reference as you go through this meeting and then also as you go through the open comments period in the coming days and weeks as you go through that process.

So the five guidances that you asked that we address and then any other guidance, I want to go through those rather quickly if we can

right now and address them.

So the first one is the ANDA submission content and format. And some points we wanted to bring to light is while each application is responsible for the best possible submission, there have been several historic barriers to fully address all explanations, especially for more complex products.

So as we move forward, and I know the FDA and OGD and the Policy Department within OGD are working rapidly to get policies in place to be able to address all this, we want to make sure that we're looking broadly across all activities and all areas from the ANDA submission standpoint.

Interactions and advice from FDA regarding specific ANDA issues typically have been too limited. Lack of pre-ANDA consultations, for example. Limited transparency has reduced predictability of applicants, and in many cases it is a one-way communication process we think that needs to be changed to definitely be a two-way communication process.

Inconsistencies among reviewers is another issue that we identify, so having a robust and a quality submission we absolutely agree and support. We also have to have robust processes on the FDA end where there is consistency among reviewers that are reviewing these robust quality submissions.

Retrospective applications of new criteria that have come into place since the date of the original submission, in some cases years afterwards, are taken into consideration while the ANDA has been sitting at the FDA for a number of months and even years before it's actually picked up, and so that needs to be taken into consideration as well.

Since the implementation of GDUFA, all informal contact between reviewers and applicants has ceased and has not been replaced with any meaningful alternative, results in major reduction in transparency, and so we would ask the FDA to review comments that we have provided before that was on August 11th for the content and format.

There is significant information in there that addresses many of the points and beyond of what I've just addressed.

And, finally, we would recommend that the Agency and GPhA collaborate to develop a guidance to address common quality issues related to submissions and reviewer consistency.

Next is controlled correspondence related to the generic drug development. GPhA has significant concerns regarding certain aspects of this draft guidance. To meet our shared aims of reducing the review cycles, FDA should encourage early engagement and feedback in advance of submissions in order to minimize FDA review timeframes and expedite patient access to generics.

What is the Agency's plan for reviewing and providing a response to controlled correspondence pending an Agency's response prior to Fiscal Year 2015?

Next is ANDA submissions, amendments, and easily correctable deficiencies. GPhA

believes a significant portion of the issues identified during the technical reviews can be classified as Easily Correctable Deficiencies, or ECDs, and communicated to applicants during the review process. Industry is able to respond to ECDs in a very short timeframe, on average 5 working days, upon receipt of the ECD, which can facilitate the review process and enhance efficiencies for both the Agency and for industry.

In the spirit of the goals letter, we request more opportunity to resolve questions via phone and mail, which is a more efficient process for both the Agency and industry resources to ensure timely transparency access to medications. And again I would point the FDA and the panel to the comments that GPhA provided on September 9th regarding this draft guidance.

Next is prior approval supplements under GDUFA. The draft guidance helps outline the Agency's implementation of GDUFA allowing greater predictability for industry and more timely review of supplements, clarification requested on changes

in GDUFA metrics when additions to amendments on PASs is requested, and providing valuable clarification on GMP inspection cycles, and risk-based approach. And again we ask that you refer to the GPhA full comments that were provided on September 9th of this year.

And then the fifth guidance that was provided in the docket to be addressed in this meeting we're not able to address at this point in time because that draft guidance just came out yesterday, so we're in the process of reading and reviewing rapidly, but we'll save that comment for our follow-up comments to the docket.

Some additional comments to guidance that we would like to make in addition to the five that were there, and one has already been addressed, but we would like to address it again because it's very important to the entire industry. The Inactive Ingredient Database, or IID, is an important area of need for us. The IID is a critical tool for the generic industry at large. The IID supports ANDAs and should be

complete, accurate, and transparent. The industry should have access to the MDI for all routes of administration. And again we ask that you refer to the GPhA member comments that were provided during the regulatory priorities open session that was in the May timeframe. And as a final note, we believe that providing further investment by the Agency to the IIDs should greatly reduce the number of control correspondences that you are getting currently and are somewhat being addressed in the new draft guidance.

Other additional policies. As stated in my opening comments, access is key to public health and an aim of GDUFA. Therefore communications and communications with applicants is important and should be provided, and priorities based on public health needs, target action dates, which have been introduced, and other related actions for ANDAs are not included in the cohort metrics, and we think that they should be.

A realistic plan based upon dedicated

resources to address the enormous backlog of ANDAs and prior approval supplements should be reviewed and addressed.

Continued meaningful interactions with industry while planning new guidances before enforcing those draft guidances would be greatly appreciated, and we think that would help both the Agency and the industry as we move forward.

Pre-ANDA consultation meetings and communications we believe is an important and a key component to moving forward with GDUFA.

Central repository or bulletin board announcements to industry to post-current thinking on ANDA data requirements, webinars, et cetera, so that there are no surprises on either side would be greatly appreciated.

Provide specific timeframes, for example, 60 days or similar, of controlled correspondence to answer suitability petitions. And more details, as I said before, will be provided in the open docket in the periods coming up in the next few weeks.

And then what other GDUFA implementation topics are needed for the guidance. Guidance clarifying QBD, QOS, requirements and expectations we think is an important guidance to review and consider. Industry needs a consistent approach of predictability.

To date, guidance documents have focused on processes rather than on what is quality for an ANDA submission for an agency. So as we've talked at different meetings and different time points, we talk about quality submissions, and we absolutely support that premise, but we want to know what is out there to help us define what is a quality submission, we don't think it's there. So again -- and I've said this before, but I think it's worth repeating, GPhA would like to recommend that the FDA collaborate with the industry to develop a guidance to address common quality issues on ANDA submissions.

Thank you.

MS. NGUYEN: Thank you.

(Beginning to clap.)

MS. NGUYEN: Questions from the panel?

MR. FLANAGAN: Someone started to clap.

(Laughter.)

MR. GAUGH: Just flies, I think they were trying to --

(Laughter.)

MR. FLANAGAN: So, Mr. Gaugh, thanks for all the detail, it's very helpful. Lots of potential areas of improvement you identified.

MR. GAUGH: Yes.

MR. FLANAGAN: When we're thinking through what the most urgent priorities should be and the next tranche of policy improvements that we make, how important is communications transparency? And I have a follow-up question.

MR. GAUGH: That would be number one.

MR. FLANAGAN: So some of the things that we've contemplated doing to improve communications transparency, sort of a transition management tool as we get into goal dates, are target action dates for pre-Year 3 submissions when we pick one up for review, assigning a target

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action date, and notifying the applicant with caveats of when we hope to take action on that submission so that folks know when something is under review.

In the ECD space, having more real time communications potentially working on pre-CR majors, and for the most commercially significant and most important from a public health perspective, first generics, which we'll discuss in much greater detail this afternoon, possibly offering some sort of -- providing some sort of mid-review status update, would all those things be helpful or any of them not a good idea?

MR. GAUGH: So I would answer with a caveat. Absolutely all of those would be helpful, and we do applaud that the FDA is moving in that direction, and there has been a lot of conversation back and forth over many months between GPhA and the FDA about getting to some of these points, and so we greatly appreciate that.

I think the thing that concerns us and my colleague who was up here just before talking

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about inspections and fees, that's completely understandable where he's coming from, but additionally to that and on the finish-fill dosage side, our companies -- and I hate to say it quite this way, but I'm going to, live and die by when they are going to get their ANDAs approved, and the decisions that they have to make to prepare for that, and that preparation is a bit of a runway. So you can't get approval today and launch tomorrow if you don't know that today is your approval date. So there needs to be some further clarity, and you're providing some of that through what you discussed but with a backlog of over 3,000, probably pushing more towards 3,200, 3,300, that's a significant number of products that are very important to the industry as well as to the American public and the health care system. And I know you have a priority review process in mind. We just know that there are products that are going to fall at the bottom end of that priority, and those companies still need clarity on where they are and what they can plan for the

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future. So we want to make sure that you're thinking about that and taking that into consideration.

Thank you.

MR. FLANAGAN: Thank you.

MS. NGUYEN: I have a question.

MR. GAUGH: Yes.

MS. NGUYEN: How much time do you need to prepare for product launch?

MR. GAUGH: So that's a great question and kind of a what if, I guess, but in the realm of 4 to 6 months at a minimum, and sometimes it's a full year. So depending upon the product that we're talking about, some products have API, for example, sources if there is only one source for that API, and that API is very expensive, for example, so it's not something that's, quote, held in inventory by either the finished dose company or by the API manufacturer. So giving them some lead time to produce their API, getting that API into the finished dosage manufacturing process, getting into the

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manufacturing process, all takes considerable time. So I would say expedited in best case scenario, everything sitting in inventory, probably 4 months, but it could take upwards of 12 or longer months depending upon the circumstances.

MS. NGUYEN: So in the case where you need a year to prepare for launch, and we provide you with a target action date of 4 months, that's not enough time.

MR. GAUGH: No, but it's clarity --

MS. NGUYEN: It's better than nothing.

MR. GAUGH: It's better than nothing, yes. And it's clarity that we have. And again we're making business decisions off of what we know. It's very hard to make business decisions off of what we don't know. So that's why we're looking for any type of information and a target action date of only 4 months, no, is not enough time, but some of the information that we provided for consideration for options for other communication time points would add to that timeframe.

MS. NGUYEN: And this vein of discussion, this is more focused on backlog and your one year to application since as we enter Year 3, you will have the clarity that you seek.

MR. GAUGH: Absolutely. That's in the metrics, yes. So this is absolutely backlog Year 1, Year 2, that we're talking about specifically.

MR. FLANAGAN: So actually I have a follow- up question which it may be hard for you to generalize. There may not be a tidy answer. But given the volume of the submissions -- right? -- and our obligation to move the freight along, it's probably not feasible in the immediate short term for each RPM to consult in depth with each applicant concerning the status of each submission, and like discern the best regulatory path forward. It's very resource intensive and requires a lot of experience and sophistication. Right? Are there individual data points that are more helpful than others when your member companies are trying to do the calculus on whether to launch a product? For example, anecdotally

we've heard from a lot of people that if the submission is doing well in chemistry, that they feel like that's disproportionately important, and I know it's hard to generalize, but to the extent that you can, could you please?

MR. GAUGH: Yes. And so you're right, it is hard to generalize, and I think probably the best option is to say that we have provided some comments to the FDA on communications and on various different example time points that could be used, and we'll add those comments to this docket as well, and we would refer you back to those.

MR. FLANAGAN: Very well. Thank you.

MR. GAUGH: Thank you.

MS. NGUYEN: Thank you.

It looks like next we have a 15-minute break. So I have let's reconvene at 10:05. I have 9:49. And as a reminder, the Wi-Fi network is "Guest Net," and the user name and password are "FDA," all caps.

(Break.)

MS. NGUYEN: I think we're going to get started in a minute, so if you could please find your seats.

Okay, thanks, everyone. During the break, the Acting Director of the Office of Generic Drugs arrived, Cook Uhl. Could you please introduce yourself?

DR. UHL: Am I on?

MS. NGUYEN: Yep.

DR. UHL: There's no color here to tell me I'm on or not.

MS. NGUYEN: You're always on.

DR. UHL: All right. Good morning. Kathleen Uhl, Acting Director of OGD. Thank you.

MS. NGUYEN: Thank you. So we'll just go right into the next set of presentations. Up next is Robert Vincent. Please when you start your presentation state your name and your affiliation.

MR. FLANAGAN: Is Marcie next?

MS. NGUYEN: Marcie is not going in the morning.

MR. VINCENT: Okay. Good morning. Thank you. I'm Rob Vincent, with Teva Pharmaceuticals USA. And I thank you for the opportunity to speak this morning and provide comments with regard to the GDUFA implementations.

The first thing I thought was important was we should note that there certainly have been already some benefits seen from the movement taken toward GDUFA for the industry. First off, the implementation of the complete response letter or concept has certainly been an improvement. It gives industry a concept of where each of the disciplines is at with regard to their review, how significant the issues may be within each of the disciplines as opposed to getting discipline-specific letters. The chemistry could be further along in biopharmaceutics or compliance or another area further behind depending on the given file, so this gives us a better picture of the overall application review.

The issuance of the multiple guidances that have come out regarding providing greater

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clarity on what the Agency expectation is for the original ANDAs and prior approval supplements certainly is a benefit. Any guidance is better than being left to shoot for a target that we can't see.

We also have seen more timely response on new post-approval submissions that are being sent to the Agency as well as the backlog submissions has certainly been getting addressed.

And also the early complete assessment reviews of DMFs certainly helped in terms of knowing that our DMFs are acceptable for review. The issues there have been taken care of, or at least are acceptable for -- excuse me, not taking care of -- they're essentially complete to allow full review, and we are certainly in anticipation of the 3-year metrics at greater clarity to review timing allows us to, as was said earlier, make better business plans with regard to our business of providing drugs to the consumer.

The challenges that we have had to date. For one, the timing of the guidances has been a

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little close to the start of Cohort 3, so there hasn't been a whole lot of time to comment or to prepare comments, although I also understand that this is not a small feat that we're attempting, there is a lot of work to be done, so it's not unexpected, but it's a little difficult to deal with multiple issuance of guidance one on top of the other.

And while the spirit of GDUFA was intended to increase transparency and predictability in the review process and timing, there have been a few little snags in there. Currently the communications from the PMs regarding applications has been less informative than it was even in the pre-GDUFA days. When you call for a status, any meaningful information is not provided, it's usually something more along the lines of, "It's in review. Call back in 3 months." A little difficult to like again make any business decisions based on the limited bit of information on that.

Another example is the controlled

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correspondence guidance expressly states you're not to check on status. Now, I understand when we get to the metric where you're expecting a response in 2 months, you don't want to take up that time in the 2-month period responding to various industries' requests on status, but when it gets beyond the metric date, technically there is nothing in the guidance that would allow you to call in to check status. It could effectively hang out in limbo.

And also pre-ANDA meeting requests.

This is something that requires a very timely feedback from the Agency, and yet they're being excluded from the controlled correspondence metric, which again is not encouraging or it's not helping with regard to the predictability and the review process or timing.

And then, of course, again just the controlled correspondence guidance, having excluded so many things from consideration under that guidance is causing concern because they were items that would have been considered controlled

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correspondence previously.

Now, my intent here really was not to provide specific comment on the guidances that have been issued so far but more so the questions that were raised by OGD to try to address some of those. So specific comments to the guidances we'll be issuing in writing to the docket.

But as far as, are there GDUFA implementation issues related to the five guidances that have not been addressed? And again I say that submissions that don't fall into the metric, and I'm of course now drawing a blank for the actual numbers, but say it's, what, 60 percent in the first year, I realize you're targeting as many as you can. Your goal is at least 60. Those that don't make it into the metric, though, there is no time limitation given. And I realize some of them are going to be complicated and take more time, but at some point they can't be allowed to fall into yet another backlog situation or recreate the backlog situation.

We're also looking for ideas to when the

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GDUFA guidances themselves are targeted to become official. The hope is that once they are official, they'll become more consistently applied and enforced across all of the application reviews and again gives us a better gauge as to how to predict issues with the Agency.

And again I'll stress that just the controlled correspondence guidance just seems to have removed far too many of the topics. The more complicated issues are the ones that really are the ones that we need Agency feedback on and your input, and those seem to be the ones that have been expressly removed from the controlled correspondence guidance.

Other GDUFA implementation topics that are in need of guidance, defining again -- and I'm going to hit on the controlled correspondence because that seems to be the one that we've had the biggest issue with, is defining a process and timing for those topics that have been excluded from controlled correspondence. If they are going to remain excluded from the controlled

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correspondence, then there needs to be a process by which we can handle these more complex issues, or those may require multiple discipline reviews. Just because they're difficult doesn't mean they should be allowed to be set aside.

And then, let's see, are there topics or issues related to generic drug development not directly affected or as a result of GDUFA that need development of guidance? And this one seems to keep coming up, the inactive ingredient database. The accuracy and completeness of the current database is lacking. There have been instances where we believe that ingredients had originally been in the database, had been removed either because the application reference had been withdrawn, but no indication as to whether it was withdrawn for reasons of safety. If it wasn't withdrawn from safety, could it or should it stay within the database? By addressing the issues with the inactive ingredient database, we believe it will actually decrease the number of controlled correspondences coming to the Agency, which will

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help you meet any of the metrics going forward and will allow you to better utilize your resources.

There also needs to be clarity with regard to single dose versus maximum daily dose issues with regard to inactive ingredients. We've heard tell that the bar to get an application accepted is, is your formulation acceptable from an inactive ingredients on a single unit that your max daily is a review issue? If your application gets issued -- or excuse me, accepted but then can ultimately become approvable, it kind of defeats the purpose. So not having that information at the time of filing certainly creates an issue for industry, and the addition of that information into the database I think would ease the process on both sides of the -- both for the Agency as well as for industry as well as dosage form interchangeability.

Can an ingredient that was used in a buckle formulation be used to justify a sublingual or a transmucosal, likely a topical in a transdermal, can they be interchangeable?

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Other topics will be, of course, complex drug products, LARs, rings, combination products where a drug and device are closely related or the device is regulating the actual delivery of the drug, not just quantity, but duration, abuse-deterrents, which I know there have been recent discussions with the agency concerning that particular topic.

And finally, one which I know is based in law, but Section 1113 of FDASIA was originally aimed to extend the Paragraph 4 applicants period to obtain a timely tentative approval without forfeiting the eligibility for exclusivity, but due to the language of the law, there is an ambiguity as to regarding what this length of period is. Is it 30, 36, or 40 months?

So whether it be some sort of guidance with regard to where that particular interpretation may be would certainly be helpful for the industry in determining -- in helping us to determine, are we still eligible? Have we forfeited? And it affects our business decisions

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in preparation for launch.
So that's the end of my presentation.
So thank you.
MS. NGUYEN: Thank you.
Questions?
MR. FLANAGAN: Thank you very much for the specificity. This is not a passive-aggressive request, I'm just really seeking clarity. On the complex drug product and combination drug product issues, have you all submitted comments to the science side of OGD as they formulate their regulatory science agenda? To what extent is this a science issue versus a policy issue? Can you comment on the interplay between science and policy on that bucket of tough issues?
MR. VINCENT: Oh, boy. That would be tough to do. You're right. With some of these topics, the complex, the device oriented, there is a very much of an intertwining of both the policy and the science. It's very difficult to separate the two issues.
With regard to have there been comments

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or questions or communications with the science staff within OGD, I believe there have been members, at least within my organization, that have reached out to have some of those discussions. Some of them have been favorable and productive, and others not as much as we would have liked. Certainly, again, any communication is better than radio silence, so we certainly welcome the communication and the opportunity.
As far as policy goes, on that one I'm going to have to defer, on that I'm not as familiar with where the company has taken a stance.
DR. UHL: Yeah. So can I just expand a little bit on what Keith is saying, and maybe I'll put words in your mouth. I apologize, Keith. It's usually the other way around, that the lawyer puts the words in somebody's mouth, but no worries here.
There is a process for regulatory science with GDUFA, there is a regulatory science program with money and grants and research, and

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there is -- I respect your opinion of that they're close and they're intertwined, however, if you don't have the scientific basis, it's hard to create the policy in certain circumstances, and it would be helpful for us for you to tease that out in the comments that you submit to the docket because what are the scientific gaps drives the GDUFA research program. What are the policy gaps? So are there particular guidances that you would like some clarity on or would like to see? That's fine. If there's a scientific gap, that's kind of a separate issue. So it's helpful for us to have them nuanced and teased out to assist us because this is multiple components moving forward in the entire program.
So to the extent that you could, Teva, or other companies could in their comments to the docket, it would help us tremendously.
MR. FLANAGAN: Because we already know that complex drug products are a regulatory challenge for us.
DR. UHL: Right.

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MR. FLANAGAN: The issue is which subissues and which types of products should we focus our regulatory -- your regulatory resources on.
DR. UHL: Right. Right. It will help us in a prioritization scheme because there are limitless numbers -- well, maybe not limitless numbers, but we do know there are a number of products for which there are no generics. There is a finite amount of resources that we have to create either the science base or the policy base for those. So it would be helpful to get that kind of input.
So can I follow up with a second type of question? Thank you.
Controlled correspondence, you used a considerable amount of your time talking about that. Could you expand, and if you don't feel comfortable now, but if you could in the docket, on what specific areas you feel were removed that should be added back in, and in addition, the aspect of a process to handle more complex issues.

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Can you expand on what that process could be, should be? What would that look like?
MR. VINCENT: I'll take the second part. Actually the second part may actually be a little easier only because it's proposals or ideas of ways you could potentially approach that topic.
The complex issues, complex products, or combination products, require more in-depth knowledge of the product and the process, something that you've got a handful of people in the industry perhaps that know of that technology. Some may or may not reside within the Agency. The only way to get that information is to have more open dialogue between industry and the Agency, perhaps as -- well, actually you've already started doing some of it with the abuse-deterrents recently, there have been some communications there. There are networks on the branded side, possibly a little easier than it does on the generic side. It's a little difficult for us to get together in a room with all of our -- you know, all of the generic industry and start

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talking about areas of science because some of it gets into what's proprietary and what's our business edge. So it's a little difficult to be forthcoming in a more public environment. There are perhaps an opportunity for more one-on-one meetings between select members of the industry and members of OGD. It would be helpful and it would allow that exchange of science information that wouldn't be as accessible in a public forum. I realize that's a little more resource intensive for the Agency, having to meet individually, but otherwise I don't know that you would be able to get that free flow of ideas on the science.
MS. NGUYEN: Does that answer all the questions?
(No audible response.)
MS. NGUYEN: Could you comment on why the flow of information challenges exist more in the generic sector than in the brand sector?
MR. VINCENT: Well, that's my assumption. I've never worked in the branded side, I'll say that right off the bat, but from my

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perspective, you've got multiple generic companies potentially targeting a specific branded product. And we're all trying to find ways of developing a product that is the same but depending on given development requirements, it may have to be just a little different for legal purposes. So we're all finding different ways of making it that little different, and we're certainly not wanting to share that information with our direct competitors.
MS. NGUYEN: That's helpful. thank you. I had another question. You had mentioned that status checks are not permitted. You talked about this in the context of the controlled correspondence guidance and suggested that status checks after a metric had passed might be appropriate.
MR. VINCENT: Right.
MS. NGUYEN: Was that comment intended for just the controls metrics or all metrics?
MR. VINCENT: Certainly it would be nice for all metrics. I understand that it would be

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better if the Agency's resources were spent reviewing instead of answering calls from industry, but whether it be an application, a controlled correspondence, a prior approval supplement, you've exceeded your goal date and you've not gotten your letter, so you're not going to be one of the applications or the supplements that make it within the GDUFA metric date.
Granted, industry has not been prohibited from getting a status check, but like I said earlier, the status checks that we've been getting haven't been exactly meaningful in helping us have any kind of business intelligence with regard to the review of those submissions. So if those applications or those supplements or those controlled correspondences that have not met the metric or the action date, if we could get a more meaningful correspondence on that, that might be a middle ground to work with. It's certainly one idea.
MS. NGUYEN: And by status check, you mean when we'll get you the answer, or what more

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information would you like?
MR. VINCENT: Timing would be helpful certainly. If there is any indication as to -- well, I'll go back several years when, you know, you might be able to get the comment that chemistry review is just wrapping up, we should have those -- we're hoping to have those questions issued within the next 2 weeks. Bioreview is done, they found it acceptable. That's something I didn't know before. So that gives me a better gauge as to how far my application is in the review process.
So it can be timing. It can be somewhat -- I realize you can't necessarily give the content of the comments, but even if there is a gauge as to whether it's major or minor ECD would certainly be helpful.
MS. NGUYEN: So at the start of your presentation, you were highlighting the benefit of receiving complete response letters --
MR. VINCENT: Right.
MS. NGUYEN: -- that gave you

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information on the different disciplines and the application status with respect to those reviews. Could you, following on your comments, tell us about the benefit, if any, of having information about pre-CR majors? Which would be not a complete response.
MR. VINCENT: Right. Uh --
MS. NGUYEN: Is this something you want us to work on?
MR. VINCENT: Right. Having information pre-CR majors. Good question. That one requires some thought.
MR. FLANAGAN: Is the answer that you get significant deficiencies more rapidly so you can start to attack them and move your submission forward more rapidly than you otherwise would have if you had to wait for the CR?
MR. VINCENT: Wait for the response, right.
MR. FLANAGAN: Can I ask a related -- we're over time, but --
MS. NGUYEN: May we have more time,

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Larry?
MR. FLANAGAN: It's an easy question. Don't worry.
UNIDENTIFIED MALE SPEAKER: Okay. Whew.
(Laughter.)
MR. FLANAGAN: So one of the challenges we have is the commitment letter only gives us credit towards a GDUFA action if it's a complete response; right? So that means the commitment letter calls for us to have all the reviews completed and to have inspections done and compliance status determination and everything you would want to know wrapped up in one package, and there's the benefit of getting a complete response, which you highlight. However, the downside is it involves delay as you wait for all the pieces to come together. Right?
MR. VINCENT: Right.
MR. FLANAGAN: We are thinking, as I had an exchange with Mr. Gaugh, we're thinking about ways that we can show some flexibility because of the downside of that commitment letter

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requirement. If we were doing things like issuing pre-CR majors and on occasion if the scientific and technical review is complete and we didn't have the inspection, how supportive do you think industry would be about giving us wiggle room on that because every time that we do something to try to be helpful, like I just described, it hurts us from a GDUFA perspective. We cannot take credit for that action.
What are your thoughts on that?
MS. NGUYEN: That was not a short question.
MR. FLANAGAN: It was pretty easy. It was like a softball question that you're supposed to say --
(Laughter.)
MR. VINCENT: Okay. To that, I'll ask the first part of the question: Would getting that forewarning of some of those major issues ahead of the CR major be helpful? Absolutely. And depending -- I'm sure there are certain circumstances where if the issue is major enough,

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a company could decide, you know what? I almost have to go back and redevelop the product to potentially do new studies. I don't have the resources to do that, and they could withdraw the application at that point, thereby not consuming your resources, continuing on in the reviews.

So when issues are major enough, I would support -- I would think that would certainly give industry a leg up, it gives us more time to respond, we'll be able to respond to the major when it comes in, in a more timely manner, and keep the whole review process going much better. So to that, I don't know that anyone would argue with getting information early, especially if it's major to the development.

The other one -- the other part of the question actually, I don't know, it's somewhat of the softball part of the question in that, how do you do it in such a way that you can relay that information and still get some sort of credit? Because it leads into the ultimate -- your credit only comes in at the complete response. Should

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there be consideration for that? Absolutely, especially when it runs into a situation where the application may eventually get withdrawn. There will be no issuance of a major letter, yet you've consumed some of your resources in identifying some of these issues. So my guess is you're going to have to go back in and look at the policy and potentially within GDUFA2 structure something in there that would allow for that communication during that initial review period, but it's something I think overall industry would certainly welcome.

MS. NGUYEN: Thank you. Any other comments from the panel?

(No audible response.)

MS. NGUYEN: So this is a general comment. You know, we've asked a couple of questions of you and of the room. If folks have comments, please submit them to the docket. The docket number for today is FDA-2014-N-1168. You may know that we had a regulatory science public hearing earlier this year. If your comments are

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more appropriate to be submitted to that docket, please do so or submit comments to both dockets. That way, we and the right folks can consider them as we develop our priorities for the coming year.

Thank you.

Next up is Marcie McClintic Coates, from Mylan.

MR. FLANAGAN: No.

MS. NGUYEN: No.

MR. FLANAGAN: It's Good Keith.

MS. NGUYEN: Good Keith. Oh, I'm sorry. I'm out of order. Did I just say "Good Keith" on the microphone?

(Laughter.)

MS. NGUYEN: Keith Webber. I'm sorry, I don't have my correct papers in front of me. So could you please state your affiliation?

DR. WEBBER: Yes. Keith Webber. I am affiliated with the generics industry in general, with Perrigo Company specifically. And I first want to start out with thanking the FDA for providing this venue for us to provide comments

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regarding recent GDUFA guidance documents as well as other topics which could use guidance.

And I want to start out, let's see, with figuring out how to use this. There we go.

I need to start out with some disclaimers. Number one, my comments at this public hearing are not meant to be a specific benefit to my company, Perrigo, but they are really intended to improve the general collaborative effort between the generic drug industry and the FDA to accelerate the development and approval of generic alternatives to brand name pharmaceuticals. And finally, I haven't received any specific compensation for this presentation.

Next on the agenda, I would like to say thanks to the FDA for the GDUFA invitation activities that you've gone through so far. Quarterly meetings with industry, representatives through GPhA, and other venues at the FDA we have greatly appreciated. Our publication of the FDA processes and procedures in your maps online is very helpful for us to understand how the FDA

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addresses issues and deals with applications. The publication of guidance for industry that we're talking about today I think has been very helpful to the industry.

The meeting with industry via the small business and industry assistance process I think has been appreciated by many as well. And then you've also held webinars to provide information to the Agency with regard to GDUFA implementation and other topics.

Today you presented us in a Federal Register Notice with two basic areas, one is on the draft guidances and other GDUFA issues that are related to the draft guidances, and then other topics that need guidance addressed. That's the main area I'm going to speak about. I have one slide which covers the afternoon on 180-day exclusivity. I'll probably throw that in this morning if I can, but will not speak this afternoon on that topic since it's really not the main thrust of my presentation.

Let me start out to say many of the

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comments I have in my presentation are much more specific than you've heard so far, and I hope that's appreciated. We will be submitting comments to the docket as well, but I thought that to hit on some really focused concepts with regard to or focused areas within the guidance document would be helpful.

Thumbs-up mean good, we like it. In the controlled correspondence related to generic drug development guidance document, the citizens petition is being preempted by controlled correspondence -- or preempting controlled correspondence, I said it wrong -- is understood. I mean, there are different requirements, different regulatory issues there.

I think generally the out-of-scope topics and out-of-scope entities that are described in that guidance document are presented with sufficient clarity, although there are some questions that we have in that regard. Number one, CC questions requiring policy development will not be answered. I can understand the

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complexity of policy development. I think we do have some concerns about how broadly that might be applied, not to have it be sort of a pat answer, "Oh, this is policy development, we're going to get out, we won't answer that."

So what falls under policy development, further guidance in that would be helpful. And requests that will not be considered controlled correspondence, bioequivalent study design requests, clinical protocol design requests. I understand those are fairly complicated or can be. But as was brought up by another speaker, what is the alternative there? If we can get meetings with OGD to discuss those issues in a timely manner, that I think would be sufficient and perhaps preferable to a controlled correspondence, but that depends on being able to get those meetings.

Let's see. Next, Number 3, inactive ingredients can be addressed in one controlled correspondence. Given the timelines, I can understand that. To some extent, however, it's likely to increase the number of controlled

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correspondence you receive. There is no reason that a manufacturer can't submit two controlled correspondence, one with three, one with one, if they have four questions. So it's not really going to do I think much in terms of workload other than increase it in terms of tracking those documents, getting responses sent out on those, et cetera. So that might be something to consider changing.

The FDA does not review proposed formulations that are not required to be Q1/Q2 equivalent. I know this has been a policy before. It does create some difficulties for the industry in that if a biowaiver is needed or dependent upon a Q1/Q2 formulation, then we really should be able to get an answer on those because that could result in a Refuse- to-receive, and a Q1/Q2 may not be required for approval, but if it's required for getting in the door, then we need to know that.

The FDA will not respond to status requests regarding pending controlled

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correspondences. I think if the GDUFA guideline deadline has passed, then we should be able to request a status update on that controlled correspondence because oftentimes things that are submitted in controlled correspondence are critical to decision in terms of product development.

This slide here addresses the RTR guidance which was actually just finalized yesterday, so I won't go into much more detail in this other than to say my first comment there regarding the five-day response time for filing deficiencies we felt was too short, but we do notice that that was up to 7 days, not quite the 10 we hoped for, but that's a good move in the right direction.

Now I'll move on to the ANDA content and format guidance. This is a thumbs-up. It's a very valuable and appreciated guidance document by industry. It provides a lot of good information. There are some very specific comments related to that document. First off, in Module 1,

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information is asked to demonstrate sameness to the RLD for inactive ingredients and that they don't impact safety and efficacy. It seems like in Module 1 it's asking for depth in detail of information that really I think would be better put into Module 2 and 3. So if that's not your intent, maybe further guidance in that area would be helpful.

In Module 2, the CTD summaries, thumbs-up. Question-based review I think is something that's been very successful and helpful.

Let's see. Now moving on to Module 3, drug substance section. Information on drug substance manufacturers ask for three different numbers, a Central File Number, the Facility Identifier Number, and the Data Universal Numbering System number. It seems like there are an awful lot of numbers there. Probably the FEI number and a DUNS number would be sufficient. We would request or suggest that some of the GDUFA IT funds be funneled toward developing electronic cross-referencing system that would eliminate some

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of the redundant facility identifiers.

In the section on reference standards, it says that reference to DMF alone is inadequate. I think we need more clarity there because oftentimes API manufacturers will have noncommercial reference standards that we don't know about as a finished dosage form manufacturer, and so it would be good to know where we can reference the DMF and where we can't.

Now, in regard to drug product in Module 3, the description for drug product, Section P1, states that manufacturers of colors and flavors can provide information directly to the reviewer. It would be good to know more specifically how that can be done within the ANDA submission. And information about the manufacturing of the drug product asks for complete testing description of the facilities performing their testing. We're not totally averse to redundancy in the application, but this information is also asked for in S4.2 and P5.2. So if it's possible to avoid redundancy, that would be helpful.

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P3.4 asks about controls of critical steps, and they ask for acceptance criteria and test results for exhibit batches. Does this include the same release testing that's requested in P5.1? We're saying it's sort of redundant for a potentially duplicative area.

The process validation information that's asked for in P3.5, our experience has been the process validation has historically been done post-approval and so we question, is this a change in policy asking for process validation pre-approval? So that's something we could use some more information on.

Some sections on Nodule 3 with regard to the regional information. Again, any information on components. It asks for certificates of analysis for drug substance lots and active ingredient lots, packaging component lots. And again this seems redundant with the information that's asked in other areas of the CTD, so that might be something else to look at in terms of revising the guidance.

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Moving on to the guidance on ANDA amendments and ECDs, Easily Correctable Deficiencies. This was one of the major comments we had, was regarding major amendments. It says that a request by the Agency for full-term stability data would be a major amendment. We find this to be problematic in that if full-term stability is needed, it may in and of itself require a 12-plus-month delay in getting that response to the Agency if that data has to be generated, which it would have to be generated. So adding 10 months to the review rather than a standard 3 months doesn't seem to be really justified by the length of time it takes to review stability data, it doesn't take that much extra time, and so it's an additional burden of up to 22 months to the Agency -- to the industry.

Moving to the guidance on prior approval supplements, we appreciate the documentation. CGMP inspection cycle for the different types of facilities. That's very good. And the acceptance of comparability protocols in lieu of multiple

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prior approval supplements is very much appreciated and is something we would like to see more of in the industry.

We could use more clarity on what types of changes can be bundled into a single prior approval supplement and which cannot. For example, if you're adding multiple API sources, is that okay? So we would like to know.

Other GDUFA implementation topics that need guidances. With regard to the post-complete response letter teleconferences that are part of the GDUFA goals letter, our experience has shown that interactive T-cons are usually not scheduled. Generally, written responses are issued to the industry. We do appreciate that we get clear timelines of when those responses will come, that's very helpful, however, the clarity of direct conversation is really lost in that process, and the written responses don't necessarily address the breadth and depth of the applicants' questions.

Finally, responding to a T-con request

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with written responses doesn't, we think, meet the GDUFA goal of interacting with the applicant, as we agreed to in the GDUFA goals letter.

Some other topics, very specific ones. Setting specifications, how that's done, we see variability there. Sampling plans are another area where we could use additional guidance, and safety of inactive ingredients. So specifically with setting specifications, we get comments, the specs are too wide, set them to the RLD data. If we set specs to the RLD, we go to (inaudible), test it, tighten it to match the process results. We matched ICH. Maybe we are asked to tighten to match the process. I think there is some focus on developing specifications that are clinically meaningful, and so this is an area where I think we really need to get better guidance.

Sampling plans, we've gotten variable questions from the Agency with regard to sampling plans, 3 samples per batch, 10 samples per batch, 5 samples per batch. There doesn't seem to be a clear policy there in terms of sampling plans.

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And then finally the safety of inactive ingredients. We would recommend that you consider a FDA approach and accept food standards for inactive ingredients in drugs. We've gotten comments that a component which is safe in foods at quite high levels is not acceptable in a drug, and that just doesn't quite make sense to the industry in general from a safety perspective. And as was said before, revising the IID to give maximum daily intake by route of administration would be very helpful. I won't go into any more details there.

With regard to this afternoon's session, I'll just say very quickly I'm sure the FDA will consider -- consideration of eligibility for 180-day exclusivity for specific products be published process. We think the process works well now, don't recommend any changes there. Disclosure of which companies are vying for exclusivity could well put companies at severe commercial disadvantage. That's one comment we have.

And again with what legal or regulatory

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mechanisms could facilitate resolving of 180-day exclusivities. The current criteria for identifying first generics seem to be sufficient, so we're okay with those. That's for my afternoon session.

And I thank you again very much for providing this venue and I'll take any questions you have.

MS. NGUYEN: Thank you, Keith. Questions.

MR. YOUNG: Keith, I have several questions focused on what seems to be the topic of the morning, the IID. So one of the points that you cover in your presentation, I don't recall if you verbalized it or not, but it is on a slide, has to do with the suggestion that because the IID is in need of repair, that essentially levels of inactive ingredients not be considered for filing purposes. Is there an alternative suggestion that would be used in lieu of that?

DR. WEBBER: I think that in lieu of that, it would be valuable to move that into a

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review issue and look at what documentation the company provides to justify the level of the inactive ingredient in their product and also to go back, as part of the review process, and ensure that the levels that are in the generic product are actually not in compliance with the levels that are currently in either foods, I would say, or in other drugs, because the IID, it's not always up to speed, and it also gives you numbers in percentages, which are hard to convert into maximum daily doses.

MR. YOUNG: And as a follow-up to that, with respect to -- and I've heard it mentioned several other times this morning, again with regard to the IID, it seems that having the MDI as a listing would be helpful. Are there other types of categories of information that industry feel would be useful to be incorporated into the IID where possible?

DR. WEBBER: If possible, I think it might be valuable to have, in addition to the maximum daily dosage, some information with regard

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to a differential between single dose or short-term acute treatment drugs versus chronic administered drugs that might be given for a lifetime.

MR. YOUNG: And my final question. When it's suggested that food levels or a food level statement could be used in lieu of a particular ID level for justification purposes, is there consideration being given to whether or not the length of administration is playing into that sort of suggestion; in other words, acute versus chronic use?

DR. WEBBER: Well, most foods are administered chronically.

(Laughter.)

DR. WEBBER: So I've really given a lot of thought to that, whereas drugs are generally given for less time, usually until the issue resolves or the illness resolves, and so I think using the food safety standards for food additives would be a worst case scenario compared to drugs.

MR. YOUNG: Thank you.

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DR. WEBBER: Thank you.

MS. NGUYEN: Go ahead.

MS. GIAQUINTO: I believe you gave QBR a thumbs-up in your presentation. Is there anything we can be doing to improve how widely used QBR is in applications currently submitted? Are there other examples we should be putting up on our website or QOS model summaries?

DR. WEBBER: I'm not really sure about that. I think that the Agency has done a fairly good job of providing guidance on use of QBR. I know there is a revised list of questions that are out for consideration, not for implementation as yet. I think that it's not clear, I think, to many in the industry how much the QOS is actually used as part of the review process, so that might be something that would be worth perhaps open public discussion as well.

MS. GIAQUINTO: Thank you.

DR. UHL: Thanks, Keith. I wonder if you could just give a little bit more clarification on the issue related to the Q1/Q2

and biowaivers.
DR. WEBBER: Sure.
DR. UHL: So is it that industry wants to be able to submit those as controls, so they basically get a response that blesses the application for filing, or what exactly is the ask?
DR. WEBBER: Yes. I think the ask is that if Q1/Q2 is required to get a biowaiver for a particular product, then we have the confidence and assurance that if we submit an application that is Q1/Q2 and we submit a biowaiver, that we would not be refused to file because we hadn't done a biostudy.
DR. UHL: Okay. Thanks.
MS. NGUYEN: I have a few detailed questions. You had mentioned in the ANDA content and format guidance that there were a couple of areas of possible redundancy.
DR. WEBBER: Mm-hmm.
MS. NGUYEN: Did you have for the three -- or for the two that you flagged, did you have a

recommendation as to whether the information on drug product manufacturers should go in 32P3 or 32P52?
DR. WEBBER: Let's see, let me go back to that one real quick if I can. Is this a slide?
MS. NGUYEN: No. It starts with "Specific Comments Continued." That one.
DR. WEBBER: This one.
MS. NGUYEN: No. I'm sorry. It's the next one right after that.
DR. WEBBER: Okay. Testing description. I think that -- I haven't really given a lot of thought to where it should go. I would suggest that it perhaps go in the earlier section, which is P3 and then -- because that's focused more on the description of the facilities that are performing new tests and put the actual tests and description of tests themselves into the other sections, just off the top of my head, that's what I would do.
MS. NGUYEN: Okay. Thank you. On the next slide, information on components.

DR. WEBBER: Mm-hmm.
MS. NGUYEN: Should that go into P2 or S404 or any of the other ones? It looks like P2 might capture in one place information that is asked for in several other sections, so the CTD.
DR. WEBBER: Yes. And I would say that the certificates of analysis should probably go not in the P2 section, that's my own belief, that the P2 is more of an overview summary of the product development, not really delving into as much detail and specifics as perhaps a certificate of analysis would.
MS. NGUYEN: Okay. Thank you. And I had a clarifying question. It's actually three slides from that one, my slide 14, but on the post-CR letter teleconference.
DR. WEBBER: Mm-hmm.
MS. NGUYEN: So right now we give you the opportunity to request a teleconference. Could you tell me what happens so that it ends up that we don't have one getting scheduled?
DR. WEBBER: Well, generally we follow

out a procedure of submitting a request for a post-complete response teleconference and provide the information that we are looking for answers to. It's a learning experience for all in industry of how to do this. So in some cases we provide a very abbreviated description of what we need information on, and without going into huge detail, if we get a response back that, well, we're not going to have a meeting, but we will send you written responses, then the written responses may only address superficially what we were requesting information about without really delving into the information that we would provide in a meeting and a discussion that would occur in a meeting. Then we get a response back from the Agency that says we're going to send written responses and we're going to do it by this date, which is, like I said, very nice to get a specific date for those. And then usually we get the responses by that date and we move forward from there with our best guess of what we should do based on that information.

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MS. NGUYEN: But you would like more often to have a conversation about the deficiencies, not just the questions that you identify as needing clarity.

DR. WEBBER: No, well, not generally about the deficiencies, but we would like to delve more deeply into the reasoning and thought processes that the Agency had with asking that question and then be able to discuss with the Agency our reasoning for why this may be -- how it should be addressed, for instance, what information we might have that would address it in a particular way and not just generally to meet and discuss about the overall deficiencies, but we still continue to be very specific.

The result of that I think is going to be that there will be -- if we continue to not get meetings, the meeting requests are going to get much, much more detailed, asking very, very specific questions, get very long and become actually a review document in and of themselves.

MR. FLANAGAN: So it's just the

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substantive issues, you would also seek or recommend additional clarity regarding the process there; right?

DR. WEBBER: You mean in this particular venue or in --

MR. FLANAGAN: Well, on how the process will unfold post-CR.

DR. WEBBER: What I really am looking for is that we would have -- more often than not, we would have a meeting with the Agency to discuss the post -- teleconference with the Agency to discuss the post-CRL questions rather than getting written responses.

MR. FLANAGAN: Okay.

DR. UHL: And, Keith, to clarify on that because it sounds to me like what you're saying is you really want to have an in-depth discussion and conversation. So can you expand on that or elaborate on that given the context of the commitment letter that refers to these post-CR meetings as 30-minute teleconferences?

DR. WEBBER: I think that we still

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believe they could be 30-minute teleconferences, but I think that the face-to-face interaction, not face-to-face, but telephone-to-telephone interaction, with the Agency is much more productive to talk with the scientists directly than it is to just throw something in terms of questions to the Agency, they throw back answers, and we move on from there.

DR. UHL: Okay. Thanks.

MS. NGUYEN: I don't know if you can give a general answer to this question, but in this teleconference, do you find that there are times when FDA has misunderstood the content of the information provided in the application and you would like to use the teleconference as an opportunity to clarify as opposed to seek more information on how to respond to the deficiency?

DR. WEBBER: Well --

MS. NGUYEN: Are you seeking to change our mind?

(Laughter.)

DR. WEBBER: In some cases, yes. In

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some cases, yes. There have been instances where we have questioned a CR comment and the Agency has gone back, looked at it, and said, "You're right, we're going to take that out of the letter." And so sometimes we're successful at changing the mind. Sometimes it is just a matter of determining or finding out how we should address that question. If there is a particular issue related to a tox study, let's say, we could provide within our request a description of the tox study we plan to do. We could have a 30-minute teleconference that says, okay, the Agency says, yeah, we like this, we like that, we don't like this, and getting that type of response, which requires really an interaction in a single response from the Agency really isn't sufficient to efficiently and quickly resolve the issue and move us toward product on the market.

MS. NGUYEN: Thank you. Are there other questions from the panel?

DR. UHL: So just for my clarification on this then. So essentially these post-CR

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meetings are you looking for something that's more than just a teleconference to discuss the content of the CR letter.

DR. WEBBER: We're looking for a teleconference to discuss specific questions that are in the CR letter and get clear direction and understanding of how to move forward with our responses.

DR. UHL: Okay. Thank you.

MS. NGUYEN: Thank you. Other questions?

(No audible response.)

MS. NGUYEN: Okay. Thank you.

DR. WEBBER: Thank you very much.

MS. NGUYEN: I think that concludes the morning presentations, so we will now move into the open comment session. I think, is it just three? We have three presenters, so I think there is time to allow each commenter to speak for 10 minutes.

Our first commenter is Candis Edwards.

MS. EDWARDS: Good morning. Candis

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Edwards from Amneal Pharmaceuticals. I didn't know I had 10 minutes, so I can slow down a little bit, I won't talk as fast.

MS. NGUYEN: Or we can ask you more questions.

MS. EDWARDS: Yeah. Absolutely.

So I wanted to address a couple of issues since I had a short period of time. We will provide more detailed comments to the docket, but I wanted to address controlled correspondences specifically. The recent practices in OGD's modernization of the controlled correspondence system has resulted in controlled correspondences being closed at the Agency's discretion without providing an answer to the questions posed since the ANDA itself was already submitted, and what was happening was that the CC was pending in the queue for an extended period of time which actually surpassed the development of the ANDA from the firm's perspective, so the ANDA was filed. And this results in an at-risk filing for the ANDA holder because we don't have the answer.

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We really feel that the CC should still be addressed by the Agency rather than close out so that the sponsor has an opportunity to withdraw the ANDA if appropriate, thereby you would actually avoid unnecessary expenditure of OGD review resources. So we would ask that you continue or at least have a discussion before they're arbitrarily closed out.

Also, with regard to controlled correspondence, it's recommended that the Agency issue a guidance for OGD/sponsor meetings to address ANDA development issues. And I'll compare it to the type A, B, and C meetings under PDUFA, understanding that the differences are for generics there are many companies going after one product, and on the PDUFA side you have one company, usually one product, but there might be something that we can gain from that process.

The meetings I believe would minimize the need for controlled correspondence because the controlled correspondence issue addresses one -- excuse me, the controlled correspondence program

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addresses one issue at a time, and sometimes the answers are taken out of context of the entire development program, and so it results in the inability of the ANDA sponsor to proceed in a timely manner with product development. So what am I saying? I've got multiple controlled correspondences on one product where if I had an opportunity to have a predevelopment meeting, I would get answers to all of the questions that I need, so I'm very much in favor of more meetings in order to address these issues.

With regard to the Easily Correctible Deficiency guidance, I have two comments. OGD's current practice involves attempting to identify a non-exhaustive list of examples of ECDs, and it sort of reminds me of when we were back in the SUPAC days and we were trying to figure out what goes here and what doesn't as opposed to looking at the principle of true risk assessment and actually being able to categorize the risks associated with a certain change, and using that information then to make the decision as to what

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the appropriate filing mechanism was. So it seems that we're sort of taking that same approach with ECDs. And Amneal recommends that there also be a possibility that OGD can base a classification of a deficiency as an ECD on a sponsor's ability to respond to the deficiency with some predetermined time period, for example, 10 days, because I think the key, the real key, is once you identified a deficiency, how long is it going to take for the sponsor to get information back to you as opposed to which actual category it falls in. So that would be a recommendation, to include that.

I also would recommend that OGD adapt practices which are utilized during NDA review whereby a project manager is authorized to engage in a telephone discussion with a sponsor in order to obtain rapid clarification on uncomplicated review questions, which if resolved, are then usually followed up by some formal correspondence to that, and the file within some agreed upon timeframe. That might also move the process along a little quicker.

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My last comment, it deals with a definition of first generics. I know that this is a topic that will be addressed in the afternoon, but I'll still take this opportunity, unless you prefer me to hold this till the afternoon because I didn't realize they were separated out.

MS. NGUYEN: If you could hold it till the afternoon, we'll have a different panel --

MS. EDWARDS: Okay. Just sign up and then I'll come back up again.

MS. NGUYEN: Please. We'll have a separate panel that will --

MS. EDWARDS: Okay. So I'll hold off on the last comment.

MS. NGUYEN: Thank you.

MR. FLANAGAN: You wanted to leave, didn't you?

MS. EDWARDS: Pardon me?

MR. FLANAGAN: You wanted to leave us.

(Laughter.)

MS. EDWARDS: No, I'm here for the day. This is my lifeblood. So those are the two

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comments I wanted to give.

MS. NGUYEN: Thank you, Candis.

MS. EDWARDS: Okay.

MS. NGUYEN: Questions?

DR. UHL: Thanks, Candis for those comments. Could you clarify a little bit on your first issue about closing out a control when an application is submitted? That's on a company-specific basis?

MS. EDWARDS: Mm-hmm.

DR. UHL: So the company submitted the control, the same company decided to submit the application --

MS. EDWARDS: Before getting it.

DR. UHL: Before the control was closed.

MS. EDWARDS: Right.

DR. UHL: So help me understand why you would still want that control answered while the application is in-house under review.

MS. EDWARDS: Because for the company it's an at-risk file in, there was a question that I had to understand how to proceed. So since I

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didn't get an answer in a time that was in line with the product development, I went ahead and used my best judgment and did what I thought hopefully I would get an answer of yes to.

DR. UHL: Right.

MS. EDWARDS: And that's included in the file. So either you're going to look at it right then when you have it in front of you or you're going to put it down and you're going to come back to it when you do either acceptance to file or review of the ANDA. It's still going to have to be addressed. So I think since it's already made its way up in the queue, it's beneficial, since you've utilized that time, to just go ahead and address the issue. I may withdraw it and the application may go away, thereby saving review time subsequently.

MR. FLANAGAN: But doesn't the answer to the outstanding question come in the CR?

MS. EDWARDS: Yes, it does, but I could have withdrawn it. Do you understand what I'm saying? You might have said -- and I don't want

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to use examples, it's hard to do this without examples, but the answer might have been your proposal is not acceptable. Well, if I knew that was the answer, I would not have proceeded in that direction in my development, and I would not have filed the ANDA, then I would have taken an alternative approach that would have been acceptable. So it's the value -- I think the whole concept here is the value of getting the answers up front. The more that we can get clarification and get our answers up front to our issues, the less resources are going to be utilized by OGD, and these applications are going to start to sail through the system, and I think that's really what I'm going to.

DR. UHL: So you would say that if you had a control that wasn't answered and you took the risk essentially -- right?

MS. EDWARDS: Right.

DR. UHL: -- of submitting an application, and somewhere during that -- so we're assuming you would submit after October 1, and

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there would be GDUFA goal dates, so sometime in there you would get a response to that control.

MS. EDWARDS: Mm-hmm.

DR. UHL: The applicant would make a decision potentially to withdraw that application.

MS. EDWARDS: Right, potentially.

DR. UHL: So I would posit the argument, though, that once the application comes in, we're investing resources, the whole time to be moving that through the GDUFA chain.

MS. EDWARDS: Right.

DR. UHL: We would answer the control in the context of the filing review, the scientific review, et cetera. You're -- I'm just getting --

MS. EDWARDS: Right.

DR. UHL: You don't want it then.

MS. EDWARDS: The only thing is that the resources that you're going to use in the review process are much more intensive than the resources you're going to use in the controlled correspondence. And I think that once we start to approach goal dates for responses to control

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correspondence, I think these situations will go away because the company won't have to wait 9 months or a year for an answer. So really what we're probably having this (inaudible) situation, because of the backlog, because of backlog in applications, as well as backlog in controlled correspondences, so that is also contributing.

So I guess what I'm saying is at least that there would be a dialogue before it was arbitrarily closed out to speak with the sponsors and say, "Hey, would it be beneficial to answer this? I know you filed." You know, there is another situation where the ANDA may be open-ended, maybe a controlled correspondence in response to a complete response. So there are a couple of situations, but again it's just been arbitrarily closed with no interaction or discussion. I think that's the main point.

DR. UHL: So I'm just trying to seek clarification because in my mind I'm hearing mixed, this is kind of pre-GDUFA without goal dates, which was past practice, this is --

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MS. EDWARDS: Yeah. Right.

DR. UHL: So you're still making the recommendation that effective October 1, when controls come in with goal dates and there are applications, your recommendation is all those controls get closed out with a response irrespective of whether or not an application has been submitted related to that issue.

MS. EDWARDS: Yes. You're talking post-goal date. I think the question is --

DR. UHL: We're only 14 days to goal date --

MS. EDWARDS: I know.

(Laughter.)

DR. UHL: -- so unless you're submitting a whole bunch today --

MS. EDWARDS: No.

DR. UHL: -- we're really darn close to that.

MS. EDWARDS: What I'm saying is you're asking me to draw this line in the sand. It's probably hard now because I think the situation

I'm describing is relevant because there are a lot of controlled correspondences in the queue that have been there for a long time. It will improve. This is only the first year that you're going to have to face your metrics and achieve your goals. As you progress, it will improve, and this situation will probably not exist.

DR. UHL: Okay. Thanks for that clarity.

MS. EDWARDS: Okay.

MS. NGUYEN: I just have a quick question. Could you -- you had mentioned that we -- in the current amendments guidance, we have provided a list of examples of Easily Correctible Deficiencies, and you suggest that we classify those based on the time it would take for a company to respond to those deficiencies. I think we heard in other presentations today that there is significant variation in financial resources among companies. Could you pose a timeframe that would be equitable for small companies and large?

MS. EDWARDS: Okay. I'm not going to do

that here, but I will do that in my written comments.

MS. NGUYEN: Thank you.

MS. EDWARDS: That's a good point and it's something that I did think about, so since I only had 5 minutes, I will do it myself.

MS. NGUYEN: Thank you very much.

MS. EDWARDS: Okay.

MS. NGUYEN: Other questions? I think we're over time.

MS. EDWARDS: Okay. Thank you.

MS. NGUYEN: Thank you, Candis.

Next up we have Satish.

MR. PEJAVER: My questions are related more --

MS. NGUYEN: I'm sorry. Could you state your name and affiliation?

MR. PEJAVER: Yes. Satish Pejaver, from InnoPharma.

MS. NGUYEN: Thank you.

MR. PEJAVER: Again, my questions are related more towards timelines in terms of how we

get feedback from FDA. And I just want to take some specific examples. These are based on our experiences at InnoPharma. The first one I want to talk about is like CBE-30. So CBE-30, you know, there is a timeline defined by the nomenclature itself that you need to get some kind of feedback from FDA possibly within 30 days. So there have been instances where we have one instance where we filed a CBE-30 and we didn't get a response within the 30 days, but we met all the CBE-30 requirements, but then after 9 months we got rejection of the CBE-30 and the conversion of a CBE-30 to a PAS. So I think from a business perspective, I mean, that can be disastrous because you're following the guidelines and it says CBE-30, and then if you don't get a response in 30 days, you say go ahead and market the product.

So I think that's something that again is just a comment. I don't know how it needs to be addressed, but definitely if there is an issue with a CBE-30 submission, then we should get

feedback, "Hold," or, "We are reviewing it," or, "It's fine." So some kind of feedback. I think that puts us in jeopardy in terms of how we operate as a company.

The other timely aspect -- and I think many people in this room will have the same comment -- is about acceptance of the ANDA. I mean, before the GDUFA, we had some sense on when we would get an acceptance, and it's typically in a 2-month timeframe. Now it varies all over the place. I mean, I do understand we're going through a transition scenario, but the timelines are very -- I mean, it can vary. We have one which is we haven't gotten a response for 18 months. So it's very difficult again from a business perspective, and we find quality and we don't get a response for 18 months, and there is no open communication in terms of what's happening.

So I think, again, my question or comment is, is there metrics for acceptance of ANDAs? And I think there should be. And it's

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something that we are battling with right now. I would like to get some feedback on that if possible today.

The other thing is on controlled correspondence right now, post-October 1st, we have 70-percent response within 4 months. So I think the clarification there that we're looking for is, what is a 70-percent comprised of? Like how is 70-percent defined? Is there some kind of Tier 1/Tier 2 criteria which would fall under the 70 percent? And I think some of the simpler things, again, with, let's say, Q1/Q2, people have raised that question before. So Q1/Q2, I think it can be easy to respond before the timeline. Before the pre-GDUFA days it was 6 months, not 6 months, actually 2 months, and now I don't get a feel for when we'll get a response on that. It again varies. It's never within 2 months, but it varies quite a bit. So some kind of clarification on that, as particularly Q1/Q2, because that defines how we are going through our development process and how we need to develop the product

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there, so it's very, very important criteria from a business perspective as well.

So the other question on controlled correspondence also in the pending controlled correspondence is, how are they going to be handled post-October 1st? So anything that's submitted October 1st falls into the 70-percent metrics and the 4-month metrics, but what about the pending controlled correspondence? Is there some clarification, some guidance, on how that's going to be handled?

A couple of other comments that I have, new controlled correspondence guidance conflicts with the commitment letter from FDA. Just one example would be --

MR. FLANAGAN: Conflicts with what?

MR. PEJAVER: With the commitment letter. So, for example, the commitment for clinical division feedback said you require one additional month for that feedback to come in. As for the new controlled correspondence guidance, anything enrolled in clinical does not fall into

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the metrics. So that actually doesn't jive.

The other comment I have is on stability guidelines and the Q1A-E document, which is final. There are some clarifications that are required, you know, especially for sterile injection, injectables, secondary packaging of injectables, powder fills. So again some clarification on these pieces of information we can definitely put into the docket. How is that typically handled by FDA?

So this is a list of comments that I had, and I guess if you need any more clarification, I can definitely provide that.

MR. FLANAGAN: Thank you very much for all those comments. My colleagues are going to remind me that I'm not really supposed to answer questions. Right? You raised a laundry list of comments. Please do submit all of those to the docket because I was writing furiously, but you had a significant volume of them.

MR. PEJAVER: Sure.

MR. FLANAGAN: I do have a couple

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comments, although my colleagues may join me. The first thing you raised was CBE-30s and the delayed response. I was a co-presenter yesterday at an FDA PQRI conference with Lawrence Yu, who is the Acting Director of OPS, and Susan Rosencrance, who is a senior leader in the CMC organization, and they presented a lot of data concerning CMC's aggressive attack on the supplement backlog, which I think actually Dr. Webber mentioned as well. So we're aware of the significant volume of work we have in that space and are making good progress attacking it. I would also note that only PASs have metric goals pursuant to GDUFA, but we still want to attack the CBEs.

MR. PEJAVER: Mm-hmm.

MR. FLANAGAN: On the filing issues -- and Johnny may wish to supplement or correct my remarks -- but we're aware of those issues as well. Pursuant to GDUFA, the clock starts to tick at submission, not when we figure out what we want to do with the submission, and we issued the finalized RTR guidance yesterday and concurrently

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issued a draft guidance concerning RTR for basically failure to explain, failure to how --

MS. NGUYEN: Provide information on purities.

MR. FLANAGAN: Thank you. And that's going to be the -- that's maybe the first in a series of draft guidances because there are recurring discipline-specific filing rather than review issues that we should RTR for when people send us stuff that we shouldn't accept that penalizes everyone else who is sending in a quality submission, and we should be making improvements to RTR over time, it's just that we want to do it in a manner consistent with our procedural obligations and in a way that it's transparent and gives industry an opportunity to comment.

And the last thing that I would touch on is a common question. You asked, okay, so assume that the metric for Year 3 for controls is 70 percent within 4 months. How do you decide which goes in the 70 percent and which goes in the 30

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percent? We don't have like a clever master plan to divide them into buckets we're going to try and hit and buckets we're on purpose going to miss. We're going to try to get 100 percent.

MR. PEJAVER: Sure.

MR. FLANAGAN: So that's the answer.

DR. UHL: So I appreciate your request of us that you get feedback today and leave here. I want to kind of jump in where Keith was because I'm thinking that Part 15 hearings are not something that the generic industry is necessarily very familiar with or something that they engage the Agency with frequently, and so the purpose of a Part 15 hearing is for us to hear, to listen, and to ask stakeholders for clarification on particular issues. And we've had several of these and we will continue to have public hearings and Part 15 hearings to allow us to get feedback from our stakeholders to clarify what we are doing internally. Okay. So I understand your need. I just want to set your expectations that that's not the purpose of today. And I'm sure you got some

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clarity from Keith.

I would like a bit of clarification on one of the things that you mentioned, was the acceptance criteria. You're talking about a filing decision or an approval decision?

MR. PEJAVER: A filing decision.

DR. UHL: A filing decision.

MR. PEJAVER: Yeah.

DR. UHL: Thank you. I just wanted to be clear that that's what you were meaning. Thank you.

MR. PEJAVER: Just one last comment again on ANDAs that have been submitted and have not been accepted yet, and some clarification on how those ANDAs are going to be handled because they don't fall under the GDUFA metrics. That's what I understand. So some clarification on that would be great as well.

Thank you very much.

MS. NGUYEN: I have a question for you. Thank you for your comments. You had mentioned -- you started your comments with the discussion

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about the CBE-30s that were denied to a prior approval supplement 9 months later. Do you have the clarity that you need to know whether to submit a prior approval supplement or a CBE-30?

MR. PEJAVER: There are guidelines for CBE-30. In some cases, there are some grey areas, but when it's somewhat clear-cut as for the guidelines, we assume that if FDA does not come back in 30 days, that it meets the requirements. It would be great to get feedback within the 30 days no matter what because in some cases there are some grey areas where FDA may decide to be more conservative or they understand the position of the industry and they grant the CBE-30, but without any dialogue, it's very difficult.

In this particular case, we followed the guidelines. So I think the haziness on the submission was somewhat limited, was pretty clear-cut, so it was a surprise to get the feedback 9 months later.

MS. NGUYEN: I would like, if you're able to submit comments to the docket, more

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information on some of those gray areas. We would like fewer gray areas over time so that there was more clarity as to how you should proceed with change.

MR. PEJAVER: Okay.

MS. NGUYEN: Thank you.

MR. PEJAVER: Okay. Thank you.

MS. NGUYEN: Anything else from the panel members?

(No audible response.)

MS. NGUYEN: And our last commenter for this morning?

MR. ROTH: Hi. I'm Gil Roth, the President of the Pharma and BioPharma Outsourcing Association. I want to thank you for the opportunity to speak today. I founded the association earlier this year to help organize and represent contract manufacturers and contract development manufacturing organizations, we'll call them CMOs for the sake of this comment session. This came after 14 years of covering the industry as the editor of Contract Pharma

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Magazine.

And our main area of interest at this hearing is facility fees for final dosage for manufacturers. I was gratified to hear Mr. Pressman's presentation earlier about the small business issues related to those fees, and we're coming from somewhat different directions, but I think we have some of the same goals. Several of our members are interested in a small business exemption under GDUFA as well as perhaps a tiered structure for CMOs as opposed to companies that are manufacturing generics for themselves. It's a very different business being a contract manufacturer than being a pharma company or a generic company operating under much different margins.

Within the field, we have some companies that might have a single generic client that they do one week of work for per year, and yet they face the same facility fee that a major, major generic facility is going to pay. Not all contracts are made to accommodate that sort of fee

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being transferred, and it's a very anecdotal industry, but I have anecdotes of companies that have told me they're essentially looking to get out of manufacturing generics because these fees make it unprofitable for them as well as for the client company they're working with.

Now, one of our members has helped -- well, a congressman, Representative Robert Hurt, Republican in Virginia, he and Phil Roe in Tennessee have introduced HR-3631, a Small Manufacturer Protection Act, which empowers the Secretary at FDA to issue small business exemptions when GDUFA might create barriers to entry. I believe the threshold for that is companies that are $20 million and smaller, and that bill is currently sitting in the Health Committee.

I'm here because this is our coming out party in a sense. This is the first public appearance the association has made.

MS. NGUYEN: Congratulations.

MR. ROTH: Thank you very much. We're

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interested in reaching out to FDA in helping to inform them a bit more about how the CMO industry differs from the branded pharma industry, from the generics industry. Like I said, they operate on very different margins. Some of them are carved out of existing pharma companies. In this case, some of them have generic products of their own through other businesses. I should note that the interest in GDUFA does not reflect the entirety of the membership of the PBOA. Some of these companies don't handle generics at all, some are biologics focused, but still they're contract manufacturers and they don't seem to be represented in the way GDUFA was structured in its initial incarnation. We're hoping going forward with the renewal that we can have some effect and help negotiate some way of differentiating CMOs from pure generic companies under the facility fees going forward, particularly for final dosage form.

And that is essentially all I have to say. We are planning on submitting comments to the

docket in the weeks ahead to again try and pave the road here, but if you have any questions, I would love to start a conversation.

MS. NGUYEN: Thank you.

MR. FLANAGAN: Welcome to the excitement of GDUFA.

MR. ROTH: Thank you very much.

(Laughter.)

MS. NGUYEN: It's always a party.

MR. ROTH: Well, this all began because I was reporting on GDUFA for Contract Pharma Magazine, where I was the editor, and the number of contract manufacturers who said to me, "We don't know what we're doing under this. We can't pass these fees along to our clients," they were, I don't want to say blindsided, we knew fees were coming. I don't think they knew exactly how it would be structured and how they would be implemented. We want to be part of the party, I guess.

MS. NGUYEN: Do you have -- can you give me a ballpark estimate on how many players would

fit into the under $20 million exemption?

MR. ROTH: Not entirely. It's an industry that's dominated by a few very, very large companies and a very large number of small companies, and some of those come and go. If anything, when I was building the membership list for this, I looked over the self-identified facilities list under GDUFA to see which companies I knew which companies didn't appear to be generic firms of their own, and start figuring out who was a small CMO, who I don't want to say get caught in the net, but showed up as a self-identified manufacturer of generics.

MS. NGUYEN: So was it a lot?

MR. ROTH: There's a bunch. I will try and get that information for you.

MS. NGUYEN: Yeah. I just want a feel for what would happen if we were to work on an exemption. I think a presenter earlier had talked about a sliding scale fee structure. You're talking about an exemption which would be something different. I don't know if you would

also -- if you like what we currently do in PDUFA and whether that would be acceptable.

MR. ROTH: And that's what I was wondering. Under PDUFA, there is both a small business exemption and facility fees are applied directly to the drug filers, not to the individual manufacturing sites. Both of those did not carry through to GDUFA. So we want to see about how that can be implemented.

One of the ideas we had was simply a checkbox of sorts under the self-identified facilities list to ask companies, do you or any of your subsidiaries own any NDAs of your own? If they don't, it's a contract manufacturer, it's not a generic company, and that might be a good way of splitting the pie to separate final dosage form into companies making them for themselves versus ones that are making them for clients.

MS. NGUYEN: Thank you.

Other questions from the panel?

DR. UHL: I was just wondering if you could elaborate on your choice of the $20 million.

MR. ROTH: Oh, that's not my choice. That's in the small business -- that's in HR-3631.

DR. UHL: Okay. Even that, how was that put? I mean, do you have any knowledge of that, that selection?

MR. ROTH: I don't know how that number was settled on, but it might be something that's come up in small business waivers in the past, but I'm afraid I don't know how they settled on the number.

DR. UHL: Okay. Thank you.

MS. NGUYEN: Other questions?

(No audible response.)

MS. NGUYEN: We'll look forward to seeing your comments in the docket.

MR. ROTH: Thank you very much.

MS. NGUYEN: So that concludes the morning session. We are at 11:47. Let's reconvene at 1:05. So we'll follow the agenda and just meet back here in an hour and 15. Thank you.

(Lunch.)

MS. TOUFANIAN: Good afternoon. We'll

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go ahead and get started. My name is Maryll Toufanian. I am an Acting Division Director within the Office of Generic Drug Policy. First, we would like to thank everybody for their participation this morning. We thought it was a really informative and helpful discussion.

This afternoon we'll be shifting gears a bit. I'll relay that the process is similar to this morning in that we have two speakers who have prepared remarks, and then we'll give an opportunity for folks who would like to comment on the issues that we'll be discussing, some of whom I believe have registered earlier today whose names will be projected on the list, and then if we have any additional time, we'll go ahead and permit additional comments.

This afternoon's policy discussion concerns two topics of GDUFA implementation that are informed by the unique incentives for generic drug manufacturers embedded into the Hatch-Waxman amendments. All of us are familiar with the 180-day exclusivity, so I won't get into the nuances

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of that, but before we discuss our criteria -- or, excuse me, our topics of discussion today, I would like to give the new panel -- you'll see some fresh faces up here -- an opportunity to introduce themselves. These are folks that are on the front line of considering the issues we'll be discussing today, many of whom will be familiar to the folks in the room.

MR. FLANAGAN: I'm Keith Flanagan. I'm the Transition Lead for Policy in OGD.

MR. REED: Dave Reed, Regulatory Counsel in OGD.

MS. DETTELBACH: I'm Kim Dettelbach. I'm Senior Counsel in the Office of Chief Counsel.

MR. SHIMER: Martin Shimer. I'm the Deputy Director of the Division working with Maryll.

DR. UHL: And good afternoon. I'm Kathleen Uhl, the Acting Director of the Office of Generic Drugs at CDER.

MS. TOUFANIAN: Thank you. So as I indicated, we have identified two topics on which

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we really look forward to getting comments from stakeholders involved in GDUFA implementation.

The first concerns, what is actually a criterion for Agency prioritization set forth in the commitment letter, the notion of a category of a first generic who will be receiving priority review, and what we have discovered based on informal comments is that description and categorization set forth in the commitment letter is not as clear as we would like, or it's not as easily defined as we thought. We have received differing definitions. Is a first generic a first ANDA that is submitted for a particular RLD? Is it a first-to-file ANDA that contains a Paragraph 4 challenging patents with a brand drug? Is it the first generic that's approved, that is approvable, the first generic that is marketed or marketable, and/or is it the most important number one priority for a specific company?

Having received these informal and somewhat differing or diverging understandings of what a first generic is, we thought it was

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essential to invite stakeholder comment on what is the appropriate definition of a first generic for the purposes of agency prioritization of ANDA review.

And the second topic we'll be receiving comments on is the Agency's consideration of 180-day exclusivity. I think everyone is well aware of what that is and that the Agency's consideration in decisions with respect to 180-day exclusivity are complex, fact-specific, ever shifting, almost always occurring prior to approval and almost always involving confidential commercial information, and that being said, we have received again a number of informal comments from a variety of stakeholders asking whether there is a way to make that process more transparent and potentially open to public participation.

As I indicated, many of these decisions are fact specific, but they deal with issues that recur for a variety of applications and for a variety of products. So we are soliciting

comments on if there are mechanisms mindful of the confidential nature of some of these determinations, are there mechanisms to make part or all of those considerations public?

The folks in the room are the folks that deal with these issues on a daily basis, and we thought it would be very helpful to get comments on those as well.

In addition, we're welcoming comments on other elements with respect to the sort of non -- I don't want to say non-scientific, but the more policy or legal elements of GDUFA implementation where additional guidance or additional clarity from the Agency would be beneficial.

So with that, we'll go ahead and start. I believe Robert is -- no? You're all set?

MR. VINCENT: I'm (off mike).

MS. TOUFANIAN: Okay. I'm sorry. Then, Marcie, if you would like to go ahead and join us. Please go ahead and just introduce yourself and identify your affiliation.

MS. McCLINTIC COATES: Sure. Well, good

afternoon and thank you. My name is Marcie McClintic Coates, and I serve as Mylan's Vice President and Head of Global Regulatory Affairs and also as a former member of the GPhA GDUFA Negotiating Team.

Mylan has a 53-year history of working closely with FDA, and we appreciate the opportunity to provide comments today, particularly given a lot of involvement in the development on negotiating of the GDUFA program along with our industry colleagues.

We look forward to supplementing the docket today with additional detail regarding all of the questions that have been published in the Federal Register Notice, and we thank the Agency for creating this forum today. I think it's well served and a continuation of having these goes a long way for both industry and FDA, so thank you.

For today, I will share some general but important considerations that really should shape our thinking as we implement GDUFA to ensure that the true intent of the program is operationalized

in a way that's consistent with the key aims that we sought for in the negotiations of the three public health aims of improved safety, access, and transparency, and certainly consistent with the key underpinnings that make our industry so unique, the Hatch-Waxman system that we have.

GDUFA was one of the most significant pieces of legislation impacting the generic drug industry since the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as Hatch- Waxman, which essentially created the generic drug industry as we know it today and interestingly next week will celebrate its 30-year anniversary.

Since the passage of this act, generics have played an increasingly vital role in the nation's public health, as FDA has approved more than 8,000 generic equivalents to brand name drugs, resulting in 85 percent generic utilization in the U.S. and saving the country over a trillion and a half dollars in just the last decade.

Now, much of that success has come

directly from the very unique Hatch-Waxman framework that Congress put in place to expedite generic competition to give patients faster access to more affordable medicine on the very earliest possible date that no legal barrier approval exists.

Now, exactly 4 years ago today on September 10, 2010, FDA had a very similar public forum as this welcoming dialogue on what a generic user fee program ought to look like, and what did industry think about? So I went back and revisited our comments then and comments that many of our colleagues have put forth as we started to really look at the need for a program, and one of the comments that we shared, Mylan's CEO shared, at the time that I think is still relevant is while it's widely recognized that Hatch-Waxman has successfully delivered significant savings to consumers, no one could have predicted in 1984 that that framework would over time tax the FDA system due to the complexity of the global marketplace. Today's reality means we must

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address the issue through a holistic user fee approach, one that supports the mission and true intent of Hatch-Waxman at the same time generating much needed funding for the FDA and assurance for product safety amidst the globalizing industry that the Agency regulates.

Now, over the time period leading up to GDUFA, median review times had hit 31 months, they had doubled over the last decade, and, quite frankly, as we all know, the Agency's resources had just not kept up with that demand nor the ability to inspect facilities located in the U.S. and outside the U.S. at the same frequency and occurrence and thus contributing to these delays because a recent inspection history is, of course, needed before you can get approval.

Now, what was happening prior to then, as we know, we were inadvertently forfeiting exclusivity as an industry. As you know, the generic drug industry has 180-day exclusivity, it's the sole exclusivity that exists for generics, and in 2003, the Medicare Modernization

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Act updated those Hatch-Waxman amendments and provided forfeiture provisions finding that if a company fails to get a tentative approval within 30 months, you will lose your 180, and as that number -- in 2003, when that was created, it took 16 months median review time to get a tentative approval at FDA. And now that we're at 30, 31 months prior to the start of GDUFA, companies were inadvertently forfeiting through no fault of their own and thus threatening this important exclusivity that Congress had put in place to incentivize companies to take on the expensive -- the extensive legal risk involved to challenge patents and at the end of the day get products into the hands of consumers faster.

So it was with all those pieces in mind, with Hatch-Waxman being at that point a century old, that industry came up with, with FDA a comprehensive user fee program that was focused on three public health stated aims of GDUFA: improved access by expediting the availability of low cost medicine by bringing greater

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predictability, increasing timeliness in the review, improved transparency by improving FDA communications and feedback within industry in order to expedite product access, and improved safety by ensuring that both foreign and domestic industry participants in the U.S. are held to consistent high quality standards and inspected biannually using a risk-based approach.

Now, as FDA is now operationalizing GDUFA and coming up with new policy development activities training within the Agency, these three overarching stated purposes of improved safety, access, and transparency should really serve as the guiding principles on all of the implementation efforts, and these are complemented by two longstanding and bedrock principles that have historically made the U.S. generic drug system the most successful in the world. Number one, FDA's relentless passion and commitment, sense of urgency, to carry out the unique Hatch-Waxman framework of getting drugs approved and into the hands of patients on the very earliest date that no legal

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barrier exists as well as, two, FDA's strong reliance on good science to continuously improve and evolve Agency thinking.

So thus GDUFA was intended to provide FDA with additional resources to essentially achieve the ultimate purpose of Hatch-Waxman that had become really strained with the growth of the industry and the number of facilities and players involved and the lack of resources at the Agency for generic drugs. And both Congress and the courts have found that Hatch-Waxman's central purpose is to implement the policy objective of getting safe and effective generics into the market as quickly as possible after patent expiration or earlier where companies are able to do so by challenging patents.

Now, the GDUFA goals letter identifies improved access as a key public health aim of GDUFA, and leading up to GDUFA, as we mentioned, the generic approval had increased to 31 months in 2011. Now, a significant amount of progress has been made to date implementing GDUFA, and we will

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outline more of those as well because they are worth noting and they're important, toward the inspection disparities, many of them, and we were having conversations at lunch with several colleagues about the improvements that have occurred, but one area that we both continue to struggle in is on the median approval times on that purpose of access. So while much has been made to hire and train and set up the infrastructure to get the generic review system a more predictable footing from the start of GDUFA, the median time for generic approval has increased to 36 months in 2013, and it's projected to be at around 43 months in 2014, although not all full data is out yet, but from the sampling that we have been able to see. And in the last year, the U.S. health care system has lost an estimated -- over a billion dollars in savings due to delays in first generic approvals missing getting approval in that earliest stage that no legal barrier exists for approval. And we, as an industry, continue to have inadvertent forfeitures for failing to get

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that timely approval. On top of that, of course, the Agency has received a record number of applications just in June alone, so the workload has not gone away either.

We are encouraged by the new Prioritization Map that has come out with FDA to try to address these challenges and to make sure that we're not losing sight of those critical products, applications that are opening the market and getting more affordable access to patients. We would urge FDA to ensure that the key principles are carried out through the prioritization of both the application submitted before October 1, 2014, as well as those that come after this date. And this is a very important point as we look at this framework and we have as a sister model to look at, is PDUFA, but I think this is really helpful to underscore this distinction.

While much of GDUFA is modeled after PDUFA, GDUFA is particularly distinguishable from PDUFA because GDUFA's goal of decreasing the time

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for approval is tied to the Hatch-Waxman amendments, which link the patent dispute process with the generic drug approval process and requires FDA to make approval determinations on applications within 180 days. And in proposing and negotiating that framework, much time was spent identifying the unique Hatch-Waxman framework that differentiates our program from following a rubber stamp, mirror image of PDUFA. And as shared during several previous public meetings as we talked through this, if the generic drug user fee program is tied solely to the certainty of an artificial timeframe alone without regard to the Hatch-Waxman framework, that encourages the earliest entry of generic competition, this would be flawed because not all applications can or should be treated equally. FDA should not simply create a cookie-cutter approach that treats all applications alike and fails to recognize the legal distinctions between each application, such as first-to-file ANDAs, subsequent ANDAs, and/or significance of a

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particular product, like one that treats an unmet medical need or otherwise a first generic or an orphan drug or some other significant public health impacting application.

Mylan recommends that FDA clarify its recent Prioritization Map with associated target action dates to prioritize those applications that have the most significant impact on the public health so that more timely approvals can be achieved. These include the availability of new first generic medicines, medicines that lack significant generic competition, including second-to-file as well as any other applications that particularly play an important role in the public health in addition to PEPFAR and drug shortage applications.

First generics should include those applications for which no other generic version of the same reference listed drug has yet been brought to the market under an approved ANDA. Consistent with the purposes of Hatch-Waxman, FDA should aim to approve applications immediately

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upon patent expiration, exclusivity expiration, expiration of a 30-month stay, commencement of a patent license date, or the earliest date that no other legal barrier to approval exists; for example, for a late statement or a forfeiture by the first applicant. FDA should prioritize any other application for which the applicants can sufficiently demonstrate a significant and compelling public health need taking into consideration factors such as whether the product will fulfill an unmet medical need or satisfy an undue economic hardship.

As the Agency assigns appropriate action dates and time to allow for a final and tentative approval, that should be aligned with the relevant Hatch-Waxman dates, and once that has been identified, these dates should have the ability to change to an earlier date just given the constantly changing dynamic nature of the Hatch-Waxman framework if it's needed. If an application has now entered into a settlement agreement, then gives the opportunity for an

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application to be approved earlier, that target action date should have that ability to respond to that dynamic and nimble nature that Congress intended to drive competition.

Additionally, all divisions within FDA that can impact the approvability of an application should be held accountable to that date. So it's not just CMC and bioequivalence and the traditional OGD review, but if something entails a consult or a citizen petition review or a review by Office of Chief Counsel, we would suggest that all of those should be -- or of wrapping up an inspection or closing out an inspection -- included here.

And with respect to submissions that are impending with FDA submitted anytime before October 1st of 2014 when the Year 3 metrics kick in, FDA should strive to maintain a level of productivity at least similar to the pre-GDUFA levels as provided in the goals letter, which says FDA will aspire to maintain pre-GDUFA level productivity as the Agency ramps up the program.

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Thus, FDA should aspire to meeting approval times of no more than 30 months of applications submitted before October 1, 2014, that are not prioritized. So the backlog is moving through toward approval.

In keeping with GDUFA's third core purpose of improving transparency and feedback with industry, we respectfully urge FDA to clarify issues relating to determining the status of pending ANDAs and approval timing so that applicants are prepared to launch immediately upon FDA approval to allow enough time to secure raw materials, plan production schedules, manufacture and coordinate distribution among many of the other pre-launch activities necessary so that industry can be prepared to provide more affordable products on Day 1.

Industry cannot plan appropriately without better predictability and potential approval times and Agency action dates. When too much is made or there are significant delays in launch, expired drug must be disposed, resulting

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in unnecessary waste. Additionally, when there isn't enough visibility to know when to expect approval, production delays are incurred counter to the purposes of Hatch-Waxman of being there on the earliest possible date.

We urge FDA to revise its internal communication policy to align the purposes of GDUFA and to improve communication and transparency with industry with particular emphasis on applications that are within at least that 6-month time period for which no legal barriers exist that would allow them to be eligible for final or tentative approval.

In conclusion, we appreciate the opportunity to share some of these general comments and considerations that shape the Agency's thinking around implementation as a whole. It's these collective principles of safety, access, and transparency, the Hatch-Waxman program, and the strong focus on science that have been the fundamental underpinning of the industry for the last 30 years and have allowed us to get

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to the savings that we're able to offer to patients, and we look forward to continuing to partner with you to navigate through implementation to ensure that GDUFA is implemented as intended to get faster medication to patients.

So thank you.

MS. TOUFANIAN: Thank you very much.

Questions from the panel?

MR. FLANAGAN: Thank you for your comments.

So I'm curious about the $1 billion number you cited.

MS. McCLINTIC COATES: Yeah.

MR. FLANAGAN: Are those submissions where there are no scientific and technical review issues outstanding inspection or compliance issues outstanding, and no outstanding Hatch-Waxman patent, legal, or related issues outstanding?

MS. McCLINTIC COATES: Yeah. It's a good question. So of what was estimated in known delays for first generics, it's a variety, and candidly I would say that some of those, I

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couldn't tell you if they have those outstanding because not the full visibility of the status of the applications are available to know where delay may sit, but the median review time for that category is around 55 months of pending Agency review.

MR. FLANAGAN: I'm sorry. So the answer to my question is we don't know?

MS. McCLINTIC COATES: Well, as part of the follow-up with the Agency, many of them vary. Some of them do have -- are pending and you know because the agencies recently ask you for a comment. I don't have full visibility into all of them because it was a blinded pulse check with (inaudible), but some of them, we don't know if things, where they're still -- some of them are kind of languishing because you don't have that full transparency about where the state may be.

MR. FLANAGAN: Well, the implication is that -- or maybe I'm being hyperdefensive -- but the implication of the number, which is large, and, you know, arguably inflammatory, is that

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there is a billion dollars in lost cost savings due to FDA dropping the ball, and my perspective is that if the submission has quality challenges and is not approvable or if there are outstanding patent exclusivity or related Hatch-Waxman issues that are out of our control, then how is it fair to say that there's a billion dollars in lost cost savings that could otherwise have been reaped if the submission is not of high quality and there are outstanding Hatch- Waxman issues?

MS. McCLINTIC COATES: Yeah, I can't speak to these are not high quality from the ones that you're referencing for the time period of which they are at, and these are ones that the date has passed by, a patent has expired or so forth. So in terms of the straightforward pending Hatch-Waxman pieces, it's not known to whether those have those, but I think the broader point that you're raising, and it's a big one, it is a shared commitment between the Agency and the industry to get there on Day 1. It is a partnership between both of us dialoguing back and

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forth. In order for us to both get there on Day 1, we have to know where things stand, and the Agency has its piece of review also. If we're both going to get there on Day 1 and you send us back comments and we then take an eternity to respond to those back, then that also pushes out Day 1.

So your point is the right one from a standpoint of it's a share between Agency and industry of where it is. It isn't necessarily that all of that is on FDA, but it's on all of us if we are missing the opportunity for Day 1s when we can strive to get there, and that's why some of the comments from this morning I think are very helpful in terms of, what can we do up front to make sure that some of the things that straggle on down the road in your review, that you can try to avoid them. So things like the controlled correspondence guidance, clarification calls that are maybe needed whenever guidances are coming back, some presubmission meetings if it necessarily warrants it, if you're dealing with a

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complex novel much like what Rob Lionberger outlined at the GPhA Fall Tech meeting. All of those sorts of things collectively go toward that. So I'm not suggesting that it's as straightforward as that, and this is a point, and no one should interpret that. It's on both of us on both sides, and it's a reality that as we look at this issue -- - and I'm pleased that the Agency is really looking at it from that Hatch- Waxman lens right now and the unique scenarios -- the reality is no two applications are alike, and as we look at the freight -- and there is over 3,000, or whatever that number is -- that's the piece that we're looking at, and what are the ones that we can take off, and how do we move them forward quicker at the end of the day, our same shared goal?

MR. FLANAGAN: And second question, you said that GDUFA contains a productivity level obligation for FDA. You did not qualify that statement. My admittedly imprecise recollection of the language exactly on point was that we had a productivity maintenance of efforts obligation

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that was basically a best efforts provision given a laundry list of other --

MS. McCLINTIC COATES: You're right, it's an aspiration. And I'm sorry, I thought I said FDA will aspire to maintain the languages, that FDA will aspire to maintain pre-GDUFA levels as FDA ramps up the program. So you're right, it's an aspiration, it's not an obligation with the program, but it's an aspiration that I suggest that we should consider in terms of addressing much of the comments and feedback from folks about this backlog and how can we make sure that the public health goals are continued to be met, that those important medicines that are in there? Is that something we can all push ourselves to strive for, both us, and the timeliness and responses with pieces, and on your end as well?

MR. REED: I have a question on priorities. You gave quite a reasonable summary of what might qualify as a first generic.

MS. McCLINTIC COATES: Yeah.

MR. REED: I think you mentioned first

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applicant to a particular RLD drug shortage and other high priority health care needs, but you also mentioned second generics, and that raises a question I have, which is, how would you propose that we prioritize within those products that have been designated for priority? I would assume that if you have a first-to-file and a second-to-file, that the one -- they wouldn't be treated as equals.

So my question is, within all of these ANDAs that are designated as priority, do you have a suggestion as to how we would prioritize within them?

MS. McCLINTIC COATES: Sure. So with respect -- and we can provide more comments certainly to the docket because, of course, all things in Hatch- Waxman are nuanced and fun, but in terms of your question here, I would say that the ultimate goal of Hatch-Waxman is to get there on the earliest date that no legal barrier to approval exists. So for that first-to-file, that we're all doing -- it's in all of our interests to

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fight for the 180, do not have inadvertent forfeitures, et cetera, to encourage that important incentive. But with respect to 181 qualifying, so for those, the legal barrier to approval, keeping with the purpose of Hatch-Waxman to get there on the moment that that legal barrier is lifted, that's going to be lifted on Day 181. So in terms of moving that thing through the process, that should be the striving goal in terms of any compliance that needs to get wrapped up, et cetera.

MR. REED: And there might be a dozen of them. So do we strive to have all dozen ready on 181?

MS. McCLINTIC COATES: I think that it is an important goal to strive toward. Every application is different in terms of where it's at in review, but in terms of the second and third and fourth generics, the overarching purpose -- and that's more of what I'm speaking from because a lot of these are fact- specific, but the overarching purpose to drive competition, we know

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that when -- we know that from 30 years in the industry that more players in the market are going to drive down to more affordable pricing, and the earlier entry that you can get there, how critical that is.

So I just want to make sure I provide that to make sure that those are not forgotten about because there are a number of important ones that are out there. And as the demand has increased, it's difficult for one supplier perhaps to absorb all of the U.S. demand for that, and so for the purposes of shortages and availability and scale and the medication that's involved, those are still very important public health priorities, that as we look at this that we want to make sure are not forgotten.

MR. REED: Thanks.

MS. TOUFANIAN: Just a follow-up question because I think it's easy for us to identify that first date and it's easy for us to identify that 181 date --

MS. McCLINTIC COATES: Yeah.

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MS. TOUFANIAN: -- but you referenced a bucket of applications for which they become available due to a settlement agreement sort of off the calendar. And obviously that is a very fluid situation and we may not be able to approve a product the day after we receive notification of a settlement.

MS. McCLINTIC COATES: Right.

MS. TOUFANIAN: Either today or I would encourage in your comments to identify some mechanisms that we could implement in our office and together with industry to make sort of those spot changes easier to administer if those are going to be contained in that first generic prioritization definition.

MS. McCLINTIC COATES: Yeah. Yeah. It's a great point because many of them, to your point, may be through a confidential settlement discussion and sharing that information, and the earlier that we can get that information to FDA obviously, that's critical. So that's a good topic I think for all of industry to consider with

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here, and I think we should add that to the docket as well to be able to provide that information.

That's just the very fluid nature of the Hatch-Waxman scheme, but our ability to pivot and to be dynamic and move, and it's a balancing act because FDA right now is putting forth any processes and policies and procedures, so given the volumes that we're dealing with, to make sure we strike that same balance that Hatch-Waxman struck to balance whenever that happens because some things are going to get rattled and changed, so how can we do that? I would urge my other industry colleagues to submit comments around exactly that point as the Agency struggles with that and we struggle with you with that to make sure that that happens.

DR. UHL: So in the spirit of clarity here, because you and Keith are going back and forth about language, I would just like to set the record straight -- and we do have a recording for this -- so since I carry my GDUFA commitment letter with me everywhere I go, Page 3 of the

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commitment letter or the goals letter or whatever it is you want to call it, so we're all talking about the same document, Roman numeral Number VII, "FDA will aspire to the extent possible to maintain levels of productivity at least similar to pre-GDUFA levels while hiring and training incremental staff necessary to achieve the program performance goals, building necessary systems, and implementing outlined program changes in Years 1 and 2 of the program." So just so we're all clear on language.

But I do have a couple questions for you, Marcie, if you wouldn't mind.

MS. McCLINTIC COATES: Sure.

DR. UHL: You state that not all applications should be treated alike. So in a GDUFA system where there are goals, GDUFA goal dates, attached to an application, how would you propose that? And maybe you're not talking about ones with goal dates and you're talking about stuff that's in Years 1 and 2.

MS. McCLINTIC COATES: Yeah. No. I

actually am referring to all of it. Just from a standpoint of from an alike standpoint, it comes back to public health. So the goal dates in the CR letters and so forth were all vehicles to help us get to that ultimate end of fulfilling that public health piece. So from that standpoint and appreciating that the applications that are submitted regardless of what goal date they may have to try to keep them moving through given the mass volume that the Agency is working through, in terms of treatment of appreciating that these all may have different nuances, it's because of the fact that, goal dates aside, the Hatch- Waxman framework that links the patent resolution process to the approval process, that linkage that exists here and unlike anywhere else in the world, it makes applications by their very nature different and, additionally, so do the public health needs of each of those applications. So, you know, an application may be there to address a shortage, an application may be there to cover an orphan indication that hasn't had a more affordable

generic, and we would urge that as we are implementing this program aimed at giving FDA the resources needed to continue to achieve the purposes, that we not lose sight of those same purposes of allowing for the public health ones, most impacting public health ones, and the ones that are linked to Hatch-Waxman, to move through on their earliest date. The Hatch-Waxman statute continues to provide that FDA should strive for 180 days, and that's still in the statute. These goal dates are, though, intended to continue, compared to where we have been, with the volumes at 31 to get those pieces back and to help us move to a place over time the first cycle approvals.

DR. UHL: So I think it would be helpful for the Agency to hear in the docket what industry thinks public health impact is because I think that's a -- you've seen in the Prioritization Map what we think are public health priorities, but I'm hearing much broader than that from you, Marcie.

I would like another bit of clarification because one of the comments you made

was a first generic is when the product is brought to market. So are you saying that a first generic that's approved and not brought to market, because that happens obviously in some of the settlements that you guys have, where would you consider that in the scope of first generic?

MS. McCLINTIC COATES: So what I reference is that so first generics that include applications which no other generic version of the same reference has even yet brought to market. So technically in that example, you may be your traditional first-to- file qualifying for 180, going to open up the marketplace, but there are scenarios where that very first filer just decided to withdraw and they never actually marketed the product. So the American marketplace, patients continued to not have access to a generic, and so that would technically be a first generic that's opening the door for that.

So they are not necessarily a P4 traditional first-to-file. There are those scenarios. Does that help?

DR. UHL: It does. Thank you.

MS. TOUFANIAN: Anybody else?

MR. FLANAGAN: I just want to express gratitude and appreciation for the amount of time you invested in preparing for this. You took it really seriously and devoted a lot of thought to it. So thank you.

MS. McCLINTIC COATES: Thank you for your time. I appreciate the opportunity and look forward to working with you more as we work to tackle our shared challenge of getting access. Thank you.

MS. TOUFANIAN: Thank you very much, Marcie. Unfortunately, the agenda I have in my book may be out of date, so are we moving to --

MR. FLANAGAN: Is that on? It's open? Is it open?

UNIDENTIFIED MALE SPEAKER: No.

MR. FLANAGAN: It's open mic, though not totally open.

MS. TOUFANIAN: I believe that certain individuals did indicate a wish to speak. And

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we're having some technical difficulties.
(Pause.)
MS. TOUFANIAN: Terrific. It looks like Ken Cappel. And I have to apologize in advance, I am reading sideways, so I will obviously mispronounce some of these names.
Ken, can you go ahead and introduce yourself and indicate where you're from?
MR. CAPPEL: Sure. Good afternoon. My name is Ken Cappel. I'm the Vice President of Global Intellectual Property for Amneal Pharmaceuticals. I would like you to know that I'm a pharmacist as well. I take my responsibilities to the patients very seriously. And I'm also an attorney and take my responsibilities to the client very seriously.
I gather I have a little extra time, so I'm going to do my whole statement.
Amneal would like to thank you and the Agency for holding this conference. We appreciate the opportunity to assist the FDA in matters that are important to the public health and the generic

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industry.
The Agency and our industry are aligned in that together we seek to provide the U.S. health care system with cost effective medicines that are equally safe and effective when compared with our brand counterparts. This is clearly our common goal.
Our parents, grandparents, and children, our neighbors and friends, and countless other patients benefit from the availability of generic medications. In fact, this very sentiment is reflected in the following quote from Amneal's website. "We at Amneal understand that every product the company manufactures is destined for someone's loved one. Quite simply, together we have a responsibility to these individuals. Hearings like this provide an opportunity to facilitate dialogue and change. Ultimately we hope to achieve our common goal."
As background, Amneal is a U.S. company headquartered in New Jersey with additional key sites in New York, Kentucky, and other locations

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outside the U.S. Amneal currently employs more than 2,300 people globally. Over half of these R&D, manufacturing operations, and other professionals are employed within the United States.
Our portfolio of approved products includes about 100 solid, oral, topical, and liquid finish dosage forms. We currently have over 100 ANDAs pending at the FDA and several of these filings are believed to be first-to-file opportunities. Obviously these filings are exceptionally important to Amneal.
Amneal has achieved exceptional growth over the past 10 years. This growth has resulted in the creation of over 1,000 U.S.-based jobs. Amneal's expansion is supported by a strong commitment to investing in R&D and growing its infrastructure to support manufacturing in the United States and abroad.
Amneal's ability to reinvest depends heavily on the revenues generated by sales of products which, without timely FDA approval, will

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almost certainly fall short of the expected return on investment needed to sustain growth. Amneal fully recognizes that this is a two-way street, improving transparency in the approval process specifically regarding first-to-file products will help to achieve our common goal.
GDUFA was supposed to improve many aspects of the ANDA approval pathway. Notably, Amneal expected that GDUFA fees would improve communication and feedback from the FDA, which in turn would lead to higher quality ANDA filings and decreased approval times. Unfortunately, this has not yet been realized.
Amneal would like to address GDUFA and 180- day exclusivity. Specifically, we are deeply concerned with the lack of communication surrounding first-to-file opportunities and the need to obtain tentative approval within the 30 months of ANDA filing.
As you know, to be eligible for 180 days of marketing exclusivity, a generic filer must be the first applicant to file a substantially

complete ANDA containing a paragraph for certification. Congress enacted numerous amendments to the Hatch-Waxman Act under the 2003 Medicare Modernization Act, and under the amended statute, the first applicant could be deemed to forfeit its eligibility if it failed to receive tentative approval 30 months from the date the ANDA was accepted by the FDA unless that failure to obtain tentative approval was caused by a change to the requirements for approval of the application imposed after the date on which the application was filed.

There is a lack of communication from the FDA on these first-to-file applications, which creates uncertainty for the applicant and the other ANDA filers. This unpredictability actually creates additional work for the Agency because the industry that's really seeking feedback -- excuse me -- that's really seeking feedback from clarity typically undertakes letter writing campaigns in an effort to ascertain the status of the application as the critical 30-month date rapidly

approaches. Unpredictability also hinders launch planning and can result in a delay of generic products reaching the public as early as possible as well as potentially costing first filers significant revenues generated during the exclusivity period.

We also understand that the Agency is navigating relatively new issues regarding risk evaluation and mitigation strategies and abuse-deterrent dosage forms. Dealing with these issues may significantly delay FDA approval, which poses a risk to the 180-day exclusivity. The industry needs transparency regarding FDA's expectations and concerns in these areas. This will allow the industry to have some measure of predictability while the FDA attempts to navigate these new waters.

The FDA's anticipated use of target action dates are an important step in the right direction. Amneal now has more than 100 ANDAs pending review, none of which has a goal date. We have a heightened concern about the future of our

first-to-file submissions. As the FDA has indicated, it intends to focus on new submissions beginning October 1, 2014. The Agency has said that it will issue target action dates only for prioritized applications, and this creates an intolerable level of uncertainty around critical first-to-file ANDAs.

On behalf of Amneal, I request the FDA to issue target action dates for every first-to-file submission within 60 days. In addition, we request the FDA to open its channels to allow for early and frequent communication on these immensely important filings. Our common goal can only be met through a stronger partnership, and I assure the Agency that Amneal and the generic industry stand together with you. We recognize the hard work and dedication of the FDA, and we are committed to working with the Agency in its efforts to continually improve the ANDA approval process. Thank you again for the opportunity to speak on behalf of Amneal Pharmaceuticals.

MS. TOUFANIAN: Thank you, Ken. Any

questions from the panel?

MR. FLANAGAN: Sorry. I do have a question. Thank you very much.

So on the communications transparency issue with respect to the first-to-files, you know, we're building a robust RPM staff, and hiring and training to make that happen. They won't be able to be -- in the immediate short term, they're not going to be like legacy OGD staffers who have been here for decades and can give you a sophisticated read on the regulatory path forward on that submission; right? As a practical matter, if we're going to give you some sort of update, it probably needs to be kind of formulaic, enough into the review so that we have something to report, but far enough back from the goal date so that it gives you enough advanced notice.

It's the same question that I had for Mr. Gaugh, is in your view, which data points in general are the most helpful to you in trying to plan a product launch? What data points do you

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most crave?
MR. CAPPEL: Right. So I'm not punting, but from my experience, each product really it's like a person with its own personality, and so the issues that you're dealing with each product are so different. So, for example, chemistry may be the critical datapoint for certain products, but then if you're dealing with REMS or ADF, then the labeling is clearly critical as well. You know? So it's hard to really give you a clear answer, I wish I could, but I think it's very fact sensitive.
DR. UHL: Can I build on Keith's? Just so -- I understand your point, but there is a need for consistent processes, and so where are there similarities that would be helpful for us so that we can find these touchpoints, which Keith is trying to elucidate from you? So I understand every product is unique, but not all products are entirely unique. There are a range of similarities across them.
MR. CAPPEL: I agree.

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DR. UHL: And that would be helpful for us to hear.
MR. CAPPEL: Right. So I think maybe what we could do as an industry is go back and discuss trying to put some comments into the docket for you and maybe put different buckets of projects together, and obviously there will be one miscellaneous, which is going to be difficult, but we'll talk about that.
DR. UHL: Because you would hate to hear us say back to you that everything is unique, so we can't create any process.
MR. CAPPEL: Of course. I realize that. I realize that I've heard a lot of that today, and we talked about that at lunch, that it's a problem that we need to work together to overcome. You shouldn't be put in that position by us, and we don't want to be put in that position by the Agency.
MR. FLANAGAN: And I think the message we do want to send today as an Agency is that we do get it, we do understand that you need some

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information for product launch purposes. We understand that.
MR. CAPPEL: Great. Thank you very much for your time.
DR. UHL: Thank you.
MS. TOUFANIAN: I just have one follow-up request. I think I will be the one giving everybody homework today. One of the things you mentioned was increased communications with regard to ANDAs that are approaching a 30- or 40-month forfeiture date. I would encourage you in your comment to identify precisely when and what mechanisms you would want us to use for those types of communications.
MR. CAPPEL: Okay. Thank you very much.
MS. TOUFANIAN: Thank you.
Carolyn Huntenburg, from Momenta. Welcome.
DR. HUNTENBURG: My name is Carolyn Huntenburg. I'm with Momenta Pharmaceuticals, and I thank you for the opportunity to talk about from Momenta's perspective. Much of what I am going to

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say has been said throughout the day, so I'll go ahead and start.
Momenta believes that in order to bring new generic drugs to the market effectively, frequent and informative and timely communications between the FDA and the ANDA sponsor are critical. Timely two-way communication calls for both parties to anticipate and/or respond to the actions necessary to bring new generic drugs to market in a safe, efficient manner.
One of the key components of the GDUFA program is transparency, which includes communication to the industry. Transparency and communications were critical issues during the GDUFA notifications. One of the principle reasons for paying a user fee was to establish a predictive process that will support industry to be able to provide safe, effective, and affordable medications to patients.
Over the past year, since the implementation of GDUFA as well as complete response letters, our experience has been that

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meaningful communications about ANDA status has become significantly restricted. This restriction and allowable and substantive communication between the ANDA sponsor and FDA is dictated by OGD policy where OGD staff are not allowed to provide ANDA sponsor with any specific information regardless of whether it is critical or not until the complete response letter is received. This restrictive communication has undoubtedly delayed the sponsor's ability to react to the information when received and likely results in a delay in approval. These issues will be only further magnified by the complexity of applications received by the FDA increases.

Patients benefit from earlier approvals. If there are more timely informal communications, particularly with complex applications, the applicant can work in parallel on important additional development requirements while the FDA reviews other aspects of the filing. This will allow parallel processing and would significantly improve the advancement of approval dates.

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Currently, if all feedback is held, then the effort of the Agency is magnified in scope for each review, and the applicant sits idle during the review period, which is a highly inefficient process.

Momenta strongly urges the FDA to implement an effective ongoing and substantive communication process between the industry and the FDA throughout the ANDA review process. By doing so, the use of resources and times on both sides is conserved. The benefit of increased communication will surely reduce inefficiencies in the process that currently exist and, more importantly, assure timely access to affordable generic medicines. Thank you very much for this opportunity.

MS. TOUFANIAN: Thank you. Any questions from the panel?

(No audible response.)

MS. TOUFANIAN: Thank you for your time.

DR. HUNTENBURG: Thank you very much.

MS. TOUFANIAN: Carole?

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DR. BEN-MAIMON: I'm struggling whether or not to use these glasses or not.

I also want to thank the Agency for this open dialogue. I think if you put all of the exchanges we're having between the exchanges you have with GPhA, those at the FDA quarterly, and these ongoing forums, I think it really does add value to ensuring in the long term we get to where we need to go, which is obviously taking care of patients.

You may or may not know, I'm a physician by background. I'm President of the Generic Division of Impax Laboratories. We develop, manufacture, and sell generic drug products. We are a mid-sized company, and so I actually represent companies that are small to mid-size in some of my remarks, which may differ from some of our larger colleagues.

And you also know this is a very diversified industry. From the morning, you heard from CMOs. We have our API suppliers. We have small companies and mid-size companies, and then

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our very large colleagues. And not all of our needs are always the same, and that's a challenge for you, and we acknowledge that.

It's really interesting to me that, as Marcie stated, we're coming up on the 30-year anniversary of Hatch-Waxman, and as we all know, Hatch-Waxman struck a very subtle but very important balance between the brand and the generic industry, and it was intended to stimulate -- and I think this is really a crux of what we're talking about here -- it was intended to stimulate competition, and in stimulating competition, it actually accomplished two goals, one was cost control for pharmaceutical products, but the other was it stimulated innovation in the brand industry as well because if you had competition, you were going to start innovating and creating new things. And so keeping that balance as we move forward and ensuring that competition exists both in the industry and for branded products when appropriate is really I think what we're actually talking about as we move forward. Patients and consumers

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obviously have benefited through this competition and the availability of lower cost products.

In the last 10 years, as you heard earlier, we saved over a trillion and a half dollars. $239 billion of that was just in 2013 alone. This is as a direct result of the availability and access to generic drugs, so it's crucial that as GDUFA is implemented, we don't undermine patient access to high-quality, low-cost generics.

Competition is critical to the continued success of Hatch-Waxman. Maintaining competition serves the public good and decreases health care costs.

With that in mind, focusing on complex products where there are no generics available and a pathway for those is important. Focusing on first generics and P4 filings and ensuring access at the earliest legal point is important, but that doesn't minimize the need and let us lose sight of the need for competition where the science may be simple or where there are multiple products out

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there that could at any point become an issue for shortages. So looking at all of these applications is important.

And I'm very sensitive to the need to prioritize. And I don't want to underestimate the challenge that exists at FDA with the volumes of applications you have. That said, it is only through competition that we actually achieve our goals, increasing access and controlling costs.

So although it is critical to ensure that the first generic is approved and available at the earliest legal date, accomplishing that goal is just not enough, it doesn't get us where we need to go. In order for competition to thrive and truly maximize value to the consumer, it is essential that the Agency continue to prioritize and approve multiple applications for the same references to drug. In fact, the opening paragraphs of the GDUFA goals letter clearly lays that purpose out.

By bringing greater predictability to the review process and ensuring greater

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transparency with regard to review time, GDUFA intended to increase and expedite access to low cost, high quality generic drug products. I think it's important to remember that if you talk to generic customers, they would find that price decreases with the introduction of each and every generic drug drives down costs. These costs continue to decrease with the entry of multiple generics, even the fourth, fifth, and sometimes sixth and seventh generic drugs. So simply looking at the very first one is really the beginning of the story, it's not the end of the story.

In addition, all products have a product lifecycle. Even older products in mature markets where there have been multiple approvals and intense competition don't always exist and stay on the market. There are many products that we all know exist have 5, 7, 10 approved ANDAs, but there may only be two products commercially available. In some of these cases, ANDAs are discontinued, plants are closed, applications are withdrawn,

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whatever the reason, the market ends up being only a very few commercially available products.

Because these products have no patents, they may actually be more attractive to smaller companies because they don't have to pay the litigation fees and sometimes the cost of development or the path to approval is more straightforward. So they seem simple and they seem unimportant, but if you look at it in the eyes of the consumer, they actually are very important. And so with that said, it is really important that we continue to look at these products.

The approval of these ANDAs may aid in preventing drug shortages. As we know, it's an incredible problem, but there are many cases in the industry where there are only two products on the market, something happens to the API supplier of one, something happens to the ability of that company to manufacture, and all of a sudden we're facing a shortage in those arenas, and they're not always foreseeable. It also maintains

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competition, which will also increase and ensure the continued low cost availability of these products.

So with that in mind, first generics I think really, like I said, are incredibly important, but we need not to ignore all the others.

It is for these reasons, while I recognize the importance of reviewing and approving the first generic, that's not where we can stop. Timely approval of subsequent generics is immensely important to a healthy generic market. Each and every ANDA, whether submitted in year 3, 4, or 5 of GDUFA implementation or whether submitted in year 1 or 2, or, for that matter, sitting in the pile of more than 3,000 applications in the backlog, serves to ensure a robust generic supply. This in the end serves patients and consumers and ensures access to low cost generic drug products.

I really want to assure the Agency that all of us in this room are sensitive to the

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magnitude of what we're undertaking. Quite honestly, I've worked on the brand side and the generic side, and I think PDUFA pales in the face of GDUFA. The dollars involved are very different. The length of review, the types of data, the number of applications for any one reference listed drug is a real challenge. And so I don't think it's that we aren't sensitive to the issues, we are very sensitive to the issues, and, as Marcie said, I think we want very much to partner with the Agency.

I also want to say something else about small and mid-sized companies that I think is important. It may appear to the Agency that those companies are not engaged in this process. They are very much engaged. We just don't have the resources that some of the bigger companies do. We don't have somebody dedicated to government affairs. I am it. So we use our industry association often as a resource to help supplement some of our issues and to engage with you because we don't have the number of people that we can

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just dedicate somebody to the issues that you deal with.

And so I think if we can reach out -- if some of the smaller companies, you can reach out to them, you can hear some of the issues that we deal with that not all of the big companies may be dealing with. A lot of the smaller companies don't have P4s, they just don't do them because they don't have the legal wherewithal, they don't have the financials, to support the P4 environment, but it's the small companies that ultimately become big companies.

And I've worked for many small companies who quite honestly 20 years ago were very small and today they're really big. And so it's those small companies that actually grow and help improve and ensure the competition and the success of Hatch-Waxman. So we look forward to working with you, we look forward to the implementation of GDUFA, and we look forward to GDUFA2.

So I'll open it to questions.

MS. TOUFANIAN: Thank you very much for

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your comments. Any questions from the panel?

DR. UHL: Yeah, I have questions. So I recognize what you're saying about the smaller companies maybe not having a stake in the ground for the P4 first-to-files. So do you have any suggestions, recommendations, et cetera, around -- because your point is don't leave the other ones behind.

DR. BEN-MAIMON: Yeah.

DR. UHL: There may be circumstances where the not first-to-file is a bolus of a large number of applications.

DR. BEN-MAIMON: Yeah.

DR. UHL: So are there recommendations on how do we prioritize that or how do we look at that?

DR. BEN-MAIMON: And it's a struggle.

DR. UHL: Yeah.

DR. BEN-MAIMON: It's a struggle because obviously in an ideal world you would have the resources to approve all the applications in a timely fashion, and we know it's not likely to

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happen and it's clearly not likely to happen in my lifetime.

MR. FLANAGAN: We'll get there.

DR. BEN-MAIMON: What?

MR. FLANAGAN: We'll get there.

DR. BEN-MAIMON: So obviously at least in the short term we need to look at that.

And I've sort of toyed around with ideas, and I would like to go back, and we will file something to the docket, but the concept of really trying to look at an argument for the public good, I've sort of thought about, is there something that's similar to the benefit-risk assessment that you do on a brand product that would allow you to make the arguments on a generic product? But then that throws it sort of back in your line where you've got to go through all these benefit-risk assessments and trying to figure out, well, which one fits where?

And so I think we, as an industry, have to hash it around, but what I really wanted to do today was really introduce the concept that it's

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not so obvious. And it's important to the small companies, but more important, like I said, it's important to consumers because it's a lot of the smaller companies that are manufacturing the older drugs that aren't quite as sexy where companies have gone out of the marketplace, and we are at risk either for shortages or for less competition and therefore not meeting the requirements or the intent of Hatch-Waxman.

And so I think we need to toss it around as an industry, but I think opening the dialogue was really my intent.

MS. TOUFANIAN: Thank you.

Anything else?

MR. SHIMER: I have a comment. One of the things -- you know, I've worked at the Office of Generic Drugs for a little over 14 years now, and one of the things I've seen over time is when we do endeavor to get multiple applications approved for a specific drug product by a goal date, it's very seldom that all of those folks end up launching their products, yet that all ends up

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being work on our reviewers' shoulders, so we have multiple highly skilled technical reviewers spending a lot of time reviewing these for the end result of an approval but a product that doesn't appear in the marketplace, and we end up hearing time and again we need all these approvals to get -- drive prices down, yet ultimately when we have 10 or 12 or 14 approvals for a drug, not everybody goes to market. How would you suggest that we, as an agency, balance that in any of our considerations? Could we or should firms state that they will go to market for a specified period of time?

DR. BEN-MAIMON: So I hear you and I think that's a really important point because we all know of a bunch of different situations. There are the 10 or 12 approvals and only 6 launch. We know the resources are still spent on the others. There are situations more recently, quite honestly, where there were companies decided not to launch and were sorry because only four or five companies came out and then there was a

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shortage in the marketplace and really prices did hold up. So from a perspective of the industry, they wish they had been there.

There are situations clearly where you spend resources and we pull applications. And that's a very big issue I think is more that we can't -- we are making business decisions. If the drug isn't going to be profitable, if we can't even make back the money on our validation batches, why would we launch? And where that occurs, whether it's at 4, 5, 6, or 7, I can't tell you, but the fact of the matter is -- and I'm going to be a little bit of a bull in a china closet, and I'm not meaning to offend anybody, all of those applications pay user fees, so they're entitled to a review technically. So, I mean, if you don't want to charge the seventh, eighth, and ninth, that may be a solution. I'm only kidding. But the fact of the matter is in the user fee world, there is an obligation to pay the user fees. I mean, that's sort of I think where a lot of us feel about the backlog issue, is we paid

backlog fees.
Now, again, I understand you have thousands and thousands of applications with limited resources and lots of new people and this isn't all going to work itself through in 6 months, I get it, and we run companies and we have our own challenges, but you can see from our perspective that we obviously file the application with the intent to launch. We don't make the investment in the R&D dollars and in the GDUFA numbers and all that. Sometimes delays occur and we get in too late, and so we don't launch the product.
But I would also say one other thing, and that is that an approved product still has value, an approved ANDA still has value, and there are also situations where, at least at our company, we have chosen not to launch but 6 or 8 months later we decide the market is actually more attractive than we thought it would be. We go back and we make sure we have done all of our validation and everything and we do launch. So I

think an approved application is an application that still I think has value to every company.
MS. TOUFANIAN: Thank you very much.
MR. LAWRENCE: Good afternoon. My name is Leonard Lawrence, and I'm from Sovereign Pharmaceuticals, and we're that small company that Carole was just talking about. We have about 130 people in our company. We're a contract manufacturer, and we do contract manufacture of both generics and NDAs. We also have filed some NDAs and ANDAs under our own name for somebody else to distribute for us because we have no distribution capabilities. So we kind of fit in with all of the things that were discussed today. And so I would like to bring up some information regarding some of the things that were talked about this morning and this afternoon. I have a series of questions for you -- not questions but comments. One is we support some of the comments we're talking about on contract manufacturing this morning about maybe some exemptions for contract manufacturing, so we're pushing that to the owners

of the application. We also support the possibility of a reduced fee for us because we do make a very small profit on what we do make, so maybe a sliding scale or 10 percent of profit or something like that that might be associated with the GDUFA fees because we do push those fees on to our customers. Some are hemming and hawing about it, others are grudgingly accepting it. However, it does increase the cost of generics, and so the cost of generics are going to go up. That's eventually going to be passed on to all customers.
That said, I have a series of topics I would like to discuss. One is -- it was just brought to my attention -- that the ANDA checklist was just kaput and I think that was a bad idea, a really, really bad idea, because the content and format and the other guidance documents that are coming out are piecemeals that kind of explain some of the sections associated with that, but not having a whole entire list of what's required in an ECTD, we have that list, what's required ECTD, but not everything in there is required for an

ANDA. So it really gives companies, especially smaller companies, an opportunity to make sure that we have all the information that's needed to be included in an ANDA. In fact, one of the things, being in charge of regulatory affairs for the company, one of the things that we do is we take that list, that checklist, and we put it in Word format, and we link it, so it's like a table of contents in the application, so we link every single thing so it makes it very easy for the reviewer to say, "Okay, you got this, you got this, you got this." By taking it away, then I think it makes it more difficult for us to make sure we're not missing everything and makes it more difficult for you to make sure everything is there. So I would suggest that you reconsider bringing that back in as a tool for the industry to use.
Some of the other topics that I do have, talking about the backlog, we do have several applications in the backlog, and we're just concerned that they're not going to get lost in

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this whole transition into the GDUFA, and we feel like the GDUFA is a good idea because you have a plan to move forward because going before wasn't working really well because you kept on getting backlogs, and so it's a good thing to move forward to have a plan to move there, but we want to make sure that the applications that are in the backlog don't get lost. If you look at it in the Year 2017, I believe it says that 90 percent of the backlog will have a decision made on it. Well, that leaves 10 percent of the applications over 5 years or more without any type of decision made on it, and that's a long time. And if you have 3,000, well, you've got 300 applications, that's significant. And to a small company like us, that makes a big difference because we are dependant on these applications. We have a little bit of them, we don't have a lot of them, and we're actually getting more, but we're still dependent on these applications, so it can make or break a smaller company in what we do.

The next topic is some of the things,

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difficult things, that I come across in an application is the IID. I know it was talked about earlier today. We make some liquid products, and it's very difficult with the way it's written to use a tablet for an excipient for a liquid product because tablets don't use the same excipients as a liquid product. You don't use much glycerin or propylene glycol in a tablet than you would in a liquid, so it makes it very hard. And so we end up having to write this huge justification for having a product that -- an excipient that has been accepted in the past that now can be a refuse-to-receive. Also, being a contract manufacturer, we may know that another application has a certain level in it and it has been approved, however, we're making this other application for somebody else, and we can't cross-reference those applications, and so it makes it really difficult, so we end up having to do this complex time-consuming process to justify every time. And my suggestion is that if the IID, until the database is more fully populated, that it may

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-- we get a stay on the refuse- to-receive issue associated with that if we're within a reasonable amount of time, again if it is listed as a food product and it's listed in the CFR. There are other references. We're not trying to just give a whole -- a higher amount of excipients in there. However, but if it's been a standard across the industry for a long time, then maybe we should get a little bit of relief from that until that IID is there because it makes it very difficult for an application.

Another thing that we've come across that is a policy issue that I think needs to be addressed is the fact that some of the chemicals that we get we need to be within 1.5 micrograms per day. Well, we get that a lot. However, the FDA has already issued toxicology studies to toxicology programs saying that you can have more than that. Also, for example, one of them is a flavoring agent that's commonly used in food, yet we're to keep it down 1.5 micrograms per day, which we can, however, just to go into the

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justification for that is very, very time-consuming and onerous on us, so I would like to consider that if there is an established level of toxicity, that you look at that first before forcing that onto a complete response letter.

Also, controlled correspondences. One of the things that's associated with controlled correspondences is the fact that we are trying to develop product, but if we don't get a response back within 9 months, then it makes it very difficult because we have somebody that wants to make it and give us money to make it, which is what we're in business for, one of the reasons, and we can't make it because we don't get an answer, and so it makes it very difficult, the time delay, and I know that it will be better, but even 4 months is a long time for certain type of controlled correspondences.

And I understand there is a level of difficulty, but I didn't hear anything about prioritizing some of the controlled correspondences, ones that are easy to get done

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that are quick, 5- minute answers like Q1/Q2. That's probably not a whole difficult time. You go back to what the NDA is and you can see, are you within 5 percent? Yes or no. It doesn't seem like to be that difficult, yet it's taking months and months and months to get that type of information.

Also, putting requirements on generalized requirements, I think it's more of a procedural thing. For example, we do make some solutions and they are oral solutions, and they are pretty much water, and we keep on getting this viscosity thing coming back in there where we need to put a viscosity, and that's really the viscosity is like less than 10. Really there is not really any viscosity to it, yet we're asked to put a viscosity spec in when it really doesn't seem to make sense for it. Now, if it was a syrup which was thick or something like that, it might be applicable, but sometimes it's not applicable. So maybe look at when those type of responses come back, is it really appropriate for this type of

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product?

Also, the last thing I would like to talk about is the USP. There was a guidance document put out in 2004 on discretion use of USP compendium method changes, but then when the new draft guidance came out, it does say that for a change in USP, you need to do a CBE-30 if you're going to delete a test or you're going to relax a test. However, I understand for active ingredients that's probably not anything that you would want to do, but for excipients, it's creating a lot of difficulty because either we file it or our clients have to file a CBE-30 to do it, and by the time you get that chain moving and getting it there, the reality is if you have a new application that has the current USP in it, you're going to approve it most likely that way, so it really doesn't affect the other one, it's just a process, and you're just adding more to your CBE-30 pile.

So those are my comments.

MS. TOUFANIAN: Thank you very much.

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Any questions from the panel?

(No audible response.)

MS. TOUFANIAN: No? It sounds like you've put a lot of thought. I would encourage, as we have with all the speakers, to submit to the docket.

MR. LAWRENCE: Yes, we will be doing that. Thank you.

MS. TOUFANIAN: Thank you.

So now in the afternoon we'll go ahead and take a 15-minute break, reconvene at 2:45 for the remainder of the comments. Thank you.

(Break.)

MS. TOUFANIAN: This afternoon we'll have four more comments starting with John.

MR. DUCKER: Unlike Carole, I don't need to think about whether I need the glasses or not.

(Laughter.)

MR. DUCKER: So good afternoon, everybody. My name is John Ducker. I'm the President and CEO of Fresenius Kabi USA. So I'm not one of these technical guys, don't get too

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tough with me on the questions.

Thank you for the opportunity to share our experience of the GDUFA implementation thus far. This is a topic that is of critical importance to my company, and my hope is that through dialogue and public hearings like this one, positive change will take place in how the FDA and the generic pharmaceutical companies work together to achieve our common goal of better serving patients and those who care for them.

Fresenius Kabi is a global health care company with more than 30,000 employees that specializes in life-saving medicines and technologies for infusion, transfusion, and clinical nutrition. In the United States, we are the second largest supplier of generic injectable pharmaceuticals.

U.S. headquarters is near Chicago in Lake Zurich, Illinois. Our portfolio comprises more than 100 injectable drugs and approximately 400 dose presentations and includes oncolytics, anesthetics, analgesics, and a wide range of anti-

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infectives and other critical care drugs.
Fresenius Kabi invests heavily in research, development, and manufacturing operations in the United States and overseas, and the return on these investments relies on the timely approval of our ANDA and prior approval supplements.
The promise of GDUFA back in 2012 was to achieve three critical public health goals: improved safety through an increase in inspectors and inspections, creating a level playing field between foreign and U.S. manufacturers; improved access by expediting the approval of low cost, high quality generics; and bringing greater predictability to review timelines, and improve transparency by identifying the facilities involved in the U.S. supply chain and improving the Agency's communications and feedback to the manufacturers.
The FDA said it would need additional resources to achieve these goals and made a commitment to drug developers that with new fees

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paid to the FDA, we could expect over time measurable improvement in the backlog of drug approval applications in communications and in compliance activities.
The GDUFA commitment letter further anticipates at least the aspiration, as Cook said, that during the first 2 years of GDUFA things would not get worse and that productivity would be maintained. Unfortunately, our experience since October 2012 is just the opposite. In the 5 years prior to GDUFA, Fresenius Kabi's average approval time for an ANDA was around 17 months. Today the average is more than 36 months and rising. At the same time, a lack of communication during the approval process has added uncertainty and unpredictability that has further slowed access to lower cost generic medicines.
On the positive side, the Agency has been doing a better job of prioritizing approvals and importation of medicines where there has been a drug shortage. In some cases, our products have been approved in weeks, enabling Fresenius Kabi to

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help alleviate critical shortages. And I would like to take this opportunity to express our appreciation to FDA's Office of Drug Shortage. I think this is the type of working relationship that could serve as a model for the Agency in terms of information sharing and collaboration.
Our experience with drug shortages that are not on shortage tells -- I'm sorry, with drug approvals that are not on shortage tells a very different story. Fresenius now has more than 50 ANDAs pending review, none of which has a goal date, and we are concerned about the future of these submissions because the FDA has indicated that beginning October 1st this year it intends to focus on new submissions in order to hit obligatory performance metrics.
For the 3,300 total backlog submissions, the Agency has said it will issue target action dates only for prioritized applications. The remaining applications are therefore likely to be further delayed and the drugs that are caught in this regulatory limbo may lose value as generic

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prices fall or other companies receive approvals. These drugs represent hundreds and hundreds of millions of dollars of R&D investment to the industry.
So on behalf of Fresenius Kabi, I request that the FDA allocates dedicated resources to reduce the ANDA and PAS backlogs in a timely manner and that the Agency issues a target action date for every backlogged application within 6 months.
Many of you have a service background, and this is an expression that Keith used when he addressed the CEO Summit I think a couple of weeks ago, and it's the principle that no file will be left behind. I think that's critical, Carole talked to it earlier, and I think it's critical to us.
Turning to transparency, things unfortunately have deteriorated here as well. As you've heard, the planning and execution of a generic launch is complicated and takes many, many months. Unless manufacturers have line-of-sight to

approval dates, they cannot start these preparations since GDUFA FDA is communicating less, not more.

As an example, my company filed a Paragraph 4 ANDA in September 2012, and we have had no response from the Agency in 2 years despite Paragraph 4 filings supposedly being one of the FDA's priorities. When we inquire -- and we do regularly, believe me -- we receive a standardized response asking us to contact the Agency in 3 months. We might as well talk to an answering machine. Market formation for this drug is expected to take place in May 2015, and 2 years after filing we still have no idea of whether Fresenius Kabi will have the opportunity to participate. It is deeply frustrating and challenging to manage our business in this communications vacuum.

I think maybe some of you experience that vacuum and that frustration in the restaurant at lunchtime. You study the guidelines, the menu, you submitted your order in plenty of time, no

food arrived. You finally managed to track down your project manager or waitress who could only tell you that the kitchen has a backlog of 3,300 orders and she can't tell you when your food will arrive. Frustrating. And unfortunately we had a deadline, too, to be back here at 5 past 1:00, so I know some of you didn't get food. So you know what it's like; right? This is the experience of our life.

My second request to you, therefore, is that the FDA provides clear and open communication to applicants. If our target action date is still 2 years away, tell us so that we can tell physicians, patient groups, and GPOs, and just as important, plan our business in manufacturing. Allow us to be part of the prioritization process. Not all of our submissions have equal priority, not all of them have equal commercial value. So we would like to help the Agency focus its limited resources appropriately, and this, too, requires a greater level of communication than we have today.

So thank you for the opportunity to

speak today. I encourage you to support the changes I've outlined, as they will have a positive effect on the FDA's mission, reputation, and on the U.S. health care system. We would welcome the opportunity to work more transparently and effectively with the Agency and we hope that this meeting will be the start of such a process.

Thank you.

MS. TOUFANIAN: Thank you very much.

Any comments from the panel?

Yeah, go ahead.

DR. UHL: Thanks, John. I appreciate your comments this afternoon. So about your request that all applications be given a target action date, how would industry respond -- or think about this because that plays into the prioritization scheme as such -- because of other aspects of GDUFA, the hiring, training, et cetera, so there will be more staff and more capacity. So being given a target action date that's 2 years out, that's not fixed because that could very well move. So you would want to know about every

single application that you have pending with a target action date that's not fixed.

MR. DUCKER: Well, it depends on -- then a target action date has little value if you don't consider it to be fixed or some level of commitment. I understand that a target action date would be a date by which you anticipated giving a complete response. Now, that may not be met 100 percent of the time, that I also understand.

But we're encouraging a dialogue here. We're all adults, and I think we're not going to hold you accountable to everything you say. There seems to be a fear when we communicate with the Agency that you don't say anything to us in case. You know? And we want to find a way in which we can have a dialogue with you that is responsible on both sides, and that requires trust, and that trust will only come through more and more open communication. But, yes, specifically, I would like to know, even if that date is 48 months from now, and even if it's not a guaranteed date, I would rather know that because it allows me to

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plan. We've got this 50 ANDA backlog. We don't know whether they're going to be approved in 3 months, 6 months, or 3 years. In 2017, we think 90 percent of them might be out; right?

DR. UHL: Right.

MR. DUCKER: Or at least have a complete response.

DR. UHL: Or they'll be acted upon.

MR. DUCKER: Exactly. But, you know, we have no knowledge at all, and 2017 is a long time away, and we have to plan business. We have to set budgets, we have to decide whether we're going to lay people off waiting for those applications to arrive, whether we're going to close down manufacturing lines waiting for those applications to arrive. Any transparency, even if it's arranged, even if you took those 3,300 and said these are A's, these are B's, these are C's, these are D's, and these are E's, allow us maybe to comment on that and say, well, we think that E is really important to us. You may think it's a fifth generic, but we think it's very important

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for these reasons, can you elevate it to a C? We have that process. And then you can say, well, all the A's, they're going to have 12 months, B's are going to be 18 months, C's are going to be 24 months, whatever it is, but give us something because this complete absence of information is killing us, at least it's killing me.

DR. UHL: I don't have a follow-on question.

MS. TOUFANIAN: Thank you very much.

MR. DUCKER: Thank you.

MS. TOUFANIAN: Tim?

MR. AMES: Well, I wanted to thank the panel for the opportunity to make a comment at this open session, but for the sake of time, I'm going to make this really brief. I did want to extend my sincere appreciation to the OGD people and other people from other parts of the Agency for putting together a Part 15 meeting where we could provide you with comments and you could listen to the comments from all of us.

I was going to comment, and I'm going to

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send these into the docket on three areas where I think you could do some guidance development in the area of generic drug development. And they include post-approval changes to tentatively approved PEPFAR application to allow for CBE type changes. The next would be to provide some clarification and guidance and clarity on inspection process revolving around the biomedical research facilities involved in bioequivalence studies both of clinical and analytical facilities. And then to reiterate what David Gaugh said about the suitability petitions, how they could be addressed and provide some metrics around the suitability petition so that they could be handled in an expeditious fashion. So I thank you, and we will send in our comments to the docket.

DR. UHL: Can I just ask a clarifying question?

MS. TOUFANIAN: Yes, please do.

DR. UHL: So thanks, Tim, for that. In your comments to the docket related to clarity on

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inspections and BE studies, will you be more specific about what it is you're looking for clarity on?

MR. AMES: Absolutely.

DR. UHL: Okay. Thank you very much.

MR. AMES: We'll take care of that in the docket. And thank you.

MS. TOUFANIAN: Thank you.

Candis?

MS. EDWARDS: Thank you for allowing me to come back. So I wanted to address the definition of first generics. You may not like what I'm going to say, but I have something interesting, let's put it that way.

So in addition to these general accepted criteria for the category of first generics, which today includes a first-to-file Paragraph 4 ANDA with a 180-day exclusivity, a first-to-market ANDA for which there is no generic competition and no blocking exclusivity, and also drug shortage products -- those are the three categories that are routinely prioritized today -- I would like to

propose a couple of additional categories that could be considered to be included in the definition for first generics.

The first category would be a product for which the sponsor receives documented evidence from an external source, such as a consumer or pharmacy, wholesaler, distributor, saying that the product is not commercially available or that the product has limited availability. However, the product has not yet made it to the FDA's drug shortage list. And we've had several situations where we've experienced that and have provided that information to the Agency in order to ask for their consideration to expedite a review. And this occurs in this fluidity of this whole industry that we're in where it will come and go with the specific products, so we would ask you to look at that category of products.

Another area is a product that is supported by one APA manufacturer who would provide API to all ANDA holders. If we were able to include products in that category where someone

were coming in with a different API manufacturer than what existed, even though there might be other ANDAs approved, that would help mitigate the risk associated with a potential shortage due to a single-source API drug product, and that would definitely have a positive impact on our health care system, which is what we're looking for when we look to define or make -- broaden this definition.

And the other concept goes to asking the Agency to work with the firms to prioritize let's say the 10 top percent of ANDAs pending at OGD, pending OGD approval for longer than 18 months, that would be defined by a sponsor based on accessibility and affordability of a specific product that would potentially bring added value to patient care and also have the potential to possibly positively impact the health care market. So it goes to who was speaking before me, the same concept that says there are some -- you know, for example, Amneal has over 100 ANDAs pending. We have about 8 percent of our ANDAs pending,

actually greater than that, that are pending longer than 18 months, and so if we were able to look at that bucket of ANDAs and say if you're going to prioritize in order to address the backlog, here is how we would ask that you consider let's say the top 10 percent in that category, we would look to have these prioritized because we would feel that they would have the most impact on a health care system and provide the most added value into the whole market.

So those are some thoughts on how we could potentially broaden that scope and also help FDA to give them the ability to prioritize and have a positive impact on the marketplace.

MS. TOUFANIAN: So one clarifying question with respect to that last category. Would that be from your description that would be restricted to the backlog --

MS. EDWARDS: Probably so. That would help, yeah.

MS. TOUFANIAN: And that would be sort of a one-time identification?

MS. EDWARDS: A one-time, yes.

MS. TOUFANIAN: Any questions?

(No audible response.)

MS. TOUFANIAN: Good.

MR. READ: Just one. It strikes me that your first one could almost be described as pre-shortage.

MS. EDWARDS: It could be, yeah.

MR. READ: So it's an interesting one in terms of trying to avoid a shortage before it happens.

MS. EDWARDS: Before it occurs, yeah. And I think we get information. We may, since we're dealing in solid products, we may get information. We have more direct contact with the consumer, so we may get information before it makes it through the processes at the Agency in order to get officially identified as a drug shortage product.

MS. TOUFANIAN: Anything else?

(No audible response.)

MS. TOUFANIAN: All right. Thanks very

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much.
MS. EDWARDS: Okay. Thank you.
MR. DILORETO: Good afternoon. My name is John Diloreto. I am the Executive Director of the BULK Pharmaceuticals Task Force. And I'm going to talk about a subject that I haven't heard too much today about, and that has to do with facility inspections. I heard it broached a couple of times. But when we began our discussions a few years ago under the original negotiations with GDUFA, one of our major concerns had to do with two aspects of facility inspections. One certainly was protecting the safety of the drug supply chain making sure that any drugs coming into the country met that same high standard from foreign facilities as they do from domestic facilities. And at the time, domestic facilities were being inspected at a rate of about every 2-1/2 years. Despite a legislative requirement that they be done every 2 years, 2-1/2 years was certainly close enough that no one was going to complain. But the second aspect of that certainly

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was leveling the playing field that the domestic manufacturers had to have a quality program in place to make sure that they met their regulatory obligations while it was felt that a lot of foreign facilities were actually skating by and never being inspected in some cases. So we felt like GDUFA was an excellent opportunity to kind of bridge that gap, understanding that it was going to take several years to hire the people, train the people, put them in place before actual inspections can be done at a frequency that was considered parity between domestic and foreign facilities, which is why within the GDUFA commitments the first couple of years there aren't any real inspection goals. Those goals for inspections typically are all at the back end of GDUFA.
That said, we were a little dismayed to see within an HHS memorandum earlier this year that FDA is scaling back by 40 percent the number of domestic routine surveillance inspections that it plans to conduct in FY2014 and 2015. When we

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all signed up for the program, I don't think we expected to see a reduction in domestic facility inspections, we expected those to remain largely the same with the real increase being done on the foreign facility side, understanding that it was going to take a time for the staff and resources to be put in place to do that, but we are here expressing concern about that reduction in domestic facility inspections.
Now, you might ask, "What's the big deal? We've got a couple of years to meet our goals." We do, but we also have to keep in mind that many of our domestic facilities who are doing business with other countries have to have an inspection done every 3 years, and if we are at 2-1/2 years to begin with and we are going to reduce that number by 40 percent, that certainly means a large number of facilities which are not going to get inspected within 3 years and in fact may not within 4 or 5 years. And we understand that this is a complex situation, which is why we also were emphasizing a risk-based prioritization for when

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these facility inspections were conducted. We felt certainly pre-GDUFA there were far too many inspections being conducted at facilities because they were easy or close, not necessarily for reasons having to do with concerns over quality of products being produced at that facility.
So while we're encouraged about the program thus far, we're concerned about the reduction of domestic facilities here, and we would like to make sure that when we reach parity, that that parity is for both foreign and domestic facilities and that we're still remaining in that 2-1/2 year range, which is what we all negotiated a couple of years ago. And that's all I have.
MS. TOUFANIAN: Thank you. Any comments or questions?
(No audible response.)
MS. TOUFANIAN: All right. Thank you very much.
MR. DILORETO: You're welcome. Thank you.
MS. TOUFANIAN: So that concludes our

session today. Keith will have some closing remarks, but before that, I just want to once again encourage comments submitted to the docket. A transcript of today's proceedings, as Martha indicated at the beginning of the day, should be available in about a month. And we encourage you to watch FDA's websites for other developments.

MR. FLANAGAN: And my only closing remark is I would like to thank our colleagues who put this together. That's Connie Wisner, Shaniece Bowens, Tawni Schwemer, Ashley Jones, Shannon Bacote, Pat Downs (ph), and Kim Giordano, as well as Maryll and Martha. Thanks.

MS. TOUFANIAN: Thank you, everybody, for coming.

(Whereas, at 3:12 p.m., the Generic Drug User Fee Amendments of 2012 Public Hearing on Policy Development -- Request for Comments Part 15 Public Hearing was adjourned.)

CERTIFICATE OF COURT REPORTER

I, MICHAEL FARKAS, the reporter before whom the foregoing hearing was taken, do hereby certify that the witness whose testimony appears in the foregoing deposition was duly sworn by me; that the testimony of said witness was recorded by me and thereafter reduced to typewriting under my direction; that said deposition is a true record of the testimony given by said witness; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this deposition was taken; and, further, that I am not a relative or employee of any counsel or attorney employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.

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MICHAEL FARKAS

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I, DEBORAH ARBOGAST, do hereby certify that this transcript was prepared from audio to the best of my ability.

I am neither counsel for, nor party to this action nor am I interested in the outcome of this action.

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DEBORAH ARBOGAST