UNITED STATES OF AMERICA
DEPARTMENT OF HEALTH AND HUMAN SERVICES

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FOOD AND DRUG ADMINISTRATION

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PUBLIC MEETING ON PROPOSED RECOMMENDATIONS FOR A USER FEE PROGRAM FOR BIOSIMILAR AND INTERCHANGEABLE BIOLOGICAL PRODUCTS FOR FISCAL YEARS 2013 THROUGH 2017

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FRIDAY
DECEMBER 16, 2011

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The meeting came to order in the Great Room, Building 31, FDA White Oak Campus, 10903 New Hampshire Avenue, Silver Spring, Maryland, at 9:00 a.m, Patrick Frey, moderator, presiding.

PRESENT
PATRICK FREY, DIRECTOR, Office of Planning and Analysis,
FDA, Moderator
STEPHEN SPIELBERG, M.D., Deputy Commissioner
for Medical Products and Tobacco
THERESA MULLIN, Ph.D., Director, Office of
Planning and Informatics, FDA
ROBERT YETTER, Ph.D., Center for Biologics
Evaluation and Research
LEAH CHRISTL, Ph.D., Office of New Drugs, CDER
AMANDA EDMONDS, ESQ, Office of Chief Counsel
KATHLEEN UHL, M.D., Office of Medical Policy,
CDER
JOHN JENKINS, M.D., Office of New Drugs, CDER

ALSO PRESENT

MARISSA SCHLAIFER, Academy of Managed Care Pharmacy

SHEIN-CHUNG CHOW, Ph.D., Duke University School of Medicine

THAIR PHILLIPS, RetireSafe

AHAVIAH GLASER, Generic Pharmaceutical Association

SASCHA HAVERFIELD-GROSS, Ph.D., Pharmaceutical Research and Manufacturers of America

ANDREW EMMETT, Biotechnology Industry Organization

C-O-N-T-E-N-T-S

P-R-O-C-E-E-D-I-N-G-S

9:00 a.m.

MR. FREY: Okay. Well, good morning and welcome to this public meeting on the proposed recommendations for a user fee program for biosimilar and interchangeable biological products.

I am Patrick Frey, Director of the Office of Planning and Analysis in the Center for Drug Evaluation and Research at FDA. And I'll be your moderator for today.

First allow me to briefly review some background information to explain the purpose of this meeting. The Biologics Price Competition and Innovation Act of 2009 is part of the Patient Protection and Affordable Care Act that became law in March 2010.

It directs FDA to develop recommendations for a biosimilar user fee program for fiscal years 2013 through 2017, and requires FDA to present these recommendations to Congress by January 15th,

2012.

Currently under the new acts transition provisions, user fees for a biological product are the same, regardless of whether the biologics license application is submitted under the new biosimilar pathway or under the current approval pathway for biological products. However, this authority will expire in September 2012.

FDA opened a public comment period in May 2011 to obtain feedback on the proposed principles, fee structure, and performance goals for a biosimilars user fee program.

Following that, FDA began regular consultation meetings with members of industry and public stakeholders, including patient advocates, consumer advocates, healthcare professionals, and scientific and academic experts.

These discussions lasted from June through September 2011. After administration clearance, FDA published a Federal Register

Notice outlining the proposed recommendations on December 7th, and posted the proposed performance goals and procedures on FDA's website.

The purpose of today's meeting is to discuss these proposed recommendations and offer the public the opportunity to present its views on the recommendations. A transcript of this meeting will be posted to FDA's website within about a month.

The public also has an opportunity to provide written comments to the public docket. The deadline for these submissions is January 6th, 2012.

By January 15th, FDA must transmit its proposed recommendations for a biosimilars user fee program to Congress.

Our agenda for today begins with remarks from Dr. Stephen Spielberg, Deputy Commissioner for Medical Products and Tobacco, followed by a presentation of the proposed biosimilars user fee program recommendations

from Dr. Theresa Mullin, Director of CDER's Office of Planning and Informatics.

We will allow some time for clarifying questions regarding FDA's presentation. However, any commentary should be reserved for the open comment period.

The FDA presentation will be followed by three public stakeholder speakers representing health professionals, scientific and academic experts, and patient advocates. We'll have a short break and after we reconvene, we'll hear from three speakers representing the industry perspective.

Each speaker has been asked to provide their comments on the proposed recommendations in ten minutes or less. If we happen to have time remaining at the end of the panel, we will take any clarifying questions you may have.

After the stakeholder panels, we will proceed to the open public comment session. If you would like to provide comment

during this session, please let me know or sign up at the registration table in the lobby during the break. Currently no one is registered.

We are also webcasting this meeting to a handful people. So I'll check in periodically to see if there are any questions from that audience.

The kiosk in our lobby is serving refreshments for purchase. And the restrooms are located down the hall behind the kiosk. That's all I have. So I will turn it over to Dr. Spielberg for his comments. Dr. Spielberg?

DR. SPIELBERG: Good morning. And on behalf of all my colleagues here at FDA, I'd like to thank all of you for joining us here today to provide your input on FDA's proposed recommendations for a biosimilars user fee program.

We've collectively made a great deal of progress in advancing a biosimilars

program since the enactment of the Biosimilar Price Competition and Innovation Act in March of 2010. And today's discussion of user fee recommendations will mark another milestone.

The Act give biosimilars and interchangeable biologics the sort of opportunities that Hatch-Waxman provided for generic drugs. With the abbreviated approval pathway now authorized by statute, biosimilar biologics can be legally approved by demonstrating, among other things, that they are highly similar to an already approved reference biologic product.

This means that as modern analytical tools progress and advance, biosimilar development should require less testing in animals and humans. Development is expected to be less risky, less costly, take less time, and approved biosimilar biologics are expected to be less expensive than the reference product.

The program created by this

legislation will provide tremendous benefits for patients, making available more affordable treatments, the clinicians will know are biosimilar.

The law may also lead to the development of new industries that will expand the opportunities for technical innovation and job growth. A win-win situation.

But getting this new type of product and new program off the ground will take new measures, and we are already operating in time of tight federal budgets. The proposed user fee program for biosimilar biologics creates yet another opportunity for a win-win.

The funding from these fees, paid by sponsors of biosimilar biologics, will provide FDA with needed resources, and provide prospective manufacturers of these products with a clearer and more predictable review pathway in the new product area.

With the added fee funding, FDA

can dedicate scientific staff to clarify policies and pathways of biosimilar development, addressing important questions, such as, just how similar is similar enough, when assessing a complex biologic product?

It will provide detailed review and consultation to sponsors during the development process, to help determine the most efficient next steps in analysis, or data collection, to demonstrate biosimilarity.

It will help review the marketing applications within predictable time frames. And continue to monitor the safety of these products and ensure the public confidence in the products once they are on the market.

During the past year, FDA has engaged with public stakeholders and with the regulated industry to discuss the design of a user fee program. The package we are reviewing today is a result of those discussions.

FDA has worked with stakeholders

to fashion a recommended package and a program that will provide strong support for biosimilar review under this new user fee program, while retaining strong support for biologic innovation review under PDUFA.

This approach reflects our view that both programs and both types of products are critical to advancing the public health.

The overall fee levels of this new biosimilar program are much the same as they were for innovator drugs under PDUFA, reflecting our assessment of the level of complexity and review effort that will be involved.

The proposed performance goals for biosimilars are also comparable to PDUFA, either quickly ramping up to the 90 percent level or starting at the same 90 percent levels that are currently established for performance goals under PDUFA.

The separate program we proposed for biosimilars is specifically tailored to

the shorter development pathways and the different types of evidence that will be required in marketing applications to support determination of biosimilarity, compared to a marketing application for an innovator biologic.

We believe that having this proposed program will ensure that the vision and intention for an abbreviated pathway will be a reality for these products.

In closing, I want to thank you again for engaging with us to provide your views of the proposed recommendations. After the review of the input we receive today, as well as through the public docket, we will prepare final recommendations for transmission to Congress in January 2012. Again, thank you all for being here today and providing your input.

MR. FREY: Thank you, Dr. Spielberg. Now we'll have a presentation from Dr. Theresa Mullin. And while she's getting

set up, if I can ask the FDA panel to introduce themselves quickly?

DR. YETTER: I'm Bob Yetter. I am the Associate Director for Review Management at the Center for Biologics Evaluation and Research.

DR. CHRISTL: Leah Christl. I'm the Associate Director for Biosimilars in the Office of New Drugs and the Center for Drug Evaluation and Research.

MS. EDMONDS: Amanda Edmonds. I'm an attorney in the Office of Chief Counsel.

DR. UHL: Kathleen Uhl. I'm the Deputy Office Director in the Office of Medical Policy in the Center for Drug Evaluation and Research.

DR. JENKINS: Good morning. I'm John Jenkins. I'm the Director of the Office of New Drugs in CDER.

DR. MULLIN: Good morning. I'm Theresa Mullin, Director of the Office of Planning and Informatics in the Center for

Drugs. And thank you so much for joining us here today.

This public meeting is one of the final milestones, as Dr. Spielberg was saying, in this process of our putting together a package of recommendations to forward to the appropriate committees in January.

So let's begin with the statutory directive to basically put forward a package for user fees. BPCIA directed FDA to develop recommendations for a user fee program for the biosimilar biologic products, otherwise known as 351(k) applications.

And in putting that package of recommendations together, we would follow a process that is rather similar to the sort of process we followed with the Prescription Drug User Fee Act reauthorization that we wrapped up the process of our consultations last spring.

And in this case again, consult with the scientific and academic experts,

healthcare professionals, patient and consumer groups, and others. And we put out a notice last spring to try to elicit interest and have people participate in that process, which we ran last summer, present those recommendations following, you know, getting a package put together, going through administration review and clearance after FDA completes its steps in the process, to have that package ready to forward to the Hill.

Before we do that, we actually have briefed the committees at a high level about this package that we were recommending -- because of the sequence of these things and the statute, that came first, to do those briefings.

We published a Federal Register Notice as you know. We're allowing a 30-day comment period that will take us through the end of the year a little bit into 2012.

This meeting is another opportunity to get your comments and input on

this package. And we will revise the recommendations as necessary before transmitting it to the Hill. And we hope to be on track to do that by mid-January.

And so this just lays out a time line showing you that process because this package of -- even the authorization for this program happened in March of 2010. The time frame for getting a package of recommendations on user fees follows the same time frame as PDUFA. And so we hurried up last spring to get the process underway, so that we could be compliant with that statutory time frame, putting out a request for interest from -- and who an industry would be planning to develop these products. Because it's a new industry, it's a new type of product, we needed to ask who should be participating, who plans to develop these products and thus, would create this emerging industry to negotiate with and talk about user fees with.

Similarly we asked for interest of

participating on the part of the public in discussions of recommendations.

We've put out a Federal Register Notice that described a potential program design so we could get some early feedback on that and try to start jump-starting these discussions because of the time frame.

So we held those discussions between June and September of this past year. And we've been in the process of having Department and OMB review the package since that time.

What do we hear from our public stakeholders in the course of these discussions last summer? There was concern that this program be appropriately funded because people are interested in having these products be available.

The promise of a more -- greater selection or availability of choices, and more affordable 351(k) products is very appealing to the public.

They wanted us to work with industry however, to make sure these products are safe and truly interchangeable, emphasize the healthcare impact of these products, allowing physicians to have products that they know are interchangeable with other biologics is considered another really valuable aspect of this.

Make sure there is sufficient funding, so that there is a level of certainty and sponsors know what to do to develop these new products. And make sure the fees are reasonable. And of course, we aspire to that.

We heard from industry, and also in some written input that we received, that we really should try to ensure that there is an optimal regulatory pathway that can be followed. And that's through a combination of consultation in the review process, and guidance that we would be providing to industry to help expedite early development and growth of this industry.

Ensure that there are sufficient resources so that we can do a review in a timely manner. That we would not be having to trade off support for 351(k) and 351(a), that's the innovator biologics, both of those programs are extremely important and we took that to heart.

And these products are complex and so we need to make sure we have the same level of post-market safety review and surveillance that we do with new drugs. And, again, have enough resources to accomplish this, but at the same time not discourage development of these products by charging a fee that's more than fair.

Now the challenge we face here, as I mentioned, is that this is really a new industry, a new type of product. So how do you structure a user fee program where there's emerging activity and interest early on in the development process, but not a mature industry?

What you see on -- so with the 351(a) products, the PDUFA-type biologics, new drugs, on the left we had, at the start of that program in the early 1990s, there was a fairly mature industry, on average about 120 new drug applications or biologic licensing applications that total NDA or BLA submissions, about 120 a year.

About 200 establishments were out there making these products, about 2000 drugs are still under patent and being marketed, that's essentially the fee structure for PDUFA. We put on those three elements.

And there was also a pretty well established history of appropriations funding for that program. And so the fees were added to those appropriations.

None of those things are in place really for these biosimilar biologics. And so we've had some challenge in trying to determine how to structure a fee program that would get us started and enable this industry

to start growing.

We're also in a tough budget climate as well, so we have limited expectations for lots of new appropriations for this program because we know there are many, many priorities competing for appropriated funds right now. And so we know that that's also a factor and a challenge.

So in developing this program, we came up with the four design criteria based on what we had gotten in the input from a PAR-15 hearing last winter, and other input that we had received from the stakeholders.

So we wanted to ensure that we had adequate capacity to do 351(k) review and get this program up and running, and successful, and not create unnecessary delay. We want 351(k) products to be developed, so we want to encourage that.

We think the complexity of these reviews and the development process is comparable, although different from 351(a)s,

and so we think a similar level of resourcing is going to be necessary for these reviews, as it is currently available for 351(a) for the PDUFA-type products.

We wanted to create a fee structure, however, that acknowledged that we don't have any marketing applications yet, or facilities, or products that are already on the market. And so how can we forward shift resources so that we are getting fee collections now, even during development?

To support the guidance and interactions with sponsors during development, which we think is really going to be critical to minimize the uncertainties and make that process as efficient and cost-efficient as possible. So that was our challenge.

And we also wanted to avoid redirecting money from 351(a) or, again, having to sort of have these programs compete. They both serve very important functions.

And so this is the fee structure

that we have agreed upon with industry to support or recommend to Department and OMB, and that we're sending forward to recommend to Congress.

And it's structured using the underlying -- kind of referencing the PDUFA fee structure. We basically are proposing that an annual fee be paid by a sponsor once they're established in a development program.

So once there's significant work going into a particular IND, and the companies come in and begin to meet with us, that we would charge an initial fee and then subsequently, an annual fee that would be set at ten percent of a PDUFA NDA fee.

And that would paid for each product in the biosimilar product development, otherwise known as BPD phase.

And basically in the first year it would be triggered by the submission of an IND, or by the request for a meeting that's going to go into some depth on a particular

product and subsequently, would be charged annually.

Those fees that are paid on that, the cumulative amount of BPD phase fee that's being paid would be subtracted from what would be paid when the marketing application was submitted to us.

So it essentially works out to be the same amount that would've been paid if you were a PDUFA product, but we forward-shifted some of those resources to support development phase review.

A sponsor can choose to deactivate or stop a development program. And basically has to withdraw the IND, but will not have to pay that annual fee anymore if that's done.

If they want to reenter the program, there's a reactivation fee that would be charged that's essentially twice the annual fee amount.

That's to discourage people from going in and out. But we think that it will

also give companies a way to, if they can't afford to fund more than one program at a time, or they need to sort of sequence their efforts, that this allows them some flexibility to do that.

Once a product is on the market, that product would start to pay an annual product fee. And the establishment in which that product is made, would have to pay an establishment fee.

Okay. The way we've structured these meetings are to provide a maximum flexibility for companies. And even though these little boxes are all lined up across, in a linear fashion, that's not the way we conceived this program working.

You can -- the Type 1, 2, 3, and 4 meetings represent meetings with -- and they're going to be described in guidance that we'll be issuing in the second quarter of fiscal year 2014, but essentially they have different time frames associated with them.

From the time of request to the time the meeting is held, different levels of complexity or depth of data that's being submitted to FDA to take a look at before the meeting, and that's why the different time frames come into play.

So the level of review that's being requested by the sponsor will vary. We heard that a lot from companies that, they're taking different approaches to how they're going to develop 351(k)s.

And we want to allow for and concur to that flexibility because this is new and we don't want to sort of stifle the innovation involved in figuring out how to develop 351(k)s.

The first meeting that a company may want to have to come in and talk to us, they're thinking about developing a 351(k), is a meeting that we would not be charging a fee for. That kind of exploratory conversation, come in and those meetings are free, if you

will.

But the others would indicate that you are now on a development pathway for a particular product. And those would be subject to, if it's the first time you're talking to us about a BPD Type 1, 2, 3, or 4 meeting, that would sort of trigger the start of payment of those BPD phase fees.

What kinds of activities are covered under this program and would be supported by the user fees? This is just to illustrate. This is similar to many of our other user fee programs. These are the components, necessary activities that are part of a pre-market review program.

So under the Review heading it would include meetings with sponsors, our review of INDs, our review of marketing applications, pre-approval advertising, supplements to the application, and post-market studies that might be necessary.

Our development of guidance

associated with this program, pre-approval inspections, and other post-marketing activities associated with biosimilar biologics. That's pretty standard.

Another component of this program that's very important is that there is a spending trigger. This is very common in our medical product user fee programs.

But there is a statutory condition that requires the Agency to spend at least $20 million, adjusted for inflation each year, from our non-user fee funds. So in other words, from our budget appropriations on biosimilar biologics activities, in order to have the authority to collect and spend the user fee funds for this program.

That way we have a balance of public input, public funding, and industry funding, as we do with our other medical product user fee programs.

It also gives this program a way to get started because it's so early on. We

don't expect large fee collections in the initial years.

This is to illustrate the ramp-up of the performance goals for this program. And as Dr. Spielberg was saying, there are a number of goals that are similar to those in the Prescription Drug User Fee Act.

And we'll start those at the 90 percent of cohort, being performed at that time frame, that we use in PDUFA to make these programs as comparable as possible, make the 351(k) program as attractive as possible as well to sponsors, because we want these kinds of products to be developed.

For these new types of review, we are ramping up rather aggressively to the 90 percent level. 3- for the review of an original biosimilar biologic product, we'll start at 70 percent of the cohort received, will be reviewed in ten months and acted upon in ten months, and ramp it up to 90 percent by the final year of the first five years of the

program.

And resubmissions will be reviewed in six months of the receipt date according to the same ramp-up.

There are a number of other goals. These are to make again, make the program comparable to what kinds of consultations and performance goals are available to 351(a) developers.

And so we're committing to the same time frames for the review and procedural goals for a sort of first cycle review performance like we have in the Prescription Drug User Fee Act.

The review of proprietary names, major dispute resolution, clinical holds, and special protocol assessments, as well as the meeting management time frames for setting up meetings. The time frames for having the meeting will be different as I mentioned before.

This is the next step for us after

we have this meeting, is to take the input that we've received through the docket and that we hear from you today.

And look at that against the recommendations that we're putting forward, try to determine if we need to make changes to that package. And then transmit those recommendations to Congress about mid-January. Thank you.

MR. FREY: Thank you, Theresa. Are there any clarifying questions from those in the room? All right, seeing none, I'll excuse the FDA panel and invite the public stakeholder panel up front, please?

So you're up first, right? Okay, so our first speaker will be Marissa Schlaifer, the Director of Pharmacy Affairs at the Academy of Managed Care Pharmacy.

MS. SCHLAIFER: I have to hold, okay. Or do you want me to talk, is it--thank you, Patrick. The Academy of Managed Care Pharmacy is pleased to provide comments to the

Food and Drug Administration on its proposed recommendations for a program for biosimilar and interchangeable biologic product applications for fiscal year 2013 through 2017.

And I'll start out by saying, I think my comments were already summarized by Dr. Mullin in her slide of the public stakeholder comments. So pretty much everything I'm going to say was up on her slide. So you did a great job there.

AMCP is a national professional association of pharmacists and other healthcare professionals, who serve society by the application of sound medication management principles and strategies to achieve positive patient outcomes.

The Academy's 6000 members develop and provide a diversified range of clinical, educational, and business management services and strategies, on behalf of the more than 200 million Americans covered by managed care

pharmacy benefits.

The Academy is pleased to share comments relating to the development of the user fee program for biosimilar and interchangeable biologic product applications submitted under the Public Health Services Act.

In addition, AMCP appreciated the opportunity to participate in the public stakeholder meetings that were held from June through September of 2011.

AMCP believes that funding the FDA at a dollar level sufficient so it may fulfill obligations to ensure medication safety and to develop an expedited approval process for biosimilars is absolutely necessary.

As a member of the Alliance for a Stronger FDA, AMCP believes funding the FDA at a dollar level sufficient so it may fulfill its obligation to insure medication safety is absolutely necessary.

The Alliance for a Stronger FDA

works to insure annual appropriations that will adequately fund the FDA's essential missions. Absent this funding to be provided in total by the federal government, the Academy supports a user fee program for biosimilar and interchangeable biological product applications.

Millions of Americans depend on biologic therapies and advances being made in the field of biotechnology. The field of biotechnology holds such great promise for the development of many new biologic products to treat such serious diseases as cancer, multiple sclerosis, anemia, and rheumatoid arthritis.

Biologics are certain to play an increasingly important role in the country's healthcare system, both in terms of scientific improvements in the treatment of disease and increased drug costs.

The Academy believes that an expedited approval process for biosimilar

products provides a needed incentive for the development of new therapeutic products that hold a promise of preventing, treating, or curing otherwise inevitable, untreatable, and incurable diseases.

This process will help ensure greater access to new therapies at costs significantly below those of brand name biologics.

Safe alternatives to some biologic drugs have existed for more than 20 years. An appropriately funded process for a regulatory pathway for FDA approval of these products is essential.

The Academy supports the following specific initiatives related to biosimilars. Applicants seeking approval of biosimilars should be required to conduct clinical studies as part of the approval process, if the FDA determines on a case by case basis that such studies are necessary.

Applicants seeking approval of

biosimilar products should be required to conduct postmarket studies as a precondition for approval, if the FDA determines on a case by case basis that such studies are necessary.

The FDA should have authority to determine whether or not an approved biosimilar is interchangeable with the innovator drug. And the manufacturer of an approved biosimilar should be allowed to use the same government-approved name as the innovator product.

The Academy believes that the FDA must have appropriate funding for the expedited approval pathway for biosimilar and interchangeable biologic products to function in a timely manner, while ensuring that such products are safe and effective.

The Academy will not address the specific dollar amounts necessary, but AMCP emphasizes the important positive healthcare impact of more cost effective alternatives for existing biologic agents. Thank you.

MR. FREY: Thank you, Marissa. Next we have Shein-Chung Chow, Professor at the Department of Biostatistics and Bioinformatics at Duke University School of Medicine.

DR. CHOW: Thank you. My name is Shein-Chung Chow. I'm from Duke University. And first I would like to thank the FDA for providing me this opportunity to share some of my thoughts regarding biosimilarity and the interchangeability from a scientific and academic perspective. Next.

In the next ten minutes also I will present some scientific controversial issues to justify why the user fee program is necessary for the regulation, and policy development, and the development of standards for a biosimilar product.

Basically, I think for biosimilarity I will touch the issues regarding the selection of the study endpoints, criteria for the biosimilarity, and

a non-inferiority versus equivalency.

And for the interchangeability, I will talk a little bit about the definition, and the concept of the alternating versus the switching, and some little comment on study design.

As stated in the Biologics Price Competition and Innovation Act, the biosimilar product is a product that is highly similar to the reference product, notwithstanding minor differences in clinically inactive components. And there are no clinically meaningful differences in terms of safety, purity, and potency.

And unlike the generic drug product with identical active ingredients, we are dealing with a similar, but not the identical issues for the biosimilar products.

Here we have the -- based on the definition from the BPCI regarding biosimilarity, actually we have two issues.

One is the, how similar is

considered so-called highly similar? And the second thing is, that in addition to the safety, purity, and the potency, should we consider similar in all spectrums of good drug characteristics?

And the list actually triggered the questions for the selection of a study endpoint for assessment of biosimilarity.

As we know that in practice it is almost impossible to demonstrate that a biosimilar product is highly similar to the reference product in all aspects of the good drug characteristics in a single study.

From here, I think that even we are interested in the demonstrating of biosimilarity in terms of safety and efficacy. Definitely we will choose the clinical endpoints.

We wanted to consider some kind of the parameters for the quality attribute for the manufacturing process and we may consider, I think that some kind CMC, the endpoints.

And for the drug adoptions, we may concede it at PK/PD, the endpoints and so on. Here I think there will be some controversial issues. Supposedly we have so many study endpoints to choose from in order to establish a so-called biosimilarity among the biosimilar products.

The question is that, which endpoints is telling the truth? Which can really be demonstrated biosimilar among the -- biosimilar products.

And how do we -- how do these, I mean the end points, translate to one another? And then, the next question is, how many studies do we need in order to demonstrate that they are biosimilar?

So the next issue I would like to talk a little bit about is the criteria for biosimilarity. As we know, the traditional approach is a one-fits-all criteria for the assessment of the average bioequivalence for generic drug products.

Here, we have also the sum -- the scientific, I mean, the issues. Now one-fits-all in the criteria may not be appropriate for biosimilar products, because it does not take into consideration of the variability, why biosimilar products are sensitive to variability.

And the next thing is that they are similar but not identical. As we know, that the biosimilar products are very sensitive to the variability. Usually I think we are dealing with the similar not the identical.

So the difference is in the two mean responses for the biosimilar product could be up to five to ten percent. Because they are not of the same, the identical active ingredient.

So I think the criteria that we should consider the so-called flexible criteria. Flexible in a sense that this criteria should adjust for variability and/or

the therapeutic index of the reference product.

The next issue I would like to attach is regarding the non-inferiority versus equivalency. There is a lot of discussion in the academia, in the literature regarding which way it should be going.

So if we take a look at this, this give a little bit of an idea in terms of the relationship between the non-inferiority and the equivalence.

If you consider mu (subscript) s is the mean response for the reference product. And then I think the delta is the equivalence limit. So if the test product, the mean response is within the mu s minus delta and the mu s plus delta, we consider that equivalence.

So the non-inferiority concept is related into the one side, if you consider left side. And then everything below the mu s minus delta is considered inferiority.

Everything beyond the point, that's non-inferiority.

If you take that right-hand side and the mu s plus delta, and then the right-hand side that's considered superiority and everything below that, that's considered non-superiority. So the concept of the non-inferiority actually is a so-called one-sided equivalence.

So this is a summary of the relationship between the non-inferiority and the equivalence. You can see that non-inferiority is a one-sided equivalence. And the non-inferiority consists of the concept for the equivalence and the superiority.

Superiority may be tested after the non-inferiority has been established. Non-inferiority is not the same as the equivalence. And the non-inferiority consequently is not the similarity.

Non-inferiority margin should be the same as the equivalence limit. And the

sample size calculation, in terms of the non-inferiority, tests for non-inferiority and tests for equivalence are not the same.

So based on the relationship between non-inferiority and the equivalence, I think that recently they have some clinical strategy for test for non-inferiority for the biosimilar product.

Basically, the concept is to utilize the concept of so-called asymmetric equivalence limit. And these are the strategies that we first considered to establish the non-inferiority. And then we would test for the non-superiority.

So in this case, I think that we were dealing with the, under the concept of the asymmetric equivalence limit, we were dealing with the two alpha, alpha-1 and alpha-2. And this will enable us to adapt a flexible biosimilarity criteria.

And then again, this also raise two critical issues. And the first issue is

the selection of the non-inferiority margin. And perhaps, I think that we can consult with the guidance recently published by the FDA in 2010.

But the other issue is the choice of the alpha-1, alpha-2, if we want to utilize the concept of asymmetric equivalence limit, in order to control our error rate of alpha.

So now I'm going to go on to talk about interchangeability. According to the BPCI, I mean, the definition of the interchangeability is actually considered two parts, part A and part B.

And for Part A, the biological product is biosimilar to the reference product and it can be expected to produce the same clinical results in any given patients.

Based on this Part A definition for the interchangeability, actually we can tell that there is a clear distinction between the biosimilarity and the interchangeability.

And one thing that I think, based

on the definition, number two, there actually is a concern whether it is possible to show that the same clinical result in any given patient.

Okay. The second part of the interchangeability, is referred to the risk of alternating or switching between the biosimilar product and the reference product.

The concept of switching and alternating can be summarized like this. For switching, I think it's referred to a switch from one biologic product to another.

That could be from a reference product to the test product, or from the test product to the reference product, reference to reference, or the test to test.

And the concept of alternating is a switch from one biologic product to another, and then switch back to the original biologic product. So that could include the reference to the test, test to the reference, and from the test to the reference and then back to the

test product.

So in order to address interchangeability, I think the measurements for the interchangeability and the criteria, and the statistical methods for assessment of "switching and alternating" should be developed accordingly.

How to do that? I think there is some recommendation. In order to address the switching, now Balaam's design, 4x2 crossover design, may be useful. And in order to address the alternating, then I think that maybe 2x3 dual design may be useful.

In order to address both switching and alternating, the modified Balaam's design, TT, RR, TRT, RTR are maybe useful.

Now I would like to summarize my presentation. For the biosimilarity, endpoint selection depends upon the drug characteristics of interest. For example, I mean the safety, purity, quality, or the efficacy, the potency, or something like that.

Criteria for biosimilarity should focus on variability. Because the biosimilar products are very sensitive to variability.

The concept of demonstration of a one-sided equivalence, that means the non-inferiority, with asymmetric equivalence limit may be useful.

For the interchangeability, it is difficult, if not impossible, to demonstrate "same clinical result in any given patient" in practice.

However, I think that it is possible to demonstrate same clinical result in any given patient with certain assurance. Based on all of this, I guess detailed regulatory guidances are needed.

So in summary, I think that user fees are necessary for regulation, and policy development, and also development of standards for the biosimilar product. Thank you.

MR. FREY: Thank you very much. Our next speaker is Thair Phillips, President

of RetireSafe.

MR. PHILLIPS: Thank you. I appreciate the opportunity to be here and to speak. I'm Thair Phillips. I'm the President and CEO of RetireSafe. We're a 20-year-old organization that advocates and educates for older Americans.

I'm here to speak for the 400,000 nationwide supporters, and their families and friends, who rely upon the safety and efficacy of the medicines they take.

These are the people who take the medicines that you approve. These are the people who rely on you to understand some of those slides that the good doctor from Duke put up.

And rely on me to understand them enough that I can advocate for them, who may not understand all of the intricacies, but certainly understand the safety that they rely on.

Science is on the verge of

discovering new cures in the large and complex molecule biologics. These new cures have shown to be difficult to create, let alone duplicate. My constituency depends on the fact that the medicines they get from their neighborhood pharmacy are safe and that they will work.

They may not understand the nuances of large molecule biologics, but they certainly understand and rely on the fact that their medicine is safe. They also have benefited from the fact that many of these life-saving and life-changing medicines are now available in generic versions which save them money.

Older Americans hope that the marketplace will soon also provide access to biosimilars, just as they did to generics. That being said, we realize that the process of manufacturing biosimilars is far more difficult and complex than generics have been.

We are here to support the FDA in

moving forward on this pathway, but to say as well that the safety of the patient who will take biosimilars must always be the prime concern.

We believe the rigorous evaluation process which are applied to the development and manufacture of biologics need to be appropriately translated to the manufacturing of biosimilars. Public safety and patient health demand no less.

User fees are key to this process. We believe that the user fee process that works for evaluating new medicines is appropriate for the evaluation of biosimilars, given the complexity of the manufacturing process.

We think it is important for Congress to recognize the impact on the FDA in ensuring safe biosimilars and to allot the needed funds required to accomplish this important task.

We'd hate to see revenue diverted

from approving new cures to dealing with biosimilars simply because there were not adequate user fees or the funding allotted by Congress was not sufficient.

Medicine saves lives and saves money. We saw, in the introduction of Part D, that the availability of drugs to older Americans had a great impact on reducing hospital visits, which overall saved money. We see that happening at the availability of new medicines and new cures.

A cure for Alzheimer's or diabetes or heart disease will save hundreds of billions of dollars and could have a huge impact on our healthcare system. A lack of FDA resources should not be a reason for a delay in the access to new cures.

RetireSafe believes that developing a viable pathway for biosimilars is an important next step. We support it. We need it. We want it done right. Thank you.

MR. FREY: All right, thank you,

Mr. Phillips. Are there any questions from the audience or these three panelists? All right, seeing none, I think we are at our break actually. We're ahead of schedule.

Do people still want a break? Okay, I'm seeing some nods. So we will reconvene at about 10:05.

(Whereupon, the above-entitled matter went off the record at 9:51 a.m. and resumed at 10:15 a.m.)

MR. FREY: Okay. Our first speaker will be Ahaviah Glaser, Vice President for Policy and Strategic Alliances at GPhA.

MS. GLASER: Good morning, thank you very much. I've already been introduced, but my name is Ahaviah Glaser. I am new to GPhA in the role of Vice President for Policy and Strategic Alliances.

GPhA would like to thank the FDA for holding today's meeting on the user fee program for biosimilar and interchangeable biosimilar products.

We represent manufacturers and distributors of finished dose generic pharmaceuticals, bulk pharmaceutical chemicals, and suppliers to the generic industry.

Generic pharmaceuticals now fill 78 percent of all prescriptions dispensed in the United States, but consume only 25 percent of total drug spending.

Between the rapid rise in the number of biologic drugs and regularly expanding indications for the products that are already on the market, biologics are becoming an increasingly common treatment option for conditions such as cancer, rheumatoid arthritis, and multiple sclerosis.

Allowing the FDA to approve less expensive biosimilars should help patients facing the substantial out-of-pocket costs that can be associated with biologic drugs.

There are currently more than 150 biologic medicines available, many of which

have either lost patent protection or soon will be off-patent. And it is expected that by 2012, nearly half of the products approved by FDA will be biopharmaceuticals.

However, while affordable generic versions of biologics are available in 11 countries around the world, there is not yet generic versions available for most of these off-patent products in the U.S.

By every account, competition from generics in the biologic sector would save patients, insurers, and the Government billions of dollars each year in treatment costs. Estimates from various economic impact studies pin the projected savings from $42 billion on the low end, to a high of $108 billion over the first ten years.

Several of our member and affiliated companies already sponsor high-quality, safe, and effective biosimilars in Europe and other regulated markets.

GPhA is committed to enabling

access to these affordable, critical medicines for U.S. patients. In fact, this is a top priority for GPhA and quite frankly, the number one reason I left AARP to come to GPhA this last month.

While GPhA will be working for a further abbreviated pathway for biosimilars, we are pleased to see FDA's commitment to resource and implement the abbreviated pathway which was enacted as part of the Affordable Care Act, and we were honored to participate in the biosimilar user fee negotiations.

As a participant in these negotiations, GPhA expressed its support for user fee funding to a level that will provide adequate resources for the incremental increase in scientific advice and applications resulting from the new pathway.

GPhA supports and will always support consistent regulatory standards being applied to all biologics, and recognizes the FDA's need for adequate resources to fund

these new activities.

This proposed user fee agreement for biosimilar and interchangeable biological products will help make this a reality.

As negotiated, this user fee proposal will result in expedited access to low cost, to high quality generic drugs for Americans. And will further safeguard the quality and accessibility of our nation's drug supply.

On this occasion GPhA wants to affirm our commitment to continue work on a robust, equitable, and worker user fee program. This program will give FDA much-needed resources, and both industry and patients will benefit from gaining a higher degree of certainty in the timeliness in application reviews.

I thank you again for the opportunity to speak today, and I look forward to working with our partners at the FDA in the days and months to come to finalize the

establishment of this important program.

I've just cut my remarks very brief, as we are quite pleased with where things stand right now. And I'll look forward to joining the other panelists for questions. Thank you.

MR. FREY: Thank you. Our next speaker will be Sascha Haverfield-Gross. Sascha is Vice President of Scientific and Regulatory Affairs at PhRMA.

DR. HAVERFIELD-GROSS: Good morning. My name is Sascha Haverfield and I'm speaking today on behalf of the Pharmaceutical Research and Manufacturers of America, PhRMA.

PhRMA appreciates the opportunity to participate in this public meeting and share its views on the proposed biosimilars biological product authorization performance goals and procedures.

As we heard earlier today, an abbreviated approval pathway for biosimilar products and interchangeable biological

products was established in the Biologics Price Competition and Innovation Act of 2009, BPCIA.

And PhRMA, as the representative of the country's leading pharmaceutical research and biotechnology companies, has been supportive of FDA's ongoing efforts to implement BPCIA in a manner that ensures patient safety and encourages biopharmaceutical innovation.

PhRMA was a participant in the technical negotiations with the U.S. FDA. That, together with input from patient and healthcare provider groups, resulted in the Biosimilars User Fee Act, BsUFA, performance goals letter.

The draft FDA performance goals are consistent with Congressional intent to create a unique user fee program to meet the needs of biosimilar product applicants, and to provide the FDA with the means necessary to build, essentially from scratch, its capacity

for science-based review of biosimilar applications.

PhRMA believes that the draft performance goals will benefit patient safety and public health, as biosimilar products will be required to meet FDA's high standards for safety, purity, and potency.

Several of PhRMA's member companies for many years have been actively engaged in the development of innovative biological products. In addition, some of PhRMA's member companies have expressed their intent to develop biosimilar products.

PhRMA therefore supports the development of a robust user fee program for biosimilar products, to provide FDA with the resources needed to review biosimilars without diverting resources from the review of innovative medicines.

PhRMA is further supportive of the appropriation of Congressional funds for this purpose, a feature common to existing user fee

programs, to ensure that user fees supplement rather than supplant appropriations.

PhRMA believes that the review process for biosimilar and interchangeable biological products must be scientifically rigorous, timely, and, above all, protective of patient safety.

Achieving these objectives will require a clear and formalized regulatory pathway for biosimilar products, quality standards that meet standards for innovative products, and adequate pre-clinical and clinical testing to ensure that biosimilars are both safe and effective.

PhRMA recognizes that, for the purpose of this first authorization, the biosimilar user fee program must be structured differently from other user fee programs.

It will be necessary, for example, to collect user fees earlier in the biological product development process, until fees from licensing applications can provide sufficient

ongoing revenues to support the Agency's activities.

It must be understood, however, that the proposed user fee program for biosimilar products, and in particular the provision for payment of a portion of the application fee at the time of an IND submission, and yearly thereafter, is a stopgap measure subject to review at the time of BsUFA's reauthorization in 2017.

As we have heard earlier this morning, among the key aspects of FDA's proposed BsUFA performance goals is the expectation for FDA, in fiscal year 2013, to review and act on 70 percent of original biosimilar application submissions within ten months of receipt, and to review and act on 70 percent of resubmissions within six months of receipt.

As the Agency's review capacity for biosimilar products develops, review performance goals will gradually increase.

The BsUFA performance goals further provide for specific FDA sponsor meetings to facilitate the biosimilars development phase.

This provision includes a special protocol assessment mechanism for clinical study protocols that are intended to establish biosimilarity and/or interchangeability with a reference biological product, to help ensure that the study design is adequate to meet scientific and regulatory requirements for approval.

The proposal also calls for FDA to issue guidance on procedures for meetings between the Agency and sponsors prior to submission of a biosimilar licensing application. And PhRMA urges the Agency to accelerate its guidance development in this area.

Eventually, the biosimilar application process should be codified in regulations similar to all other approval pathways.

Additionally, user fees will be applied to enhance patient safety through implementation of measures to reduce medication errors related to similar-sounding proprietary names, unclear labeling, and confusing package design.

So, in summary, PhRMA supports the proposed BsUFA performance goals agreement as a means of advancing public health by making adequate resources available to FDA to build a capacity for regulatory review of biosimilar products, consistent with the Agency's high standards for patient safety and scientific rigor.

PhRMA and its member companies are committed to working closely with FDA and all stakeholders to establish a science-based approach to the development and review of biosimilar and interchangeable biological products.

PhRMA therefore urges Congress to authorize BsUFA and allocate Congressional

appropriations in support of this program for fiscal years 2013 through '17. Thank you.

MR. FREY: Thank you, Sascha. Finally, we have Andrew Emmett. Andrew is Managing Director of Science and Regulatory Affairs at BIO.

MR. EMMETT: Good morning, everyone. And on behalf of the biotechnology industry organization, thank you for the opportunity to comment on the proposed user fee program for biosimilar and interchangeable biological product applications, or BsUFA.

BIO supports FDA's ongoing implementation of a well-constructed, science-based pathway for the approval of biosimilar products that promotes patient safety.

A transparent, predictable, and balanced regulatory framework for the review and approval of biosimilars, accompanied by reasonable performance goals and a dedicated, independent funding stream will ensure that FDA can facilitate the development and

evaluation of biosimilar products, while also continuing to prioritize the review of innovative drugs and biologics, so that safe and effective new treatments, many for currently untreatable and serious diseases, can be made readily available to patients.

BIO represents more than 1100 biotechnology companies, academic institutions, and state biotechnology centers and related organizations across the U.S. and 30 other nations, and BIO members are involved in the research and development of innovative healthcare products.

Over the last 20 years, biotechnology has created hundreds of new therapies to help extend and improve the quality of life for millions of patients suffering from serious and cruel diseases, such as cancer, HIV/AIDS, arthritis, and multiple sclerosis, and our industry holds great promise for the advancement of the next generation of cures.

Throughout both the legislative consideration of the Biologics Price Competition and Innovation Act, BPCIA, and ongoing implementation of the pathway, BIO has articulated several key principles that will promote the development of an effective regulatory framework for biosimilar products.

First, ensuring patient safety. Second, recognizing scientific differences between drugs and biologics. Third, maintaining the physician/patient relationship. Preserving incentives for innovation, ensuring transparent statutory and regulatory processes, and finally, continuing to prioritize FDA review and approval of new therapies and cures.

BIO believes that the proposed user fee program is consistent with these principles and supports Congressional authorization of the program.

The establishment of a stand-alone, independent biosimilars user fee

program is consistent with Congressional intent and precedent established under other user fee programs.

BIO recognizes that a 351(k), biosimilars applications will raise novel and complex questions of science and law, requiring substantial time, expertise, and additional resources to ensure a thorough regulatory review.

BIO believes that one of the principal goals of this new user fee program must be to ensure that the workload associated with biosimilar applications does not harm the Agency's ability to efficiently review innovative drugs and biologics, and that new treatments continue to have the highest review priority.

Accordingly, we agree with FDA's principle that the Agency needs sufficient review capacity and dedicated user fee resources for 351(k) biosimilar applications to ensure that resources are not redirected

from innovator reviews.

Additionally, BIO recognizes that historically, most user fee programs have been established on a pre-existing base of appropriations.

However, given the recent establishment of the biosimilars program at FDA, only modest appropriations are currently allocated to the program, which are inadequate to meet the anticipated workload demands.

To facilitate an equitable balance of fees and appropriations, FDA and industry support a trigger provision similar to existing appropriation triggers and other user fee programs, that would ensure that FDA allocates adequate appropriations to the program.

BIO encourages Congress to recognize the importance of a well-resourced and viable biosimilars pathway at FDA, and we request that adequate new funding be appropriated for the program.

The biosimilars program also establishes a unique biosimilar product development fee, which is ultimately deducted from the sponsor's application fee.

Since there is no established biosimilars industry facility base, or product base to form a stable funding source for these activities that occur before submission of the application, it's important to front-load the fees through the product development fees, so the Agency has available resources to meet with sponsors during development and provide scientific advice and feedback.

It should be noted, however, that the assessment of a product development fee is unique to this situation with respect to biosimilar products and should not establish any precedent for IND fees under the Prescription Drug User Fee Act.

Additionally, any IND-associated fee should sunset permanently when both PDUFA and this new user fee program are reauthorized

in five years.

BIO appreciates the opportunity to comment on the particulars of the biosimilars user fee program. And we look forward to additional opportunities to engage with FDA and other stakeholders in the broader issues related to implementation of the biosimilars pathway.

A transparent, open, and science-based implementation process that engages the public and regulated industry, will only serve to strengthen the regulatory framework.

For example, we look forward to commenting on FDA's pending draft guidances. We also encourage the Agency to hold additional workshops and public meetings to facilitate an ongoing dialogue.

In particular, there are three issues directly related to FDA's workload and review process activities that BIO has raised in previous comments, and that we continue to believe the Agency should address proactively,

as part of its ongoing implementation, in order to promote transparency, confidence, and predictability and to ensure the successful use of the pathway.

First, we encourage FDA to clarify which types of applications would be accepted for review under the 351 innovator pathway versus the 351(k) biosimilar route.

The Agency should reiterate that 351(a) innovator applications will require a full complement of pre-clinical and clinical data and may not reference in any way or seek to rely on innovator products' prior approval or associated data.

Allowing a biosimilar product to utilize the 351(a) pathway would undermine the careful balance of benefits for innovators and follow-on sponsors established in the BPCIA.

Second, to ensure that limited Agency of resources are directed only to those applications that are in full compliance with the statutory requirements for exchange of

patent-related information, we propose that FDA institute a simple administrative certification process as part of the 351(k) marketing application acceptance process.

Such a mechanism will help to ensure that any patent disputes that may impact the marketing of a biosimilar can, consistent with Congressional intent, be resolved efficiently and largely prior to a biosimilar launch, while also facilitating the Agency's prerogative to devote its resources to those applications that are complying with the statute in good faith.

Finally, given that the same review divisions will review both the innovator product and the biosimilar, it's critical that FDA clearly define the process for review of 351(k) applications to assure protection against disclosure of trade secrets and confidential commercial information from a reference BLA.

And that approval of the 351(k)

application does not rely on any data or information from the reference BLA that's not publicly disclosed, publicly available.

In addition, a technical correction of FDA's disclosure regulations is necessary for harmonization with the BPCIA, reflecting the current view that biologic application information is competitively sensitive.

In conclusion, BIO supports enactment of the proposed biosimilar user fee program, which will provide FDA with adequate resources and promote predictability in FDA's biosimilar review process, while continuing to promote the development and evaluation of innovative therapies for unmet medical needs. Thank you.

MR. FREY: Thank you, Andrew. Are there any questions for the industry stakeholder panel at this time? All right, seeing none, thank you very much.

And I'll invite the FDA panel back

to the table. We have one public comment for this session. I'm told that there's a question or a comment from Bruce Leicher of Momenta Pharmaceuticals.

MR. LEICHER: Good morning. I'm Bruce Leicher and I'm Senior Vice President and General Counsel at Momenta Pharmaceuticals.

Momenta is a biotechnology company engaged in the development of biosimilar and interchangeable biologics, as well as complex generics and novel products.

We use analytical and biocharacterization tools and methods to demonstrate similarity and interchangeability. We then use these tools, in concert with process understanding, to guide manufacturing process development.

And we believe that the science associated with better understanding of these products is rapidly advancing, I think as you heard this morning.

And as a result of the enactment of this pathway, it's encouraged that, and that for the pathway to succeed, the Agency will require significant resources and staffing. And for that reason, a separate user fee program that assures timely and adequate funding is essential for that success.

And for this reason alone, we applaud the Agency for its recommendations and all the hard work they've put into working with stakeholders over the past six months.

I would like to highlight why. As Dr. Mullin noted earlier, fee collection before an application is filed is a key aspect of this program. Substantive pre-application meetings will encourage investment in new approaches and methods that are critical for the development of high-quality and safe biosimilar products.

It also recognizes that multiple technical approaches should be encouraged and

that the pathway needs flexibility to allow for today's and tomorrow's innovative development options.

The meeting process allows for applicants to propose how they will demonstrate similarity and interchangeability and satisfy the statutory requirements, without dictating a particular approach.

It contemplates that the science is evolving and will continue to evolve. And that development of biosimilars will require new Agency expertise and staffing.

Second, we fully support a biosimilar user fee that is equivalent to the PDUFA fee. Without this full fee, funding, in our view, would just be inadequate.

Third, we enthusiastically support the meeting process, the inclusion of metrics, and more importantly, the requirement that the Agency provide written advice following each meeting.

This process encourages each

applicant to propose innovative approaches to demonstrate that a biosimilar product candidate is highly similar and/or interchangeable.

Applicants will be able to engage with scientific staff at the Agency in a transparent and timely way to ensure that biosimilars are safe, pure, and potent.

We also support the inclusion of meetings that allow for timely review of protocols, as well the inclusion of a dispute resolution mechanism, like that available under PDUFA.

We'd prefer that metrics start at closer to 100 percent achievement, and encourage the Agency to strive to do so, and particularly with the meeting process. We recognize that it's going to ramp up over the first few years.

Our view is that meetings, if they're well conducted, offer the opportunity to actually accelerate development and reduce

the level of effort for all involved.

Finally, we support the inclusion of establishment fees and product fees to ensure, as others noted, that the inspection and post-approval monitoring activities that the Agency has to maintain do not create conflicting demands that can dilute resources that need to be available for new applications.

And while we're really pleased with where the Agency's proposal has come out, we do have some concerns as we approach the upcoming legislative process. During the legislative debate, proposals were made and rejected by Congress because they could've undermined the success of the pathway.

Some of these proposals could be raised again on the Hill and, if added to the bill, seriously undermine the pathway's attractiveness and future success.

We urge the Agency to oppose these potential modifications. For example, the

BPCI Act made substantive guidance on how to develop a biosimilar or interchangeable biologic optional for review of applications.

This affords the Agency the scientific discretion to determine whether and to what extent non-clinical and clinical data are required.

This discretion is essential to driving applicants to innovate and propose new and better ways of developing similar and interchangeable products.

The meeting process creates a constructive process for doing this and implements a policy that does not mandate that one-size-fits-all and can assure quality.

Similarly, some have or may advocate that as part of the application fee process, applicants certify that they've delivered their confidential 351 application to a reference brand product company under the patent exchange portion of the law.

The BPCI Act is explicit in that

it does not embroil the Agency in the patent clearance and exchange process. The BPCI Act assigns to private litigants and the courts management of when and whether an applicant can decide to turn over its application to trigger the patent exchange and litigation process.

The law provides for an explicit legal remedy for failure to do so and does not delegate authority to the Agency.

Just as with a full BLA, the Agency should maintain the confidentiality of the application. And it's up to the applicant to elect whether to disclose.

Finally, some have or may advocate that, as part of the proprietary name review process, separate non-proprietary names be created for each biosimilar and interchangeable biologic.

We believe that biosimilar is just that, highly similar. And that some form of differentiation, whether through better track

and trace programs, perhaps in naming or in labeling, may be appropriate.

But an interchangeable biologic, by definition, is interchangeable under the law without the review or intervention of a physician, and must share the same non-proprietary name and perhaps, for that matter, labeling, to facilitate the objectives of the law.

We urge the Agency to reject any proposal that would handicap the pathway and the incentive to develop affordable interchangeable biologics.

To sum up, we're very pleased with the Agency's proposal to adopt biosimilar user fees that are coupled with substantive review meetings, mandatory advice metrics, and an assurance of staffing and resources.

We believe this reflects forward thinking on the Agency's part and we look forward to the enactment of the user fee bill.

MR. FREY: All right, thank you

for that comment. Are there any other comments in the room? I believe I see two mics, if anybody wants to step up.

All right, seeing none, I think we'll move to close. Okay.

Just a few thanks to the panelists for providing your input. Thank you to the FDA staff, Rokhsana Safaai-Jazi and Manju Thomas, and the White Oak Conference Center for helping to set up this meeting.

Quick reminder that the docket closes for public comment on January 6. Tick-tock, get your comments in. And there are instructions in the notice about how to submit comments. And if there's nothing else, we'll close. Have a safe holiday and see you later.

(Whereupon, the above-entitled matter went off the record at 10:43 a.m.)