U.S. DEPARTMENT OF HEALTH AND

HUMAN SERIVCES

FOOD AND DRUG ADMINISTRATION

PUBLIC MEETING

ON BIOSMILAR USER FEE ACT

(BsUFA)

Friday, December 18, 2015

FDA White Oak Campus,
10903 New Hampshire Ave.,
Bldg. 31 Conference Center
Silver Spring, MD

Reported by: Christine Allen,
Capital Reporting Company

A G E N D A

P R O C E E D I N G S

(9:03 a.m.)

DR. TOIGO: Good morning, everybody, and welcome to this public meeting on the reauthorization of the Biosimilar User Fee Act. My name is Terry Toigo and I'm the Associate Director for Drug Safety Operations in the Center for Drug Evaluation and Research. My job is to be your moderator today.

Today's meeting is an important step to begin to gather input from stakeholders on features of the BsUFA program in advance of the discussions that will occur with the regulated industry.

We have a full agenda for today's meeting. We will start with Dr. Janet Woodcock, Director of the Center for Drug Evaluation and Research, and she will get us started with opening remarks. You don't have to come up yet, Janet. I'm going to go through the logistics.

That will be followed by Leah Christl, who is the Associate Director for Therapeutic

Biologics in the Office of New Drugs in CDER, and she will provide a presentation on the BsUFA background and the reauthorization process.

Then we will have panels. The panels will provide perspectives from the following types of groups. We will have consumer and patient advocates, health care professionals, the regulated industry, and then our last panel will be scientific and academic experts.

After the panel presentations, Theresa Mullin, Director of the Office of Strategic Programs in CDER, will then provide some remarks.

At the end of that, there will be an opportunity for public comment. If you wish to speak during the public comment session, you need to sign up at the registration desk, and I ask that you do that before we have the break, then we can figure out how we want to set up the last session. If you want to speak, if something comes up in the first part of the meeting and you decide then you want to speak, as long as you can sign in with the folks at the registration desk, we can

take care of that.

Each of our panelists will have 10 minutes to present the perspective from their organizations, and we are going to ask you to adhere to that time frame. It will be my job to let you know when you approach your time limit, and your microphone will not cut off, but I will politely ask you to move on if you get to your 10 minute time frame.

FDA provided two questions in the Federal Register Notice to help panelists in the preparation of their comments. The two questions: What is your assessment of the overall performance of the BsUFA program to date, and what aspects of the BsUFA performance goals should be retained, changed, or discontinued to further strengthen and improve the program.

BsUFA reauthorization deals with process enhancements and funding issues. Policy issues are beyond the scope of the reauthorization process. There is also a public docket that will be open until January 19 to which you can submit public

comments, and speakers, if you have additional comments after your presentations and you want to submit something in writing, we ask that you do that to the docket.

Brief logistics, housekeeping items. We will have a 20 minute break at 10:30. Food and beverages are in the lobby. I'm sure most of you are familiar with that process, since you have been here before. The restrooms are down the hall and to the right.

That is our opening and logistics. I'm going to turn it over to Dr. Woodcock, and she's going to get us started for today. Thank you all for coming. We appreciate your participation in this process.

DR. WOODCOCK: Thanks, Terry. Good morning, everyone. Here we are, bright and early, talking about the user fee program. I'd like to thank everyone for coming today to this meeting. It's really important to us to have public input as we go through this renegotiation process.

The purpose of the public meeting really

is to hear the stakeholder views from the wide variety of stakeholders as we consider whether to retain, to change, or discontinue the current BsUFA performance goals in any next BsUFA that there might be. That is really the purpose of the meeting. We really want to hear input from everyone about that.

The first Biosimilar User Fee Act or BsUFA was over three years ago and allowed FDA to begin development of the infrastructure it needed to support this new program. We started out with nothing, and we didn't really have an appropriation for this program, so it was foreseen that we would develop a user fee program to support these activities. We had to get started before we had appropriation or before we had any money for the program.

We created for the industry when we started the BsUFA program -- we had the statute first, then we got BsUFA, is what I was trying to say. BsUFA really allowed us to begin this infrastructure and to figure out how to do funding

of the program when in fact we didn't have any marketed products.

We created the biosimilar product development program, and that provided a mechanism and structure for collection of development phased fees, which is quite different than our other user fee programs that are related strictly to applications and marketed products.

We did this because the development phase for this was unknown, developing a biosimilar was viewed to be intense, and since the biosimilars by definition are supposed to have less in the clinical development phase, it was felt there would be much more in the product development and comparison phase, and that would be during the IND process.

This allowed the agency to work toward devoting additional resources to meeting with companies regarding products they were developing to help streamline that development process, so that companies as they were developing the new biosimilars could do the right things and could

get good advice from the agency about what we were looking for.

Hopefully, this whole pipeline, once it became mature, would lead to safe, effective, and possibly more accessible biosimilar products for patients.

The accomplishments of this program -- first of all, we did approve the first biosimilar in the United States in March of 2015. That was RCO, everyone knows, or Filgrastim-sndz, which is a biosimilar to Neupogen or Filgrastim, which is a reference product that is licensed by the FDA, and the indication is to stimulate white blood cell growth in patients with cancer and help them fight infection. It has a number of other uses. We published three final guidance's in 2015, and we have published five draft guidance's since 2012.

We are aware that development of biosimilars is really a global activity, that there has been a program going on in Europe for longer than we have had legislation for biosimilars, so we work with the international

regulators and others, like the World Health Organization and so forth, on all the different matters that have to do with biosimilars in all these different regions.

We hope to make sure we do have regulatory convergence so there is more or less an uniform global structure around biosimilars and how they are developed and how they are regulated.

We have begun and we want to continue outreach efforts toward the public and clinicians about biosimilars. I think I've concluded that really targeted outreach, when you approve a Filgrastim, the hematologic community, the oncologists, they are going to be the most interested in that. Your dermatologists aren't going to be interested.

We're not going to try to educate the world on these. We're going to try to educate the relevant specialties that use the reference molecules about the biosimilars in a timely manner, when a biosimilar is coming available, so they can understand.

I can say for my community, the rheumatologic community, there has been ongoing discussion. I've been at their annual meetings for years talking to them about this. Leah Christl has come with me sometimes and talked about it.

I can say there is still considerable concern by the clinical community about the use of biosimilar products and what's going to happen. It's the unknown. Going forward in the next program, as more biosimilars become available, this part of the activity is going to become more important.

We certainly saw that years ago with the generics program. There was a considerable amount of resistance in the clinical community with the use of generics, that they were inferior. There is still some residual of that but not very much since 88 percent of dispensed drugs in the United States are generic drugs. At the beginning of the program, we forget, because it was a long time ago, there was clinical resistance.

That is going to be an increasingly

important part of the program. First, we built the infrastructure, the conceptual framework for how biosimilar would be evaluated and how its biosimilarity would be evaluated. We need to build and publish the conceptual framework for the inter- changeability part, and we are working on that.

Then we had to develop the infrastructure of the machine to get the reviews done, and how we would structure the review process for biosimilars and all that would work, and we have done that, and then anticipating approval of a number of biosimilars over the next several years, we're going to have to figure out how to work with the clinical community and help educate them about this.

There are challenges as this program is dynamically evolving. There is a large number of industry biosimilar development programs underway, and that is terrific. That is really good news, I think, for consumers. It means we are going to have a robust program.

As of November 2015, there were 59 programs in the biosimilar product development program. That doesn't mean that is every single biosimilar program there is in the world. That means that's the people who have signed up for our program and are paying user fees, and are getting advice from us. That is a lot of entities.

As I said, when we started out, when the statute was enacted, we didn't get additional resources for this program. We have carved those resources out ourselves out of our appropriation that was existing and we have some increment from the biosimilar development program from the fees that we charge under that, which is the current user fee program, and then there is the application fee.

We really need to figure out going forward, if we get a significant proportion of these 59 products come forward and turn into applications for marketing, how we are going to get this work done, and how the biosimilar program in the future would be funded to support getting

this work done.

We do have challenges at FDA. We continue at CEDR to have challenges in recruiting and retaining critical staff for review of the biosimilar development programs and the application submissions. This is very complicated science. I think it's very fun, but the people that have to do it every day are also highly sought after in the outside, for much more competitive salary positions outside.

We need to be able to offer a desirable program here that we can get those scientists and clinicians in-house and build our biosimilar development program.

With those challenges, that's what we need to think about as we think about the future of the program. That is what we think about. We also need to know from our stakeholders, many of whom are represented here in this room, what do you think about as what needs to be considered as we consider a second user fee program.

I know it's hard for everyone because

although we have approved one biosimilar, it's not as if it's like the new drug program, the generic program, we're approving hundreds of applications every year, or in the case of generic, maybe approaching 1,000 products.

How do we structure a user fee program, what are the needs, what aspects should be considered from each one of the stakeholders.

To reiterate, the purpose of this meeting is to hear stakeholder views as we consider whether to retain, to change, or discontinue the current BsUFA performance goals in the next BsUFA program. We'd like to know from those of you here, what is your assessment of the overall performance of the BsUFA program to date, what is your experience, if you have experience with it, and what aspects of the BsUFA performance goals should be retained, changed, or discontinued to further strengthen and improve the program.

I would also ask what do you envision, if you could fast forward three to four years, think about those 59 development programs, what do

you envision the biosimilar review program looking like and needing to look like five years from now, and then if so, how we would be able to build that program to meet the needs.

We look forward to hearing all your views on the reauthorization of this critical program, and this is truly the kick-off of starting to think about the future for this program. Thanks very much. Thank you, Terry.

DR. TOIGO: Thank you, Janet.

(Applause.)

DR. TOIGO: Our next speaker is Dr. Leah Christl, the Associate Director for Therapeutic Biologics in OND and CDER.

DR. CHRISTL: Good morning, everyone. I'm going to take just a little bit of your time and go through the BsUFA program and the reauthorization process.

What I'll do is give a little bit of background about BsUFA and the fee structure, speak very briefly about the workload and performance, talk about some additional

accomplishments under BsUFA, speak very briefly about the reauthorization process, just to orient folks who might not be as familiar with this process as others, and then touch on FDA's goals for BsUFA 2.

The Act directed that FDA develop recommendations for a new user fee program for 351(k) applications. When the Act was passed, it amended the Federal Food, Drug and Cosmetic Act to include 351(k) applications and the definition of "human drug application," enabling FDA to collect the same fees for 351(k) and 351(a) BLAs through September of 2012.

At the time, the Act had directed FDA to think about a user fee program for the biosimilar products, whether those would be their own user fee program or whether they would get rolled and under PDUFA, how they would do that. FDA did develop recommendations to Congress for a separate user fee program for 351(k) applications through fiscal years 2013 to 2017. Again, we could have kept them under PDUFA or created a new user fee

program.

What we did was create this new user fee program or BsUFA. On July 9, 2012, the President signed FDASIA, which included the authorization of BsUFA. With that passage, BsUFA then allows FDA to collect user fees from the biosimilar biological product industry to supplement the non-user fee appropriations that the agency spends on the process for review of these products. Again, this was October 2012 through September 2017.

The basic BsUFA construct is the same construct as any user fee program. These fee funds are added to appropriated non-user fee funds and are intended to increase staffing and other resources to ensure a predictable review process. The user fees are intended to pay for services that benefit those who are paying the fees.

The fee discussions with industry, again, this was mentioned previously, they focused on desired enhancements in terms of specific aspects of activities and the process for the review of biosimilar biological product

applications.

Part of those discussions and negotiations look at what new or enhanced processes FDA or industry would want to seek during that period of the user fee program, discussions about what's technically feasible, what resources are required to implement and sustain those enhancements, and again, the user fee negotiations, and the construct of user fee negotiations does not include a discussion of policy.

Our experience with this user fee program and every user fee program, I think, is the devil is in the details. What are the details? The BsUFA user fees are intended to support FDA staff work against an increasing performance level. The way BsUFA 1 was set up is there are a number of goals, many of them are listed here in this chart. We did note that not all the commitments are listed there.

As you can see, for some of them they had an increasing goal over the five years of the

user fee program, some of them starting at a 70 percent goal to whatever activity it was within a certain time frame, and then increasing up to 90 percent performance for certain goals by the end of the user fee program in 2017.

The goals that are listed here include application reviews, supplement review, including manufacturing supplements, looking at special protocol assessments, clinical hold responses, and then there were a number of goals around scheduling and holding meetings. Again, not all the commitments are listed here. We do have some additional commitments about conveying filing issues or review issues and reviewing non-proprietary names.

The current fee structure, there were a number of principles that guided the BsUFA program. We wanted to ensure sufficient review capacity to support the biosimilar review, to prevent unnecessary delays in development and approval of the 351(k) products.

There was an assumption made that the

351(k) fees should be comparable to the 351(a) fees for a standard review because of comparable complexities of the review process and the products.

We wanted to create a fee structure to ensure that funds were available to support critical development fees for review activities. Again, as Dr. Woodcock had mentioned, there wasn't an existing industry, so we looked very much at the development phase review activities as a part of BsUFA, and really tried to build the program around focusing very heavily on the development phase activities.

Also, we were very cognizant of avoiding redirection of resources from 351(a) application review under PDUFA to 351(k) activities.

The current fee structure that was enacted as part of BsUFA 1, there are a number of fees that are here, one of the unique aspects of the BsUFA program is this concept of a biosimilar product development fee, and there is an initial or an annual fee, and this is per product, so it

is for each product in the BPD phase, and that was set at 10 percent of the human drug application fee for that given fiscal year.

When a sponsor joins, they pay the initial fee, and then as long as they are in the program, it's an annual fee. It's not a fee for service type of system. There's an annual fee that covers the interactions with the FDA, be it meetings, exchanges through written correspondence, so on and so forth.

If a sponsor does withdraw from the program for a certain period of time and wants to rejoin and get engaged with FDA about the development of that product, they would pay a reactivation fee, which was set at twice the initial BPDC, and then after that, as long as they are in the program, they would then pay the annual fee.

Like the other user fee program, under PDUFA, there is also an application fee, and again, that is for each biosimilar product that will be submitted in the individual application,

and that was set equal to the human drug application fee under PDUFA less the sum of the initial and annual and reactivation fee that had already been paid for that product.

There is also an establishment and product fee that would be for approved products, and these are annual fees that you can see here.

Very briefly about performance and workload that we have seen so far under BsUFA 1, I will just very quickly touch on last year, so fiscal year 2014, BsUFA review meeting on performance. All of the goals are listed up here. It's a busy slide.

The first section of the blue bars deals with where current performance is for each of those different metrics. The red line in both cases is the goal for that existing year. Again, some of these had increasing goals over time, so you can see on that top portion, the goal for that fiscal year for all of those performance elements was 70 percent, and on the bottom portion of the slide, for those elements, it was 90 percent goal

for performance.

You can see based on that red line there are blue bars that are one side and blue bars that are on the other. There are some things we are meeting the goals on as of last year, and there are some things that the agency has not met the goals, particularly around meeting scheduling, so that would be when meetings were held within the certain time frames that were agreed to in the BsUFA negotiations.

You can see, for example, the third line down would be the BPD Type 2 meetings, and the performance was under 70 percent. For the BPD Type 3 meetings, it was above the 70 percent goal.

The other portion of the slide, you can see the number of submissions that would have been subject to that particular goal in that given fiscal year. This gives you an idea of the amount of workload that would be against those particular goals in addition to FDA's performance for fiscal year 2014 on these goals. This is combined CDER and CBER performance for fiscal year 2014.

In addition to the BsUFA performance goals that I just touched on, there were a number of different accomplishments that we wanted to note that were occurring under BsUFA 1. Again, this is a new program, so there had to be an establishment of the actual program and the review process and how it is that FDA was going to interact with sponsors in terms of development of these products.

FDA established three committees to ensure consistency in the regulatory approach and guidance to sponsors for proposed biosimilar product development programs, intended for submission under 351(k), the PHS Act, and then related issues.

The committees that were charged with discussing and coordinating issues were the CDER/CBER biosimilar implementation committee, BIC, and then each of the centers has their own biosimilar review committee. The biosimilar implementation committee was focused on policy issues, guidance developments, looking at

developing policy around the development and approval of the biosimilar products.

The biosimilar review committees were charged with more scientific aspects of implementation of BsUFA, so looking at the policy, if it was scientific policy, ensuring implementation, and all these committees were also intended to provide an aspect of central oversight to help promote consistency in the agency's approach as we developed this program.

CEDR also developed the OND therapeutic biologics and biosimilars staff, of which I am the lead. This is housed in the Office of New Drugs, and the staff was created again to ensure consistency in the approach and advice provided to sponsors. TBBT is one of the few organizations within CEDR that actually sees every development program. We also manage the BRCs, so we are the ones that are bringing issues before the BRC and helping to manage that.

Again, this is all around providing consistency in the advice and making sure that the

agency is being consistent in their scientific advice and the application of policy to the development and review of these products.

We also provide a central point of contact for OND and other staff in addition to industry, so there is a communication portal inside and outside of FDA for this particular review program.

The agency also held two public meetings. One was in November of 2010. This meeting was held to obtain input on specific issues and challenges. The comments and discussion that came out of that meeting helped to inform the development of the first three draft guidance's FDA published in February of 2012.

There was another public meeting that was held in May of 2012, and this was to obtain input on recently issued draft guidance's, so those draft guidance's that we issued in February, we then had a public meeting in order to receive feedback and make sure as we moved forward in finalizing those guidance's that we weren't just

taking into account the public comments that were received in the docket for these guidance's, but we provided an opportunity for stakeholder input and discussion and exchange of ideas.

To date, FDA has issued a total of eight guidance documents related to the implementation of the BPCI Act. I won't go through each of these. I will note they are separated into the guidance's that have been issued in final form. In addition, the lower portion are the draft guidance's that have been issued to date.

FDA has noted in the guidance agenda that they intend to publish additional guidance on these topics that are listed up here, and we know these are eagerly awaited by both FDA and industry.

In terms of the reauthorization process, there are some mandated things that need to occur, including a consultation phase, a public review of the recommendations, and then the transmittal of those recommendations.

This is our first step in looking at

renegotiating BsUFA and moving into the BsUFA 2 negotiations. This is an opportunity for public input, stakeholder input, as we move into the negotiation phase that will start next year.

As a part of BsUFA 2, there is going to need to be a discussion of some of the assumptions that went into BsUFA 1 that helped to form not just the performance goals but the conversation around resourcing.

There were a number of assumptions that were made including predictable workload with consistent numbers of BPD programs and meetings, along with applications that were going to be coming in.

The assumptions included that there would be eight BPD products on average, with no more than 11 at one time. You heard what Dr. Woodcock said, as of November 30, 2015, there were 59 programs in the BPD program. That is quite an increase over the 11 that was anticipated to be in the program at any one time.

There was also an assumption that there

would be one to two BPD meetings per year, per sponsor, with a total of 16 on average based on that average, eight products in the BPD program at any given time, and if you look back at the performance slide, you can see the number of meeting submissions that occurred during fiscal year 2014, so you can see it's definitely over 16.

There was also an expectation there would be 13 351(k) applications through the end of fiscal year 2015. Those companies who have submitted 351(k) BLAs have publicly disclosed -- I think folks are fairly familiar with the applications that have been publicly disclosed. Clearly, one of those applications was approved by FDA.

Again, there were assumptions that were made, if you remember, on the fee structure around not just the application fees but also product and establishment fees that would be coming in for approved products, so with an expectation there would have been 13 351(k) BLAs that would come in, there was a certain revenue stream that was

anticipated during the course of BsUFA 1 based on these assumptions.

There were also assumptions that were made regarding the resources required for reviewing the 351(k) development programs and applications. Again, this was thought to be similar to the PDUFA resource requirements for standard applications, so there being a need to discuss some of those assumptions as well regarding not just incoming submissions and that aspect of workload, but actually the work that the agency puts in.

Also, assumptions that were made around the ability to recruit and hire qualified staff for the BsUFA program. As Dr. Woodcock indicated, there are challenges that the agency has around hiring and recruiting staff with the essential expertise to be reviewing these applications.

The agency's priorities for BsUFA 2 include to review the existing BsUFA program to further increase the quality and predictability of product development and review for these products.

Again, to revisit the workload assumptions from BsUFA 1 to ensure there is adequate resourcing and accurate resourcing so we can make sure the program is functioning as soundly as it can, and we are being responsive to industry needs.

Also wanting to ensure financial soundness through fair and efficient fee structure enhancements, including financial management and reporting system enhancements. Also, there will be a focus on recruiting and retaining critical staff for the review of the biosimilar product development stage and then also the application review.

With that, I thank you very much.

DR. TOIGO: Thank you, Leah, for that background. I am now going to ask our consumer and patient panel to join us. We have representatives from AARP, the Colon Cancer Alliance, and from the Digestive Disease National Coalition.

Our first speaker for this panel is Leigh Purvis from AARP.

MS. PURVIS: Hi. Thank you for having me here today. My name is Leigh Purvis. I'm Director of Health Services Research in AARP's Public Policy Institute, and I am responsible for developing and helping to guide all of AARP's work around prescription drug issues, which I like to sum up as "I Do Drugs."

I feel like I'd be remiss in my role as a representative from a consumer organization if I did not stop and kind of level set as we're talking about these issues and kind of give you a better idea of what consumers are experiencing on the ground and why AARP finds this issue so important.

I don't think this is going to be a surprise to anyone in this room, but we have certainly caught on to the fact that biologics really represent the future of the drug industry. They represent a growing amount of the drugs that are in the pipeline. It's obvious that more and more of them are going to be coming into the market. They also represent a lot of the top

selling drugs, so we are spending a lot of money on these products.

Something else that is important to note is that the number of indications for these products is expanding, so the way we like to sum it up is that there are a lot more of them coming and a lot more people are using the ones that are already here.

Again, no surprise to anyone in this room, part of the reason that AARP has really focused on this issue is the fact that the prices associated with these products are so incredibly high. We're looking at tens of thousands of dollars at this point, which is considered a low price, so they can obviously reach hundreds of thousands of dollars.

They are also are being used again by more people. One example that we like to point to is the new PCSK9 inhibitors, the new cholesterol drugs. That is a proposed patient population of anywhere between 10 and 15 million people with an annual cost of around $14,000 per year. The

numbers associated with that are just incredible, and it really speaks to perhaps the sustainability of the system and perhaps not being able to sustain those types of spending.

Our population is particularly vulnerable to the costs associated with biologics. We use more prescription drugs than any other segment of the population, and we also use them on a chronic basis. The majority of older adults have two or more chronic conditions. When we are talking about prescription drugs, we are talking about costs that they are facing for the rest of their lives. This is not one bad year. Again, something you will face for the rest of your life.

Biologics are commonly used to treat conditions that are commonly found in older populations. This is not a population that really can absorb the costs associated with these products. The median income for Medicare beneficiaries is around $23,000, and more than one in four have less than $10,000 in savings.

If you are prescribed a very expensive

product for the rest of your life, you really do not have the means to absorb the costs associated with it.

We are kind of unique as a consumer organization in the fact that we represent consumers and we also try to keep an eye on the programs they rely on. Being cognizant of time, I'm just going to talk about Medicare Part B today, which is the part of Medicare related to physician services.

Under Medicare Part B, beneficiaries are responsible for 20 percent of their prescription drug costs. There is no out of pocket cap. If you're prescribed an incredibly expensive drug, you are looking at potentially in some cases as much as $100,000 in cost sharing every year for the rest of your life.

There is no one in this room who can absorb those kinds of costs. That is a huge concern for us. Yes, there are a lot of Medicare beneficiaries that have supplemental coverage, but the fact of the matter is the costs associated

with expensive drugs don't just disappear into the ether. They will be rolled back into the supplemental coverage cost sharing and premiums, which will eventually make that type of coverage completely financially prohibitive, which again, kind of defeats the purpose.

The Medicare program itself is spending a lot of money on biologics. In 2013, eight out of the top 10 drugs with the highest Medicare Part B expenditures were biologics. That is incredible, that is an incredible amount of money. Part B spent around $21 billion total, and again, biologics are representing a growing share of those types of costs.

All that is a very long way of saying biosimilar competition cannot come soon enough for our members and for the programs they rely on.

I have seen projections that until biosimilars become available, spending on biologics is projected to grow by more than 10 percent annually. This is not something that our health care system can absorb.

On the other hand, good news, there are a lot of biologics with patents that will be expiring in the near future, so the opportunities for competition are here. We just need to be able to take advantage of them.

There are many things that AARP does. We do not manufacture biosimilars, so there is only so much that we can say about this process, and most of it really speaks to an overarching theme that we have about biosimilars, which generally is that we want to make sure there are no unnecessary barriers to competition and to the savings that were intended by the creation of the approval pathway.

We can have some level of specificity in terms of what we think, and the two ideas that we really fall into are kind of competing but there is a balance that can be achieved here. One is we want to be sure that FDA has the resources it needs to be able to approve safe and effective biosimilars. We think that is incredibly important. Again, our members rely on these

products. We want to make sure they are reaching them, we want to make sure they are safe, we want to make sure they are effective.

However, we are a little concerned in the sense that some of these fees might be high enough that they may disincentivize manufacturers from producing these products.

In our eyes, we think it would be helpful if FDA were willing to kind of revisit these fees as they develop more real world experience with approving them, perhaps reducing them, phasing some out, or perhaps even considering similar to what we see under PDUFA, perhaps returning some of the fees if a product doesn't not actually get approved at the end of the process.

I always like to close, and this is kind of the theme of the entire presentation, close with a little bit of a recap of what this means to our members.

The costs associated with these products really are not sustainable for patients or for

payers. The health care system simply cannot take the costs associated with biologics. We need the competition.

More importantly, patients are reaching the point where they cannot access the products they need to get and stay healthy, and to us, that is just unconscionable. We have to be able to treat patients.

The final thought that we find ourselves saying about biosimilars, biologics, and really any prescription drug these days is the fact that medical advancements are meaningless unless everyone can afford access to them.

Thank you.

DR. TOGIO: Thank you, Leah. Next, we will hear from Eric Hargis, who is the CEO of the Colon Cancer Alliance.

MR. HARGIS: Thank you. I want to thank Dr. Woodcock and the FDA for the opportunity to share the patient advocacy perspective on the reauthorization of the Biosimilar User Fee Act.

The FDA is being proactive in engaging

patients in all areas of drug development and the approval process, and we appreciate that the voice of those who rely on this agency for both innovation and safety is both heard and valued.

Biologics are integral to the treatment of colorectal cancer. Thanks to innovative medicines, we are seeing an improvement in both survival and quality of life. While we recognize the value these medicines have for patients and the huge financial investment necessary to create them, their costs has a dramatic impact on patients and their families.

The cancer diagnosis doubles the rate of bankruptcy, and in almost half of the 100,000 patients who contact our organization every month are in desperate need of financial assistance. Biosimilars have the potential to lessen the financial impact on both patients and payers.

While we will not see the type of price drop common with generics, given the high cost of biologics for colorectal cancer, even a 20 percent reduction in price translates to significant

dollar savings.

The Colon Cancer Alliance would welcome biosimilars for colorectal cancer as the lower cost treatment for our community provided first the FDA approves the biosimilar based on evidence it is the therapeutic equivalence of the innovative biologic. Second, that appropriate systems are in place to track adverse events. Third, distinguishable names are used to avoid inadvertent switching, and finally, that switching from innovators to biosimilar or between biosimilars is a decision of the clinician and the patient and not the pharmacy.

To accomplish this goal, the FDA must have the financial and human resources to answer the question of how similar must the biologic be so that patients are assured that it will provide the same therapeutic benefit as the innovator biologic.

While the public may think of biosimilars in the same way as generics, demonstrating equivalence presents an entirely

different set of challenges, and we can't expect the FDA to continue this as just another task added to their already shrinking appropriations budget.

In addition, the FDA must have the necessary resources to ensure that the facilities producing biosimilars meet the same quality and safety standards as those making the innovator biologic. There is and will continue to be political pressure for the FDA to act swiftly in approving biosimilars, and the agency must withstand a rush to judgment and provide patients the assurance that a reduction in price does not come with a reduction in either efficacy or safety.

User fees have become the major source of funding for the FDA to carry out its important work, now representing more than half of the FDA budget. In the current environment, it is highly unlikely Congress will provide the funding necessary to address biosimilars, and the Colon Cancer Alliance strongly supports the

reauthorization of the Biosimilar User Fee Act of 2012 to ensure that the FDA can continue its work to make biosimilars widely available.

In addition, we believe that this or other legislation must address the unique needs the FDA has to recruit highly specialized staff. FDA must be able to go outside of HHS pay scale for a limited number of staff positions. We're not suggesting that the FDA staff generally make more money than their HHS colleagues, but the agency needs individuals with specific skills that are in high demand in both the private and public sector.

How can we justify asking users to pay a fee for timely review if the agency cannot spend some of that money to get the necessary staff talent to conduct the work.

While FDA will not be able to offer industry like salaries, going beyond HHS scale will help recruit individuals with these skills who share a passion for public service.

Again, we appreciate the opportunity to

share the patient advocacy perspective on the reauthorization of the Biosimilar User Fee Act, and we encourage all appropriate steps to ensure the FDA can make biosimilars widely available and in a timely fashion.

Thank you.

DR. TOGIO: Thank you, Eric. Our last speaker on this panel is Andrew Spiegel from the Digestive Disease National Coalition.

MR. SPIEGEL: Good morning, and thank you for the opportunity to comment on this important legislation.

While I hold a number of relevant hats in my role as a patient advocate, today as current chair, I'm honored to represent the Digestive Disease National Coalition. Founded in 1978, the DDNC is an advocacy organization comprised of more than 50 national patient and professional organizations who are concerned with ensuring that digestive diseases are on the radar of all health care policy makers.

The DDNC focuses on improving public

policies related to digestive diseases and increasing public awareness with respect to the many diseases of the digestive system.

In addition to my work with the DDNC, I am currently the Executive Director of the Global Colon Cancer Association, an advocacy organization representing the millions of patients worldwide who suffer from colorectal cancer.

Finally, I am the founding member and sit on the steering committee of the Alliance for Safe Biologic Medicines, an organization formed in 2010 to help support the FDA as they address the unique challenges biosimilars present to regulators.

For the last five years, we have worked not only with the FDA, but regulators worldwide and the World Health Organization to ensure that these unique policy and regulatory challenges are resolved in a way that places a premium on science and safety.

We commend the FDA for its commitment to bulletproof science and recognize that a long term

sustainable biosimilars program requires such an approach. The arrival of biosimilars to the U.S. promises to offer new treatment options to patients suffering from cancers, as well as other serious conditions, such as rheumatoid arthritis, psoriasis, and Crohn's Disease, as well as colitis.

The patient community is excited about the potential of biosimilars to reduce treatment costs which would increase access, but we are mindful that we cannot value speed at the expense of safety or the quantity of biosimilars over their quality.

Simply put, we recognize that in order for patients to enjoy the benefits of biosimilars, the FDA must always have the resources it needs to measure both the timely yet thorough review process.

The BsUFA was designed to do just that. It was modeled with long-standing and successful funding mechanisms for medical devices, MDUFA, and prescription drugs, PDUFA, which have both been

repeatedly reauthorized as we recommend BsUFA should be as well.

As patient advocates, we are extremely encouraged by the success of BsUFA in promoting both safe and timely introduction of biosimilars. This past March, we saw the first biosimilar, Zarxio, also called Filgrastim-sndz, approved. Numerous other products are in the various stages of the pipeline.

We can see the FDA's cautious science based approach to biosimilar approval is working. Take, for example, its use of distinguishable naming, both in the Zarxio approval and in subsequent guidance on biologic naming. It is critical for patients and providers to always be able to clearly identify which biologic product is being used throughout treatment.

Accurate attribution of adverse events to the correct biologic is also necessary for long term tracking and safety and efficacy.

While we see the FDA's long-standing commitment to transparency reflected in Zarxio's

clear naming, we feel a major obstacle to biosimilar adoption overall could be insufficient transparency on biosimilar labeling.

For example, the label of Zarxio neither identifies itself as a biosimilar, does not state whether or not it was interchangeable with its reference product, nor does it provide any analytical or clinical data demonstrating its biosimilarity. It does not tell our physicians whether its approval is based on its indication.

Say, for example, ulcerative colitis was based on trials in ulcerative colitis or Crohn's patients, where only on extrapolation from trials in rheumatoid arthritis or psoriasis patients.

Together, these omissions could impact the ability of patients and physicians to make informed treatment decisions and could potentially undermine physician confidence in biosimilars generally.

Similarly, while we are encouraged by BsUFA's progress since its introduction, we would like to see further progress and more biosimilar

approvals. The FDA has several years to assess whether the funding mechanisms provided adequate resources to thoroughly evaluate the ever-increasing number of biosimilar applications. If the FDA were to find more resources when required to get safe, effective biosimilars approved and to patients to a timely manner, we as patients would be supportive of expanding the BsUFA program as a funding mechanism.

Additionally, it is not only important that these funds are sufficient to improve review times, but that the allocated funds remain dedicated to their intended purpose, so that the FDA has the tools to perform this role.

It is important to all of us who want safe and effective biosimilars to be successfully introduced that the FDA get this right.

In closing, let me commend the FDA for its continued work in bringing biosimilars safely to the American patients. BsUFA is a critical component of the U.S. biosimilars pathway, and without reservation, we recommend it be

reauthorized.

Thank you again for the opportunity to comment on this important subject.

DR. TOGIO: Thank you, Andrew. That concludes our consumer/patient panel, and thank you for your thoughtful comments and the time you took to prepare them.

Our next panel will be the health care professionals' perspectives, and we have three organizations represented, the Academy of Managed Care Pharmacy, the American College of Rheumatology, and the American Society of Health-Systems Pharmacists.

Mary Jo, you can go right to the podium, and we will go on down.

MS. CARDEN: Thank you. Good morning. My name is Mary Jo Carden, and I serve as the Vice President of Government and Pharmacy Affairs at the Academy of Managed Care Pharmacy.

AMCP's more than 7,000 members that include pharmacists, physicians, nurses, and other health care providers and stakeholders, develop

and manage pharmacy benefits for more than 200 million Americans.

AMCP is committed to ensuring that individuals in the United States receive access to high quality, affordable, and safe medications. AMCP applauds the Food and Drug Administration for approving the first biosimilar in the United States and its consideration of others.

AMCP understands that the approval of a biosimilar is a major milestone, but more work is necessary to provide clarity about the biosimilars pathway and to encourage a robust market for biosimilars. Today, AMCP offers our perspective on the biosimilars pathway and also provides recommendations for FDA to direct user fees in the areas of post- marketing surveillance and educational efforts.

First, let me begin by talking about AMCP's position on biosimilars. AMCP supports an abbreviated pathway for approval of biosimilars in the United States. These medications play an increasingly important role for the treatment of

chronic conditions, and offer hope for many patients who had not had any access to medications.

In many cases, biological products are very costly to both patients and the health care system, and the introduction of biosimilars will help increase the competitive marketplace and offer more choices for patients that will result in increased access and lower costs.

However, to date, there are still legal and regulatory challenges to the introduction of more biosimilars to the market. FDA has issued guidance on the pathway but has not finalized its thinking in certain areas, including the issue of naming.

AMCP supports a naming convention that uses the same Government approved international non-proprietary name as the reference product. The naming convention has proved successful in the generic small molecule market and should be continued.

As proposed by the FDA, the naming

convention that affixes a four letter suffix to the INN would result in confusion to both patients, health care providers, and others. To achieve the stated purpose of achieving a robust pharmacovigilance process, AMCP supports the use of the NDC that is readily available and provides a system to identify the medication, package size, and manufacturer.

The addition of more information does not improve safety but rather adds another data element that may result in additional confusion and medication errors.

Next, AMCP supports interchangeability that recognizes products may be substituted by pharmacists and other dispensers without additional notification to prescribers. AMCP believes this reflects the spirit and the intent of BPCIA and that interchangeability is similar to the AB rating on generic products, which share highly similar characteristics.

AMCP also supports the approval of different indications for special populations

related to biosimilars.

In regard to active post-marketing surveillance, AMCP supports the use of active NDC based pharmacovigilance systems. To that end, AMCP has launched the biologics and biosimilars collective intelligence consortium, a public service initiative that will draw on large sets of identified pharmacy and medical data to provide unbiased scientific information on the safety and effectiveness of marketed biosimilars and their novel corresponding biologics.

AMCP recommends that the next steps that the FDA should take is first it should reconsider its naming guidance that would implement a hyphenated-random four letter suffix. AMCP has stated before its concern that current proposals will result in confusion to both the public and health care providers. Other identifiers, including the NDC, are already available to distinguish products.

FDA should also seek public comment on interchangeability through written comments and a

public hearing. AMCP also recommends that FDA hold a public hearing on the naming issue.

Finally, AMCP supports the use of user fees to engage in a broad stakeholder educational campaign to provide unbiased information about biosimilars. This campaign should focus on health care providers, payers, and consumers.

As the agency responsible for the public health and safety of the medication supply chain, FDA is a logical choice in providing this education. AMCP is also committed to providing education in this area and believes that a public/private partnership would be effective in ensuring that consumers understand biosimilars.

FDA's educational campaign should focus on the needs of the various stakeholders and should provide basic as well as higher level information about biosimilars to health care providers, payers, and decision makers. FDA should also assess the needs of stakeholders before releasing its information. It must also consider a variety of means to communicate this information

to accommodate people's differing levels of access to information and understanding, including websites, social media, print, apps, and video.

Again, thank you very much, and AMCP supports the FDA's process to approve biosimilars, and thank you for holding this meeting.

DR. TOGIO: Thank you, Mary Jo. Our next speaker is Augus Worthing from the American College of Rheumatology.

DR. WORTHING: Thanks very much. I'm Angus Worthing, and I'm grateful for the opportunity to be here and comment today on behalf of ACR, the American College of Rheumatology, in support of the reauthorization of BsUFA through the fiscal years 2018 through 2022.

On a personal note, it's exciting to be engaging with Government, patient groups, industry, and my colleagues in the provider arena.

I'm a practicing rheumatologist in the Metro D.C. area, and a member of the ACR Government Affairs Committee. ACR represents the vast majority of rheumatologists in the United

States. Rheumatologists, as we all know, specialize in caring for Americans with potentially disabling conditions, like rheumatoid arthritis, lupus, psoriatic arthritis, ankylosing spondylitis, gout, osteoporosis.

The FDA's approval of biologic medicines has been a miracle treatment for our patients with these and many other chronic and more rare inflammatory conditions, cancers, and other rare serious illnesses.

Not only have biologic medications reduced the burdens of joint pain and organ damage, disability and mortality from rheumatologic diseases, they have improved the quality and quantity of life for thousands of Americans. They are changing the face and course of many diseases in ways unimaginable a few years ago.

Rheumatologists utilize and work with biologics in many ways, as basic science and clinical researchers, clinician prescribers, like myself, and as monitors of on-site medication

administration in the clinic.

Rheumatologists' experience with biologics is different from other pharmaceuticals in three ways that are pertinent to our discussion today. They are highly complex, highly efficacious, and very expensive.

The ACR supports reauthorization of BsUFA because it allows the FDA to continue its vital and important work to evaluate emerging complex biopharmaceuticals, whose approval as biosimilars could reduce treatment costs.

The ACR's current position statement regarding biosimilars strongly endorses that safe and effective treatments should be available to our patients at the lowest possible cost. It also states that any decisions regarding approval of biosimilars must be driven by sound science that takes into account several observations and guiding principles, including the following two:

number one, the size and complexity and heterogeneity of biologics, and thus, biosimilars, necessitate a greater degree of scrutiny in their

analytical evaluation than what is typically required for small molecule generics.

Two, rigorous analysis of clinical trials in humans is necessary to ensure safety and efficacy of biosimilars, and provide the necessary level of confidence in their use by patients and providers.

We believe that BsUFA is a critically important means to ensure that the FDA can perform its important work and we offer the following three analyses.

Number one, about cost and access, that has been touched on before in this presentation today. The price of biologics has increased faster than other components of the health care system, and is predicted to increase further. This has led to reduced access to these valuable therapies, mainly via insurance payers' use of restrictive formularies, creation of various tiering schemes, and co-insurance.

We know that at least one in six people with rheumatoid arthritis already reduce their

medication due to cost, potentially resulting in long-term joint damage.

We physicians are extremely frustrated when we see our patients suffer because they can't obtain or use the medicines we have prescribed as recommended by the FDA.

We hope the anticipated decrease in costs resulting from the introduction of safe and effective biosimilars will increase access to agents and improve the health of all those who use them.

Number two, a brief review of BsUFA to date. As was stated at the public meeting here in December 2011, the funding from fees paid by sponsors of biosimilar products would "Provide FDA with needed resources and provide prospective manufacturers of these products with a clear and more predictable review pathway in the new product arena." The ACR supports these provisions.

As for fee amounts, it is appropriate that the fees are structured based on FDA analysis of the complexity of review required for innovator

biologics, and are sufficient for the FDA to perform the critical tasks required to ensure the safety of our patients.

Thirdly and finally, review of the BsUFA performance goals, ACR supports the performance goals of FDA to promptly and carefully review what look alike and sound alike proprietary names and specifically package labeling. The increased transparency will not only reduce medication errors but also increase prescriber confidence in biosimilar safety and efficacy data, and allow for more extensive pharmacovigilance programs.

I think it would be appropriate to add four things to product labeling or make sure four things are there, the distinct name, compared to the innovator biologic, the manufacturer, analytic data, and clinical trial data.

In summary, ACR supports reauthorization of BsUFA as one of the means for the FDA to adequately and appropriately evaluate important biopharmaceuticals that will ultimately increase our patients' access to these highly effective

treatments, as well as reduce their morbidity and mortality, and improve their quality of life.

Thank you very much.

DR. TOGIO: Thank you, Angus. Our last speaker is from ASHP, Christopher Topoleski.

MR. TOPOLESKI: Good morning. My name is Chris Topoleski. I serve as ASHP's Director of Federal Legislative Affairs. Two weeks ago, I was the Director of Regulatory Affairs, so I am holding two jobs at the moment, which as you all know is the easiest thing. I'll be doing interviews at the break if anyone wants to do reg work.

AHSP represents pharmacists who serve as patient care providers in acute and ambulatory settings. The organization's more than 43,000 members include pharmacists, student pharmacists, and pharmacy technicians.

For over 70 years, AHSP has been on the forefront of efforts to improve medication use and enhance patient safety.

I appreciate the opportunity to present

the views of AHSP on the performance of the biosimilar user fee program.

FDA's public health mission is to ensure the safety and effectiveness of drugs, biologics, and medical devices. No other agency or private sector entity serves this vital public health purpose in our society.

AHSP believes that the allocation of sufficient Federal resources to the FDA to meet its mission is a necessity, and those funds should be achieved primarily through Federal appropriations. AHSP strongly supports increased appropriations for the agency and is working to achieve that through our work with the Alliance for a Stronger FDA. We're pleased to see the increases for the FDA proposed in the recent omnibus package.

AHSP has a long-standing professional policy that supports legislation and regulations that promote greater patient access to less expensive biologic products. AHSP's policy emphasizes that safety comes first and a desire to

rush drugs to market should never surpass the need to ensure that products are safe and effective.

Drug user fees do not replace the need for increased appropriations from Congress. However, AHSP does recognize that with the agency's increasing applications for biological products with the passage of the BPCIA, biosimilar user fees represent an important and viable means to help bring safe and effective biological products to market.

My comments today will focus on the current state of post-marketing surveillance, one of the activities for which the FDA may spend the user fees collected on.

The AHSP policy shown on this slide supports a biological product naming convention as consistent with international naming standards developed by recognized authorities such as the WHO, USAN, and the United States Pharmacopeia. In addition, this naming convention is also supported by other national organizations, including the NCPDP.

These organizations have developed a harmonized biosimilar naming approach based on a shared non-proprietary name for originator biological products, related biological products, and biosimilars. Under their authority, these products essentially share the same non-proprietary name but can be individually identified through their unique NDC or other unique codified identifiers, and trade names.

FDA has proposed a non-proprietary naming process that deviates from existing standardized approaches that have been applied by international authorities such as INN and USAN.

Under FDA's proposal, a unique randomly generated suffix composed of four lower case numbers will or suffixes related to the licensed holder of the product, which could change over time, would be applied to the originator biological products, related biological products, and biosimilars.

AHSP is concerned that this approach

varies from the naming processes that are already in practice in other developed countries such as those in Europe.

Furthermore, using randomly generated suffixes would be unlikely to achieve FDA's goals of product recognition and recall by prescribers, patients, and others. Non- meaningful, unpronounceable suffixes are unlikely to be readily recalled or accurately associated with specific products.

Consistent with other standard setting groups, national pharmacy organizations and the WHO, AHSP does not believe there is a need to develop a naming convention that differs from the current standard. Without well designed testing, it is unclear whether FDA's proposal for a naming convention would achieve the high level pharmacovigilance or would cause confusion among clinicians and patients who rely principally on proprietary names for self reporting about branded products.

FDA is also planning to change the

official names for biologics with globally adopted INNs and USANs. Initially, this would apply to a small number of products but eventually would retrospectfully change the names of a broad group of existing products to include unique randomly generated four letter suffixes. Such a naming change would require extensive education and potentially require reprogramming of health information technology systems. This could result in significant risk for medication errors.

AHSP supports a biosimilar naming approach that relies on the ability to track medications by NDC or by other standard product identifiers. While all hospitals and health systems may not currently have the ability to fully track drug products by the NDC, they will be required to have that capability pursuant to the Drug Supply Chain Safety Act, which requires package level NDC tracking by 2022.

In addition, there are at least two other options available to health care organizations that could be implemented until more

permanent solutions are developed. The first is to apply the current vaccine adverse event reporting system model to the biologic and biosimilar products.

This regulatory framework already exists for vaccines in all clinical settings and could be applied by the FDA to ensure that pharmacovigilance regardless of where a patient receives the biologic.

The second option is to manually enter an NDC into the patient's electronic health record. Given that the current universe of biologic and biosimilar products proposed by the FDA is small, this could serve as an initial solution while a more permanent one is developed. The AHSP is prepared to work closely with the FDA to develop such a solution.

AHSP believes there is a great deal more to be discussed regarding the appropriate non-propriety naming policy that should be employed by the FDA. We believe it is premature to implement the draft guidance until the agency has engaged in

a robust stakeholder discussion.

Therefore, we believe it to be in the best interest of public health for the FDA to delay finalization of the guidance and proposed rule pending a meeting in accordance with 21 CFR Part 15 to hear the opinions and concerns of all related parties that would be impacted by a non-proprietary naming policy that deviates from the current conventions.

AHSP appreciates the opportunity to comment at this meeting today. We look forward to working with the agency over the coming months as they prepare for BsUFA reauthorization. Thank you.

DR. TOGIO: Thank you, Chris. That concludes our health professional panel. Thank you for taking the time to prepare the comments and come and present them. We appreciate your input.

We will now take a break. We are ahead of schedule. According to the agenda, we are supposed to be back at 10:50, but how about we are all back at 10:45, and we will start at 10:45.

Thank you.

(Recess.)

DR. TOGIO: This is last call for public speakers. I have two people who have signed up already. If you want to speak during the open public hearing, you need to come see me now.

If Kay, Juliana, David, and Michael can join me at the front, we will be ready to get started.

This is our second to last panel, and these are perspectives from the regulated industry, and we will hear from BIO, Coherus Biosciences, GPhA, and PhRMA. Kay Holcombe is going to get us started. I did not put the name tags in the right order, but that is okay, Kay, you are listed on the agenda first, so you can go first. I know you like to go first.

MS. HOLCOMBE: I just think this is an example, Terry, of the last shall be first.

The Biotechnology Industry Organization greatly appreciates the opportunity to speak with you today regarding the Biosimilar User Fee Act.

BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers, and related organizations across the United States and in more than 30 other countries.

BIO supports the timely reauthorization of BsUFA, and may I just say that when we started user fees, we created the monster acronym, UFA, and BsUFA has almost taken us over the edge, acronym-wise.

We believe that this reauthorization should strive to clarify and enhance the processes and tools FDA uses to regulate biosimilars and improve the transparency, sustainability, and financial accountability of the BsUFA program.

When BsUFA was enacted, it established a program of user fees associated with a category of products new to the U.S. market and the U.S. regulatory system. Therefore, unlike when the grandfather of user fee programs, PDUFA, began, there was no market, and neither the FDA nor other stakeholders had a good idea of what the volume of

applications, products, or facilities would be, and how long it would take for an application volume and a market to grow to the point where a user fee program constructed like PDUFA could be viable.

In discussing this reauthorization, stakeholders will have more information, although certainly not the level of understanding that existed when the other user fee programs were established. It, therefore, will be extremely important for us to learn from FDA how the program is proceeding.

While we have seen the reports of the extent to which the agency is currently meeting performance goals, it will be more important to know how the agency is allocating resources in this program, how many FTEs are required to conduct the anticipated meetings, and to evaluate applications, and the extent to which and how the agency predicts this workload will change as the number of sponsors interested in entering this market and the number of applications increase.

As PDUFA evolved over its nearly 25 years, to include multiple activities related to the review of human drug applications, we anticipate this program will evolve as well. Biosimilar user fees already are designed to support a wide range of FDA activities, including meeting with sponsors during development, BLA review, and post-market safety.

With this new to the U.S. category of products, this latter is especially important. Not because these new highly similar products are inherently higher risk, but because they are biological products that have the potential to cause unexpected immunogenic responses, because they are highly similar but not identical risks, the reference products in lieu of which they may be prescribed and used, and because they are new.

Both prescribers and patients need to be educated and well informed throughout the course of biosimilar development and use, so that this new category of products will result in a robust market.

As interest in the U.S. biosimilars market grows, the structure of this program will undoubtedly need to change. We welcome the opportunity to discuss with FDA and other stakeholders what changes make sense and how fee changes or fee structure modifications can be phased in effectively and judicially as the numbers of applications and products increase.

Beyond fee adjustments are questions of what additional activities need to be undertaken to ensure a robust and patient- centered biosimilars marketplace in the U.S., and to what extent such activities are appropriate for discussion in the context of BsUFA.

For example, there is significant interest in increasing the number of final guidance documents that will provide sponsors with greater understanding about FDA's expectations regarding data needed in biosimilar applications, both in general and in specific product categories.

While FDA has issued several final

guidance's, there are also important documents still in draft which need to move forward. Additional guidance also is needed and planned by FDA.

For example, we need guidance regarding how FDA will make determinations of interchangeability, and regarding labeling of biosimilar products. Regulatory guidance as we all know plays a critical role in the development of any new class of products, and is in the best interest of all stakeholders, whether they are companies trying to decide if this is a marketplace they can and wish to enter, or providers and patients who may want to and will use these products. Timely and appropriate regulatory guidance can help the development of a robust biosimilars market.

We understand that specific policy outcomes or change are not appropriate user fee discussions. However, the development of guidance and the time frames around such development are clearly in bounds. It will be helpful to

understand as well the extent to which existing BsUFA resources have been used for policy and guidance development, and how FDA sees this playing out in the future.

As to BsUFA performance goals, it is hard to estimate whether and how agency performance can or should improve, because of the relatively small numbers to date. We have little visibility into the length of time or the FTE effort needed to review an application, and we have similarly limited understanding of the resource needs for the other aspects of the biosimilars program that would help us determine whether the current BsUFA structure is appropriate for long term program sustainability.

The BsUFA program must continue to evolve to the benefit of patients and to support FDA's ongoing implementation of a well-constructed science based pathway for the approval of biosimilar products. To this end, for BsUFA 2, BIO will work with PhRMA to advance and support policies to achieve the goals I mentioned at the

beginning, to clarify and enhance the processes and tools FDA uses to regulate biosimilars, and to assure transparency and financial sustainability of the BsUFA program.

BIO looks forward to engaging with FDA, other stakeholders, and Congress to consider the best pathway forward to timely BsUFA reauthorization. Thank you for the opportunity to talk with you today.

DR. TOGIO: Thank you, Kay. Next, we will hear from Juliana Reed, who is speaking on behalf of The Biosimilars Forum.

MS. REED: Thank you. A special thanks to the FDA for holding the workshop today and for the invitation to speak. As mentioned, I am Juliana Reed. I am the current President of the new organization this year, The Biosimilars Forum.

A little bit about The Biosimilars Forum. We are a non-profit organization working to advance biosimilars in the United States. We are the first non-profit organization solely dedicated to biosimilars and expanding access to

biosimilars.

Right now, our member companies are developing at least 70 percent of the current proposed biosimilar products that are currently advancing at the FDA.

The members of The Biosimilars Forum and one of the reasons why we came together was because as you can see, we represent a very diverse and in some cases, especially in this town, an unlikely group of bed fellows. We came together as folks know with the biosimilars industry being a new industry. We also felt that we needed a place, and why we have the name the "forum," we needed a forum to work on this new industry and the policies that will govern this new industry.

We were able to come together, as you see, we have innovators, we have start-up's like Coherus and EPIRUS, and we have traditional generic manufacturers like Teva, altogether to support again the new biosimilars industry and to work together to advance it.

As I mentioned, the Forum represents the majority of the current programs under consideration at the FDA in biosimilars. We also are very honored to have Sandoz as a member, having the first U.S. approved biosimilar to date, but also the members represent the majority of biosimilars approved outside the U.S.

The Biosimilars Forum supports the reauthorization of the user fees. We're very glad to hear several of the things today that support the user fees, support biosimilars, but also we believe we share several of the positions and things that the FDA is seeing as well, so we look forward to working with the FDA team on the user negotiations as we go forward.

It's vital to all of our members and the biosimilar sponsors in the U.S. that we have a productive dialogue that will lead to the timely product approvals. It's important for us to continue to lower the cost of biologic drugs in the U.S.

Some considerations we would like to

move forward with as we continue this dialogue with the FDA. It is crucial that we continue to maintain our current momentum and build on our experience, but here are some key things.

One, we would like to continue with aggressive but also realistic time frames for review and approval. We would like to work with the FDA to ensure that there are adequate and skilled resources for the review of these products. Meaningful and frequent communications between biosimilar application sponsors and the agency are important to our members.

Also, as you noticed in our membership, leveraging the scientific knowledge of the experienced manufacturers and scientific experts in the industry is important to the FDA, and we look forward to supporting you on that.

Education of stakeholders including industry, providers, and patients, is a key principle and foundational goal of the Forum, and we again would like to support the FDA in that as well.

Using lessons learned to improve our outcomes and meeting expectations. This is a new industry. It is a new user fee program. We are coming with open minds and changing the lens and the paradigm of how user fees in the industry can succeed.

This is a tremendous opportunity for both the industry but also the agency and the patients, and we are all in the same place with the goal to advance a high quality and robust biosimilars market. We look forward to continuing to work with the agency and with our other stakeholders here on shaping the market and renewing the user fees.

Thank you.

DR. TOGIO: Thank you, Juliana. Our next speaker is representing the generic drug industry from GPhA and the Biosimilars Council, David Gaugh.

DR. GAUGH: Thank you. Good morning, everyone, and thank you for allowing us to speak in front of you on this very important program,

the reauthorization of BsUFA.

I'm David Gaugh, Senior Vice President for Sciences and Regulatory Affairs, representing the Generic Pharmaceutical Association, and more importantly, the Biosimilars Council, which is a division of GPhA.

The Biosimilars Council works to ensure a positive environment for patient access to biosimilar medicines. The Biosimilars Council is a leading source of information about the safety and efficacy of these affordable alternatives to the costly brand biologic products.

Areas of focus include public health, expert education, strategic partnership, government affairs, legal affairs, and regulatory policy. Of course, for those of you who would like more information about the Biosimilars Council, we have put our website on here so you can check it out.

The Biosimilars Council is currently a 13 member organization, so these companies represent the Council, and as my esteemed

colleague just before me stated, a couple of the companies, Sandoz and Teva, for example, are the lead outside the United States for biosimilars and also some of the leads on the biosimilar applications that have been filed with the agency thus far.

The impact of biosimilars on patients. Biosimilars as interchangeable biologic products holds promise not just for consumers and the pharmaceutical industry, but for sustaining a health care system with very finite resources. By 2016, it is predicted that 8 out of the top 10 most dispensed pharmaceuticals in the United States will be biologics.

In a recent study by Express Scripts, it was estimated that the potential savings of $250 billion in the next decade will occur with the approval of just 11 biosimilar products.

Where things with implementing BsUFA 1. FDA has expanded a considerable effort in drafting guidance's, some of which are now final. FDA has met with multiple sponsors to date. There are

estimated to be well over 50 products under development in the United States under the BsUFA pathway.

Although it may be too soon to judge the agency's performance on applications given the number of submissions, the BsUFA program can be elevated for the biosimilar related work that consumes the greatest amount of FDA resources - development phase support. To date, eight BLAs have been announced as submitted to the FDA, and the actions to date for five of these submissions has passed.

We only know of the review outcomes and timing of two of those five, and for the two, FDA has completed their review within the 10 month goal, Sandoz's Filgrastim, for example, with an approval, and Pfizer's epoetin alfa with a complete response letter.

Of the remaining three, we do not have public information available to us concerning their status. Overall, there are fewer biosimilar approvals at this point than what either the

industry or FDA predicted several years ago.

Where things stand, continued. Development phase support and meeting management is a predominant activity where improvement is needed. For 2013, the BsUFA performance report found that all three goals not met were related to meeting management. For 2014, which is a preliminary report, found that seven goals where there is potential to miss, six relating to meeting management.

According to the Eastern Research Group, BsUFA workload study meetings and policy development consumed a majority of the CEDR staff activities, 45 percent for meeting activities, 19 percent for policy activities, and 7 percent for BLA review.

An assessment of the current BsUFA processes. We have found interactions with FDA under BsUFA to be very constructive. We believe that a 10 month review clock for biosimilars, which is two months less than that of the standard PDUFA drug review, is justified because FDA is

granting multiple development meetings prior to the BLA submission, allowing for extensive feedback and aligning prior to the submission in order to improve the completeness of the quality of the BLAs.

These multiple meetings permitted under BsUFA enable industry to obtain extensive feedback which in turn led to improved dossiers.

At present, FDA is expanding a very significant portion of biosimilar resources on regulatory policy issues. We are hopeful that these issues will be resolved in the very near future, which will free up significant resources to provide timely and detailed feedback to the sponsors on the product reviews.

To date, FDA has issued four final and eight draft biosimilar guidance's plus a proposed rule on non-proprietary naming. It is critical that FDA continues to provide guidance's to industry and proceed with the outstanding guidance's the agency has said they would be introducing this year, which includes

interchangeability, labeling, and statistical considerations for demonstrating analytical similarities.

Additionally, FDA should prepare a guidance to address life cycle management or post-approval requirements, covering topics such as requirements for biosimilars and interchangeable biosimilars as well as supporting manufacturing changes, such as the need to establish similarity to the originator or comparability to approved biosimilars.

From a future state standpoint, increase and strengthen FDA resources and capabilities to improve the review and approval of these critical products. Staffing goals should be met at the FDA commitment levels. Advisory committees that increase the number of scientific experts from outside the agency, more analytical and functional experts with a strong understanding of the science of comparison, and the assessment of biosimilarity should be added.

These are imperative since the risk

based considerations for biosimilars are highly driven by analytical and functional data.

Maximizing the efficiencies of FDA meetings and improving the outcomes, a clear process where time lines should be established for follow up clarification to any BsUFA meeting. Application orientation meetings permitted under PDUFA and very beneficial to FDA reviewers should be encouraged under BsUFA. Additional touch points during the review of the 351(k) is very important.

Finally, Type 2 meetings should be specifically authorized to provide written advice on whether the achievement of certain pre-defined product quality attributes would enable the use of targeted clinical programs and allow for the determination of interchangeability.

FDA and the industry need to work collaboratively to create a public education campaign around biosimilars. These collaborative educational efforts will provide a key and independent source of information regarding

biosimilar products, their safety, and the scientific development.

Additionally, other key stakeholders, payers, patients, and clinicians would contribute to an extensive educational campaign.

With that, I want to thank the agency for this time and allowing us to present our position and some of our thoughts for a future under the reauthorization negotiations that will soon be taking effect, and given the strong public need for more affordable biologics, it is critical for FDA and industry to focus negotiations on efforts to ensure timely patient access to these more affordable high quality biosimilars.

The Biosimilars Council thanks FDA for their accomplishments under BsUFA 1, and we look forward to working with the agency under BsUFA 2 reauthorization. Thank you very much.

DR. TOGIO: Thank you, David. Our last speaker for this panel is Michael Levy from PhRMA.

MR. LEVY: Thank you. As just stated, my name is Michael Levy. I'm Deputy Vice

President in Science and Regulatory Advocacy at Pharmaceutical Research and Manufacturers of America, otherwise known as PhRMA.

PhRMA is pleased to have the opportunity to respond to the Food and Drug Administration's request for comments on the overall performance of the Biosimilar User Fee Act, and to participate in the upcoming reauthorization of BsUFA.

PhRMA is a voluntary non-profit association that represents the country's leading pharmaceutical research and biotechnology companies, which are devoted to inventing medicines that allow patients to live longer, healthier, and more productive lives.

PhRMA's membership includes several leading biopharmaceutical companies actively developing biosimilar medicines and working with the Food and Drug Administration to bring these to patients.

In 2011, PhRMA was a participant in the technical negotiations with FDA that together with input from groups representing patients and health

care providers resulted in the first BsUFA performance goals letter. At that time, there was little experience in reviewing and approving biosimilar medicines on which to base the content of the performance goals letter.

Now, with more collective experience, PhRMA remains committed to working with FDA and other stakeholders to reauthorize BsUFA in a data driven manner, which ensures FDA continues to receive funding necessary to review biosimilar applications in a timely manner, without diverting resources from the review of innovative medicines.

PhRMA has long backed the establishment of an approval pathway for biosimilars that involves the thorough assessment of their safety and efficacy. We supported the enactment of the Biologics Price Competition and Innovation Act, and have actively participated in FDA's ongoing efforts to implement the statute.

It is imperative to ensure that the continued implementation of BPCIA matches the original legislative intent to ensure patient

safety while at the same time balancing increased competition from biosimilar products with the need to provide biopharmaceutical researchers with certainty to make long term research and development decisions and support future medical innovation.

PhRMA's consideration of biosimilar policies is guided by our support for the following five things: a science based implementation of the BPCIA and regulatory decision making. Patient safety through effective identification of biologics and robust pharmacovigilance. Health care provider and patient choices, regulatory transparency that enables stakeholders to understand the basis for FDA's decisions, and long term stability of the biosimilar user fee through financial transparency, efficiency, and accountability.

The BsUFA agreement developed in 2012 provides the agency with the resources and regulatory framework to meet its public health mission and to ensure patient safety. BsUFA 2 and

FDA's continued policy development related to biosimilars should further advance these activities.

PhRMA is committed to working with FDA and other stakeholders to review the existing performance goals and consider enhancements that can improve the program.

To date, the agency has issued several draft and final guidance documents to assist sponsors in generating data to support biosimilar applications. FDA guidance and regulation provide insight into the agency's current thinking regarding how it will evaluate and understand significant regulatory questions.

Key guidance's that remain on the agency's agenda include but are not limited to guidance on the labeling for biosimilar biological products and guidance for industry considerations in demonstrating interchangeability to a reference product.

In addition to issuing these guidance's, the agency should provide clarity on how FDA will

interpret statutory provisions that apply to biosimilar applications. For example, those that reference innovative products that are covered by the transition provision in Section 7002 of the Affordable Care Act.

We urge the FDA to issue the necessary guidance's and regulations to implement fully the BPCIA, as these are critical to provide predictability and transparency to sponsors in order to help them design effective development strategies to meet patient needs and FDA regulatory expectations.

We agree with FDA that implementation of a robust modern pharmacovigilance program for all products is essential to ensure patient safety. All biologic medicines have the potential to cause unwanted immune responses in the body that could have serious adverse effects.

A feature called immunogenicity. Although rare, these serious safety risks may not be detectable during pre-approval clinical testing because the size of the population exposed may not

be large enough to assess very rare events. Because of this, it is even more critical that we ensure adequate pharmacovigilance systems are in place as we introduce biosimilar biological products to the marketplace.

PhRMA believes that all original biologic and biosimilar products should share a common non-proprietary name that is accompanied by a unique memorable suffix to distinguish them from one another. This will help to ensure that physicians can remember the names of the biologics that they prescribe, and patients can remember the names of the biologics that are prescribed for them. Such identifiability is essential for monitoring drug side effects, and we applaud FDA for issuing guidance on this critical policy area.

PhRMA believes that to facilitate patient-centric prescribing and choice, there should be appropriate regulatory transparency in biosimilar labeling, including a statement of biosimilarity. Biosimilar labeling should state that the product has been approved as a biosimilar

for stated indications and routes of administration. The labeling should also identify the reference product. A statement on interchangeability. Biosimilar labeling should state whether or not the FDA has made a determination of interchangeability with the reference product, and include any such FDA finding.

A description of data supporting approval. Biosimilar labeling should describe the basis of approval for each indication by identifying the relevant data for the reference product and biosimilar that support a finding of biosimilarity.

In summary, PhRMA supports the reauthorization of the Biosimilar User Fee Act in a way that is consistent with the original legislative intent.

The BsUFA performance goals agreement is a means of advancing public health by making adequate resources available to FDA for the regulatory review of biosimilar products,

consistent with the agency's high standards for scientific rigor and patient safety.

PhRMA and its member companies are committed to working closely with FDA and all stakeholders to reauthorize this important program to maintain, improve, and expand upon its science based approach to the development and review of biosimilar products.

PhRMA, therefore, urges Congress to reauthorize BsUFA in 2017, and compliment the user fees with congressional appropriations.

Thank you.

DR. TOIGO: Thank you, Mike. Thank you to our panel members for presenting the industry perspective, and for keeping to the time commitment. We appreciate your cooperation.

We have one more panel, although we have one panel of one person, so we have one person, Dr. Antonio Moreira, who is going to talk to us about the perspective of the scientific and academic community.

DR. MOREIRA: Good morning, and thank

you so much to the FDA for giving me the opportunity and inviting me to be with you this morning and present some perspectives from the scientific and academic community on the BsUFA process.

I feel a bit lonely being the only member on this panel, but I'll do my best to oblige to the request.

I am Tony Moreira, Vice Provost for Academic Affairs at the University of Maryland, Baltimore County. I'm a Professor of Chemical, Biochemical, and Environmental Engineering. I have been in the biotech business for about 35 years, both in academia and in industry. I teach courses in regulatory science at UMBC, and also I'm a member of a DARPA funded project that deals with manufacture of therapeutic proteins at the point of care, and these are applications for biosimilars, so I'm very much personally interested in the progress of the biosimilars field and what we can do in academia to support this activity.

As we look at the intent of BsUFA in terms of providing resources for the FDA to develop at the end of the day a better managed and biosimilar product review process and making sure we have high quality product therapies that come to the market as needed by the patients, we have to realize that we are talking about developing products, similar bioproducts, to very complex molecules, orders of magnitude more complex than simple chemical synthesized, well defined small molecules.

Thus, the use of the language of "highly similar" as opposed to being the same or identical product, again, because of the unique characteristics of these products as a function of the manufacturing process used for that manufacturer.

Again, the need for somehow identifying what we mean by "similar structure," and the major impact of having strong analytical technology packages that can compare the biosimilar product with the reference material from the innovator

compound.

Thus, in the definition of "biosimilar" from the BPCI Act, words like "being highly similar to the reference product," notwithstanding minor differences in clinical and active components, and the "no clinical and meaningful differences" being observed between the biological product and the reference product in terms of safety, purity, and potency.

Probably the words here "highly similar and no clinical and meaningful differences" bring about many questions from the science point of view in terms of making sound scientific decisions of the biosimilarity approach in terms of the product being defined.

I liked a previous slide from Dr. Christl's presentation because I think it provides a very good pictorial of the process for the step-wise approach in terms of generating data and evaluating what the FDA has labeled as the evaluation of the uncertainty, starting from the very strong analytical package and then moving

down the line in terms of animal studies, clinical PKPD, and potentially additional clinical studies that again are looking at the totality of the evidence, a decision being made for the process.

This leads to a pathway for biosimilar development that starts by looking at the reference product licensed in the U.S., reengineer a clone that develops then a product that will be comparable to the innovator molecule based on the analytical studies, develop the manufacturing process, and realizing again because of the complexity of these molecules, we are always talking about some differences possibly occurring between the two products.

Following the development of the manufacturing process with clinical development work, again, as defined here, leading to a demonstration of efficacy and safety after assessing immunogenicity as well, and again, some of the concepts you already heard earlier in terms of how to extrapolate across indications and the potential or not for interchangeability or

substitution decision making, again, becoming a very important part of the deliberations in terms of biosimilarity.

Again, all of these eventually lead to or come as a result of scientific studies that will support the decision-making. I think these are just in my view some of the scientific topics with the introduction of the biosimilar discussions in the U.S. that has caused us to work in terms of the development.

How to establish that the molecule profile is highly comparable to the innovator molecule, and then leading to the development of manufacturing processes, efficient, optimized, and high yield in terms of making products of final high quality.

Science and technology has advanced tremendously since the days when the innovator molecule was developed, so I think we have now novel expression systems, novel tools, improved analytics, single use systems, a lot of new technologies and knowledge that allow us to use

those to make these biosimilar products.

Science has developed to the point where there are exciting opportunities to develop products of high quality and compare them to the innovator molecule. This comes to a question of how much statistical packaging we need to establish for making these decisions, so again, I know the FDA is working on these concepts of how to develop these statistical analyses so they are scientifically sound to establish biosimilarity.

Also, the clinical trial design that will be necessary in terms of the uncertainties in decision making, a new way of looking at these studies to prove the biosimilarity.

These are whole new ways of looking at this product. It really is a paradigm shift in the regulatory approval process and review, which I think brings the scientific topics where again the development in science can be very important and helpful to make those decisions.

We are looking, as I was saying before, in my laboratory at point of care delivery, so I

think we are looking at how biosimilars even can interface in personalized therapies. It will be an interesting topic, I think, looking at ways where academic institutions, where we are doing discovery and new science and bringing new knowledge to the table, how can we be more successful in whatever we discover in the academic world that can be ultimately marketed through successful clinical trials or these approaches to biosimilarity. I think it will become quite important for us to interface with the FDA and industry.

Again, these are some of the challenges, one might call. I would rather see them as opportunities in biosimilar development. When we look at what is necessary to define the target profile of the biosimilar material, what are the methodologies necessary that are sensitive enough to look at the differences in similarities between products, and understanding what's critical in manufacturing, what are the quality attributes and related to key process parameters.

The structure and functional relationships and all the strengths of the analytical package necessary even before we initiate any pre-clinical or clinical studies. Defining how similar is similar. What can we tolerate or accept considering even the innovative molecule, of course, is also a variable in its properties.

As I said, with this paradigm shift, it brings about as far as I can see it from my academic perspective, brings in the opportunity for true innovation in biologics manufacturing, which will impact the biosimilar industry, but also the biotech industry in general. I think we are all looking at really new ways and scientifically sound approaches for biologics development at the end of the day.

When I look at these kinds of scientific opportunities, my thought is at this point is really as you look forward to the BsUFA reauthorization, which I am obviously supportive of, for the FDA to consider the academic community

as a partner as well, with the scientific opportunities that we can have in academia.

For instance, the FDA can give us guidance on what are the important questions that we should be looking at in academia that can support the FDA's mission in specifically biosimilar development. We do lots of things in academia. We look at many new technologies, new science, new discoveries.

How can we model or mold those studies and that research in order to provide information, provide knowledge to the FDA in helping answer the questions that are part of the biosimilar process flow.

Also, the FDA can help us in looking at the training of staff that is needed by the FDA. The FDA can provide the ideas for projects that our students can work on at the Master's or Ph.D. level. Not only they will be doing work that is important and useful for the FDA, but they will be trained in issues and problems and topics that then they can come and work for the FDA, in terms

of their knowledge of the regulatory science and the needs of this kind of industry.

I think that interface where we can really use the FDA as essentially the critical component to help us design our research, design our studies, so we can be helpful to the FDA, I think, will be a very important component.

I'd like to recommend highly leveraging the resources of the academic community to support these efforts.

Ultimately, I think as we look at the FDA and this industry coming together, perhaps developing best practices that we all share, and that could support these efforts going forward. Again, we can have an efficient process that brings these medicines to the market in a timely manner as needed by our patients, and as we can in the academic world and in scientific communities support the FDA and industry in making this happen.

I think bringing this triangle together and FDA thinking of academia as a catalyst to

develop these sources of knowledge that can be directly supportive of the FDA's needs in terms of their science and staffing levels, that is something the academic world is open to, and looking forward to work with the FDA and industry in these endeavors.

Thank you very much.

DR. TOIGO: Thank you, Dr. Moreira. To wrap up the panel presentations, we are going to have Theresa Mullin do some closing remarks, and then we will have a brief open public hearing session. Theresa?

DR. MULLIN: It's still morning, so good morning, everyone, and again, thank you for coming today to this meeting. It's a very important milestone for us, both in terms of this reauthorization process and also a milestone because this is the first reauthorization program which is still, as I think you have been hearing from the various stakeholders who have been able to share their views today, still a new program.

This is the first reauthorization. I

guess we would agree with some of the views that we are also trying to get a better understanding of the resources required to do these kinds of reviews and to support this program.

I'm going to just try to close with a quick recap. I have been making notes throughout the morning. Recap of some of the key messages that I think we have been hearing from you today.

I will start with we hear there is a need for biosimilar competition and to improve the affordability of needed biologic therapies, the cost of biologics can be quite high, and competition would be valuable, but yet the need for rigorous science, the bulletproof science, I think I heard, and sufficient staffing of qualified experts to really underpin and address these policy challenges, there are new regulatory challenges and policy challenges associated with biosimilars, and they take a much more complex approach to both develop them and to manufacture them than would be needed for say a small molecule generic product, generic drug.

There is a need for naming that would minimize the confusion in the health care system and at the same time support accurate, clear attribution of adverse events so that you can have effective risk management and follow up of any safety issues that may emerge in these new projects, which are again more complex as we have been hearing, and we need the resources to be able to accomplish this.

User fee reauthorization appears to be generally supported by the public in the input we have received today, and that the fee level should be in line with the cost of running this program in an efficient manner.

It was also noted that the development pathway here is different, it's different from the new drug 351(a) or from the generic drug pathway, and from a scientific standpoint, there is a paradigm shift, and this presents both challenges and opportunities to be really pursued.

Also, with all that and the paradigm shift, there is a need to really get an

understanding of the resources that are needed for this program and the structure of a program that would be successful in this case, considering that it is a different type of pathway, and the evolving program.

We hear there is a continuous desire for continued communication between FDA and sponsors as they work through these new pathways throughout development, and the need for continuing guidance and policy development, that there has been a significant part of the workload in the early years, we are really now finishing up the third year of this program, and it's acknowledged that guidance is much needed and additional guidance may also be needed.

These products are complex products, and complex policy issues and new products and new development programs sometimes raise additional new issues.

User fee negotiations and discussions I will note focus on process. They are about review, process enhancement, not policy issues.

The discussions we will be undertaking in the next several months with the regulated industry will not involve naming, they will not involve payment policy, they won't involve labeling policy.

They might involve identifying, industry may say, more guidance is needed, but not what would go in the guidance. They may identify an area where they would wish for more guidance.

We have been successful to date in funding careful, rigorous review of safety and effectiveness and providing a timely and predictable process using industry user fees by making it clear that the timely process is a value and benefit for industry, and it doesn't promise a particular answer, so we do not tie fee payment or we certainly don't return fees after doing that careful review, depending on the answer.

It's quite critical that this is the way the program be structured to ensure program integrity and public confidence in these programs, and public confidence is quite critical as we know in the case of biosimilars to ensure timely

uptake.

Finally, I want to conclude by reiterating Dr. Christl's comments about our priorities for BsUFA 2. We want to further increase the quality and predictability of this program in development of these products. We want to revisit the workload assumptions as we have been hearing, the paradigm shift, the complexity, and even the greater than we expected desire by companies for consultation throughout the development phase.

That is very important, but we may need to revisit how we structure and finance the program to ensure soundness in that financing so we can continue to sustain this program and meet the promises that our patients and others have in it, and that we recruit and retain the scientists that we need for timely review, so we are able to accomplish this.

With that, I'll close. Thank you again. We look forward to a very robust discussion to support timely reauthorization of this program.

Thank you again for coming today. Happy holidays.

DR. TOIGO: Thank you, Theresa. We have two people who have signed up to speak in the open public session. Dr. Hillel Cohen from Sandoz, and Dr. Sumant Ramachandra, from Pfizer. We will start with Dr. Cohen. Gentlemen, I will ask you to keep it to about five minutes. Thank you.

DR. COHEN: Good afternoon. I'm Hillel Cohen, Executive Director of Scientific Affairs at Sandoz, Inc., a Novartis company. We would like to thank the FDA for holding this meeting.

At present, Sandoz is the only company that has taken a product through the entire biosimilar development FDA review and approval process. We have had more than 30 meetings with the FDA to discuss development of biosimilars. Our experiences provide a unique perspective, and we welcome the opportunity to share them at this meeting.

There are many aspects of BsUFA that worked well and that we would like to retain. Our interactions with the FDA under BsUFA were

excellent and constructive. The multiple meetings permitted under BsUFA enabled us to obtain extensive feedback, which in turn led to improved dossiers.

We believe that the 10 month review clock for biosimilars was successful and is justified. The extensive interactions prior to submission allow FDA to obtain an overall familiarity with the contents of the dossier.

FDA has expended and continues to expend a very significant portion of biosimilar resources on drafting guidance's to industry to provide clarity on the development pathway and to resolve remaining regulatory and policy issues.

We are hopeful that the remaining issues will be resolved in the near future, which will allow FDA to allocate more resources to providing rapid feedback to sponsors and to product reviews.

There are several ways in which the U.S. biosimilars development pathway can be enhanced. First, it is apparent that non- biased education is needed to ensure that health care professionals

and the public understand and accept biosimilars. The FDA acknowledges this need, but at present, these activities are not funded. It is important that a mechanism be developed to address this critical need.

Second, a clear process with time lines is needed for follow up clarifications to a BsUFA meeting. The existing guidance meetings are extremely useful, but at times, there are residual uncertainties about the outcomes. A mechanism should be created to resolve any residual uncertainty from either the meeting itself or the meeting minutes. This would greatly benefit all parties.

Third, FDA is currently taking the approach that a sponsor must first obtain approval of a given biological drug, that is a biosimilar, and only after initial approval can the sponsor seek approval of the same product as an interchangeable biologic. The reason stated by the FDA is that they are not yet ready to evaluate interchangeability as a part of the initial

application.

In the interim, companies must submit a supplemental license application in order to obtain an interchangeability designation, even if the data was available, and incorporate it into the initial submission. The current supplement fee is in the neighborhood of $1 million. Congress never intended that FDA review of interchangeability be automatically subjected to an additional user fee. This situation must be addressed.

We have specific suggestions for these highlighted items, as well as other suggestions on how BsUFA could be improved. We will provide those to the groups that will discuss BsUFA reauthorization on our behalf.

Thank you very much for your time.

DR. TOIGO: Thank you, Dr. Cohen. Dr. Ramachandra?

DR. RAMACHANDRA: Thank you for the opportunity to provide Pfizer's views on the reauthorization of the biosimilar user fee

program, BsUFA 2.

My name is Sumant Ramachandra, and I'm the Senior Vice President and head of Research and Development for Pfizer's Global Established Products.

We believe that Pfizer's experience under BsUFA 1 having seven products in development in the U.S., including one product pending approval by the FDA, may offer important insights for FDA and relevant trade associations as they begin the reauthorization process.

Any potential changes to BsUFA should be data driven and informed by FDA's review performance. We encourage FDA and the trade associations to develop that evidence base during the course of the negotiations.

Despite significant progress by the agency, only one 351(k) BLA application has been approved by the FDA to date, with another seven applications still pending. Based on publicly available information, this equates to an overall 25 percent first cycle review approval rate. By

comparison, in recent years, the PDUFA program has achieved a first cycle approval rate for NMEs ranging from 80 to 95 percent. Furthermore, we estimate the number of applications will significantly increase in 2016 and 2017.

Understanding this performance and Pfizer's experience, we have identified three high level priorities for BsUFA 2. First, the program should be appropriately resourced to ensure that the FDA has adequate capacity to provide advice and feedback to biosimilar sponsors both during development and on pending applications.

Second, the FDA should commit to training and workforce development to ensure that FDA staff fully appreciate the difference between the review of a biosimilar and a new therapeutic biologic. This is a paradigm shift and defers from both novel products and generic reviews.

Third, FDA should enhance the clarity, consistency, and timeliness in its feedback to sponsors during biosimilar product development meetings and the BLA review process.

In summary, based on Pfizer's experience and leadership in biosimilars and biologics development, we look forward to contributing to the BsUFA reauthorization process. By enhancing consistency in reviews and ensuring adequate resources and staffing trained, we believe that BsUFA 2 will provide FDA with the infrastructure necessary to anticipate and respond to the next wave of biosimilar applications.

Thank you again for the opportunity to provide the views of Pfizer, and we would be happy to provide any clarifications needed through the process. Thank you very much.

DR. TOIGO: Thank you, Dr. Ramachandra.

That concludes our meeting for today. Thank you all, to the speakers who took the time to prepare and come and present, to the FDA staff who did a lot of work to get the meeting organized, and to our participants who came and participated in the process.

FDA takes seriously its responsibilities related to public input into our regulatory

processes.

Thank you, and remember that the docket is open until January 19 for any additional public comments you want to provide.

Safe travels, and that's it.

(Whereupon, at 11:42 a.m., the meeting was concluded.)

CERTIFICATE OF NOTARY PUBLIC

I, CHRISTINE ALLEN, the officer before whom the foregoing proceeding was taken, do hereby certify that the proceedings were recorded by me and thereafter reduced to typewriting under my direction; that said proceedings are a true and accurate record to the best of my knowledge, skills, and ability; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this was taken; and, further, that I am not a relative or employee of any counsel or attorney employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.

_____
CHRISTINE ALLEN
Notary Public in and for the
State of Maryland

