FOOD AND DRUG ADMINISTRATION

FACILITATING COMPETITION AND INNOVATION
IN THE BIOLOGICAL PRODUCTS MARKETPLACE
PART 15 PUBLIC HEARING

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C O N T E N T S

C O N T E N T S (cont'd)

P R O C E E D I N G

DR. SHERMAN: All right. It's nine o'clock. Let's get started. Good morning and welcome to the Part 15 hearing on Facilitating Competition and Innovation in the Biological Products Marketplace.

My name is Rachel Sherman. I'm the Principal Deputy Commissioner of Food and Drugs, and will serve as the presiding officer for this hearing. The purpose of the hearing is to provide an opportunity for broad public input on FDA's approach to enhancing competition and innovation in the biological product marketplace, including facilitating greater availability of biosimilars and interchangeable products.

Before we begin I will make a few administrative announcements. First, please silence any cell phones, as we on the panel have done, or other mobile devices, as they may interfere with the audio in the room.

Second, we ask that all attendees sign in at the registration tables outside the meeting room.

Third, the rest rooms are located in the lobby past the coffee area, to the right and down the

hallway.

And finally, and I'll mention this again, copies of today's presentations are available upon request, and the contact information is available at the registration table, and for those of you watching on webcast, we will have a slide later that will give you the contact information.

For media inquiries, our press officer is Linsey Mayor, but she's taking -- today is the first day of school at Montgomery County, so to all FDAers with school-aged kids, thank you for juggling. Sandy Walsh is here. Sandy, can you -- Sandy Walsh will be here most of the day and Lindsey -- we'll introduce Lindsey when she arrives.

If any members of the media are here today, please sign in, and if you have any questions or are interested in speaking with the FDA about this public hearing, please contact Sandy or Lindsey. Because this hearing is intended to give FDA the opportunity to listen to comments from presenters, the panelists and other FDA employees will not be available to make statements to the media.

Although there are no rules of evidence for this public hearing, I note that the lawyers on our panel outnumber the physicians, so we're all going to behave. There are some general procedural rules. No participant can interrupt the presentation of any other participant and only FDA panel members will be allowed to question the presenters.

There will be an open public comment period at the end of the day, after the presentations have finished.

Public hearings are public administrative proceedings and are subject to FDA policy and procedures for electronic media coverage. Representatives of the electronic media are permitted, subject to certain limitations, to videotape, film or otherwise record FDA public procedures, including the presentations of the speakers today.

The hearing will also be transcribed and copies of the transcript can be ordered through the docket or accessed on our website approximately 30 days after the meeting.

Turning to today, we have 27 speakers, and

each will have eight minutes to present. After each speaker presents, we will have three minutes for the panel to ask questions. If a speaker finishes early or the panel does not use the full three minutes, we intend to move on to the next speaker.

This means the speakers may find themselves asked to give their presentations before the time that it listed on the agenda, so please keep that in mind as you schedule your day.

Although we may be adjusting the speaker schedule, we intend to keep to our scheduled breaks, including lunch. For the speakers, and this is the crucial part, we have timer lights to guide you. Theresa can point to those. The light will indicate when to begin speaking and when to stop. The timer will give you a one-minute warning. It will turn yellow. You have a minute left.

If you have not concluded your remarks by the time a light turns red, I apologize in advance but I will interrupt you and ask you to stop. And any time that is over the eight minutes will unfortunately have to come out of the panel question time.

Please remember that the hearing is being transcribed, so please be sure to use the microphones. If you did not register to make an oral presentation but wish to do so, you may be able to speak during the open public comment period, which begins at approximately 3:30. If you're interested, please sign up for one of the available slots, three-minute slots, by 10:00 a.m., and that's again at the table outside.

And I will be emphasizing this throughout the day. Please submit your comments to the docket, both what you present and on any other thoughts that you have. The Federal Register notice will have -- has the detail of how to submit, and we will again have a slide later for the folks who are viewing us remotely.

And as you can see, not from this slide, but from a slide eventually, the docket will remain open until Friday, September 21st, of this year.

This hearing is being webcast live, however, it is not interactive, so webcast viewers cannot comment or ask questions, but of course they can submit to the docket.

So turning to today, thank you all for coming,

particularly, again, the morning after Labor Day, and now let's turn to our first speaker.

Oh, I'm sorry. I forgot to ask the panel to introduce themselves.

MS. ABRAM: Anna Abram, Deputy Commissioner for Policy, Legislation and Analysis.

DR. FRANKLIN: Good morning. Joe Franklin, Director, Policy Staff in the Therapeutic Biologics and Biosimilars Staff within CDER.

DR. CHRISTL: Leah Christl. I'm the Director of the Therapeutic Biologics and Biosimilars Staff in CDER.

DR. KOZLOWSKI: Steve Kozlowski, Director of the Office of Biotechnology Products and OPQ, CEDR.

DR. MALONEY: Good morning. I'm Diane Maloney, Associate Director for Policy, in the Center for Biologics.

DR. UNLU: I'm Unlu Mustafa at the Office of Chief Counsel.

DR. SHERMAN: Thank you. And before I begin, thank you to the staff for giving me the phonetic spelling, but if I butcher anyone's name, I apologize

in advance.

Our first speaker is Dr. Andrew Greenspan from Johnson & Johnson.

DR. GREENSPAN: Good morning and thank you for the opportunity to speak on this important topic. As you heard, my name is Andrew Greenspan, and I'm the Vice President of Medical Affairs responsible for immunology biologics at Janssen Biotech.

I've split my 15 years with Janssen between medical affairs and research and development. Prior to that I was a practicing internist in New Jersey. I hope my perspective will be helpful and I'd like to commend the FDA for convening today's forum.

We'll also be submitting written comments to the docket following this public hearing. At Janssen we have extensive experience with the development, manufacturing and post-marketing safety of biologics. A long history included OKT3, the first monoclonal antibody ever approved and Remicade, a TNF blocker, for which there are three approved biosimilars plus seven additional biologics across a wide range of indications.

We'd like to be clear at the outset about two points. First, we support policies for biosimilars, while ensuring an open and competitive marketplace.

Second, we believe that patient safety and clinical considerations should guide all policies related to biosimilars. From the beginning we have been a leader in advocating for a biosimilar framework in line with these principals.

As FDA considers ways to facilitate greater available of biosimilar products, it is valuable to consider the potential ramifications of various switching scenarios, which I will discuss later in my presentation.

These scenarios include patients switching from innovator to biosimilar, switching between biosimilars and multiple switches. I will be using a Remicade experience today for illustration.

We have four recommendations to share today. Policies -- FDA policies must facilitate innovation to advanced patient care and outcomes. Regulatory exclusivities and patents incentivize the development of new life-changing treatments. Developing new

biologic products is resource intensive, and the risk of failure is high, and as policies must respect the intellectual property rights of innovator companies. Policies should protect life cycle product improvements that provide benefits for patients. The FDA issued guidance that clarifies that improvements, such as new indications, will be protected under the products initially granted exclusivity, also known as umbrella exclusivity.

Second, FDA should finalize robust standards for interchangeability. Many biologics treat chronic progressive diseases requiring a lifetime of therapy. It can take years of trying multiple medications for a patient to find a therapy that is effective. As a result it our experience that many prescribers prefer not to switch a stable patient, unless there is evidence that this switch will improve outcomes.

Biosimilars, which by definition do not offer improvements in efficacy or safety, offer no clinical reason to switch. The potential risk of switching back and forth between innovator and biosimilar requires rigorous clinical evaluation.

As discussed in the draft interchangeability guidance, such studies are particularly important in the case of monoclonal antibodies with known immunogenicity concerns. For example, in a large study of Remicade in patients with rheumatoid arthritis, nearly half of patients had anti-drug antibodies after seven months.

We support well-designed and rigorous studies as described in FDA's draft interchangeability guidance, because of both their value in providing confidence to patients and prescribers and the importance of resolving these unanswered scientific questions.

Third, FDA should address biosimilar-to-biosimilar switching. This switching is already occurring in the real world. Consider the VA system. Prior to 2017 Remicade was the exclusive infliximab in the VA hospital system. In 2017 Inflectra became the preferred infliximab. And Renflexus will become the preferred infliximab starting this month. This change in the formula has already resulted in Remicade patients switching to Inflectra and will resulted in

switches from Inflectra to Renflexis.

Prescribers have many questions regarding such switching between biosimilars, with few, if any studies that evaluate the consequences of it. Biosimilar approval is based only on comparison between the innovative product and biosimilar. We ask that FDA address the clinical questions about the safety and utility of switching between biosimilars, especially if their data suggests physical, chemical or functional differences between one biosimilar and another that could translate into a clinically meaningful effect.

We also ask that FDA acknowledge the potential concerns regarding biosimilar -- switching between biosimilars, by requiring biosimilar labels to convey that there are no data about switching between biosimilars.

Additionally, we ask that FDA require manufacturers make clear in the labeling of interchangeable products that a designation of interchangeability refers only to interchangeability with the reference product.

Fourth, FDA should consider requiring post-

marketing studies for biosimilars. Post-marketing studies provide useful information about a product when it is used in ways or settings that were not evaluated during the approval process. While the purpose of post-marketing safety studies is to provide additional long-term real world data, such studies have the added benefit of increasing prescriber confidence. There are no post-marketing commitments for biosimilars.

FDA should consider working with biosimilar sponsors to establish post-marketing registries or other methods for gathering longer-term safety data, particularly on the topic of switching between biosimilars, extrapolated indications and special populations.

I'd like to address uptick in use of biosimilars. The current system is an open and competitive environment that FDA policies should maintain and foster. We're seeing that biosimilar uptick and price competition have lowered the costs for both patients and the healthcare system.

For example, the net price of infliximab products, including Remicade, is falling. Biosimilars

have access to both public and commercial channels. And, in fact, the uptick of infliximab biosimilars is consistent with biologic launches in the US immunology market, even those that provide a clear clinical benefit over the standard of care.

As we discussed earlier, when patients are stable, many prescribers prefer not to change treatments, so we should not be surprised that biosimilars take some time to penetrate the market.

The primary driver of biosimilar adopted is prescriber confidence. The more confident prescribers are in FDA biosimilar and interchangeable approvals and the safety of these products, the more uptick there will be.

Finally, policies that give an advantage to either biosimilars or reference products may limit the potential savings generated by competitive pressure.

In closing, at Janssen we support the maintenance of robust and competitive environment for biologics, including biosimilars, and environment where patient safety and clinical considerations guide FDA's biosimilar decisions and policies. We ask that FDA

provide additional clarity in the areas of biosimilar to biosimilar switching, and interchangeable status. We believe that patient and prescriber confidence and use of biosimilars will increase with assurance that FDA is implementing and enforcing rigorous standards.

Finally, our experience with Remicade shows that when biosimilars are approved and marketed, competitive pressure will meaningful reduce net price.

Thank you again for this opportunity to speak.

DR. SHERMAN: Thank you for your comments and getting us kicked off on time. Questions from the panel.

DR. KOZLOWSKI: So you mentioned the need to look at biosimilar to biosimilar switching. So how do you think that differs from switching within a product class? So anti-TNF's, you know, are switched in patients all the time between different products, so what is the difference between that scenario and biosimilar switching again? Not interchangeable products but biosimilar switching?

DR. GREENSPAN: Yeah. Thank you for the question. So the molecules that inhibit TNF are

significantly different from each other, and there have been some data suggest that there may be concerns when you switch across the class of anti-TNF's. So there is one example of a study that was published a few years ago in patients with Crohn's Disease were stable on Remicade but switched to another TNF, with just a sub-cu delivery and patients lost response, and I think that data was very informative to show that not all TNF's are created equal.

When it comes to biosimilar to biosimilar switching and how that's different, there's really no data at this point at all, and we speak to physicians who have questions around that, and I think generating data on that would be valuable. And I think the reason why it's an important question is for a couple reasons.

One is from the patient perspective, they've taken quite a bit of time to reach Remicade. Many of them are untreated for many years by the time they get Remicade. They deal with infusion reactions, as I mentioned, is not uncommon with Remicade. Often prescribers spent a lot of time optimizing the dose, so they have a lot invested in Remicade. And from a

patient perspective, there's concern about switching.

From a scientific perspective I would focus on two things. The first is immunogenicity concerns, particularly with Remicade, which I acknowledge might be less significant for other biologics, but it's quite significant for Remicade.

And the second is that there are suggestions that there may be differences in infliximab biosimilars. Actually, thank you for the question. I brought up a publication from just last week that looked at structural and functional differences between the two marketed infliximabs that did show differences in glycosylation patterns, particularly afucosylation and I think some of the FDA panelists may be familiar with this during the approval of Infectra, this came up, and in functional differences and antibody dependent cellular toxicity, they suggest that may have clinical meaningful consequences. Whether it does, I don't know, but I think it's worth on a case-by-case basis for the FDA to look into such cases like that.

DR. KOZLOWSKI: Thank you.

DR. SHERMAN: Other questions? Ms. Malone.

DR. MALONEY: I had a question. Could you just expand on your statement on the previous slide about where you say policies that advantage either biosimilars or reference products may limit the potential savings --

DR. GREENSPAN: Sure.

DR. MALONEY: -- generated by competitive pressure?

DR. GREENSPAN: Yeah, I'd be happy to. So it speaks to competition will drive down prices. We've seen that already. As one biosimilar entered the marketplace for Remicade, the price decreased. With two, the prices decreased. With increasing -- there's a third approved but not yet marketed, infliximab biosimilar, and we expect the price to continue to fall. It's probably best answered by Allen Greenspan, not Andrew Greenspan, but my understanding is more products into the marketplace, the price should continue to fall.

I will reference CMS policies. That seemed to be advantaging biosimilars, particularly on Fee 43 pricing, and that's what we were referring to.

I would just like to add on though, in the biosimilar action plan there were several suggestions about how to accelerate the development and availability of biosimilars, and some examples of those would be in silico modeling and simulation and the use of real world evidence, and we think those are great suggestions and they apply just as well to the development of biologics, so we encourage you for some of those innovative approaches to consider them to apply to biologics and all drugs, as well.

DR. SHERMAN: Any other questions? Just one point of clarification. If you could on Slide 5, you said if approved as interchangeable, it should only be with reference practice. Is that because you were assuming that's what the studies were done, or if you feel there were similar data with a biosimilar-to-biosimilar, then that could be interchangeable, as well?

DR. GREENSPAN: Yeah, thank you for the question. An opportunity to clarify. If -- the interchangeability claim should only be made with the drug that's used as a reference of that, and the

concern was that there might be confusion in the marketplace if another biosimilar, which doesn't have an interchangeability claim would be confused as an interchangeable product.

DR. SHERMAN: Thank you for the clarification. Other questions? Thank you for your remarks.

DR. GREENSPAN: Thank you.

DR. SHERMAN: Our next speaker is Mr. Randall Rutta from the American Autoimmune Related Disorders Association.

MR. RUTTA: Good morning. Thank you. I'm Randall Rutta, Federal Policy Consultant for the American Autoimmune Related Diseases Association or AARDA. Thank you on behalf of AARDA for this opportunity to participate in today's public hearing, on behalf of people living with autoimmune diseases.

The FDA's goals and key questions concerning discovery, development and marketing of biologics, biosimilars, and interchangeable products are well founded, timely and critical of critical interest to the autoimmune community. At every step AARDA believes that patient engagement is essential to the success of

the FDA in advancing its mission and role regarding the evolution of the biological products marketplace. AARDA is dedicated to the eradication of autoimmune diseases and the alleviation of suffering and negative socioeconomic impact of autoimmunity through education, public awareness, research and patient services.

As many as 50 million Americans are affected by one or more of the 100 plus autoimmune disorders that originate in an aberrant immune response and span a multiple of diverse conditions. AARDA recognizes that biologics and biosimilars are advancing patient access to new therapy options and affordable care. Patients with autoimmune diseases have extremely sensitive immune systems, which results in variations in how patients with autoimmune diseases experience their disorders, the manifestation of symptoms and the responses to treatment.

Even with small molecule drugs autoimmune patients can experience vast variations in responses due to their immune systems reactions, to both active and inactive ingredients in different medications. For highly complex therapy, such as biologicals, patients'

reactions may often vary even more greatly than the variances experienced between branded drugs and generics. We urge the FDA to insure that interchangeability determinations are not made unless it's truly the case for the statutory standard that the same clinical result can be expected in any given patient.

Data shows that patient responses to immunosuppressants and other immune modulating therapies vary greatly. As a result these drugs are often not interchangeable for particular patients and their specific experiences with autoimmunity and other co-occurring conditions.

AARDA believes that the approval of standards for a biosimilar product must meet the same standards of rigor and accountability as those set for the innovator biologic. Efficient development of biosimilar and possible future interchangeable products must use state-of-the-art experience and different biologic products that is sensitive to unique patient characteristics. Human testing that meets the highest safety standards is key, and special consideration

should be given to the application of biosimilar -- biosimilars in pediatric patients and those with complex multiple conditions.

We urge the FDA to fully enforce the rigorous statutory standard for interchangeability and to ensure that no interchangeability determinations are made unless it's truly well established, proven and unequivocally supported by data. Interchangeability between biosimilars and reference products, and between interchangeable biosimilar products themselves must be equally data driven. Patient awareness of and participation in clinical trials and other developmental steps in bringing these products to market should be optimized, including through collaboration with AARDA and other patient groups that are trusted by and have access to patients and their physicians.

In regulating biologic products, including biosimilars and the possibility of future interchangeable products, AARDA strongly encourages the FDA and other HHS agencies to support biologics and biosimilar innovation, while recognizing the important

distinctions between different therapies.

The Biologics Price Competition Innovation Act created hope for patients with autoimmune diseases with respect to encouraging the development and availability of additional therapies for a number of diseases that currently have very limited treatment options. Biosimilars hold great promise to expand the therapeutic options for patients and to encourage competition, which in turn may also lead to improved affordability for many drugs.

We support initiatives focused on biosimilars innovation and policies that facilitate appropriate access and affordability to these medicines. AARDA supports the FDA's draft guidance that would require sponsors to consider immunogenicity risks and studies conducted for potential interchangeable determinations. AARDA recommends that autoimmune disease patients be included in clinical trials, post-marketing studies and other evaluations of potential interchangeability. AARDA believes that all stakeholders including patients and their healthcare providers must have access to information that distinguishes the biosimilars from

innovative biologics for appropriate prescribing.

As noted, even small differences between biologic products can have serious implications for autoimmune patients. As a result, distinct names, identifiers and labeling are critical to facilitate prescriber and patient awareness, minimize confusion and help ensure appropriate treatment management. These steps will enable an accurate, effective use, encourage development and support the marketing of biosimilar in interchangeable products.

One fundamental priority in this area, AARDA believes patients and their physicians must have the final choice on what products a patient receives. Significant harm can result for patients, particularly vulnerable individuals with complex conditions, when medication switches or substitutions occur. Given the implications, any potential interchangeability determinations that might occur in the future must consider the safety risk that substitutions present, and must avoid disruptions in care for patients.

This includes patients who are stabilized on a biological medication, those who may incur

immunogenicity, and those for whom substitutions could cause a loss of response to the originator medicine. For patients will complex conditions who are already stabilized on a therapy, it's not appropriate to impose automatic substitutions or non-medical switching made by a pair without the intervention and consultation of the prescriber and consent of the patient.

The BPCIA allows biosimilar substitutions without a physician's intervention, only for interchangeable products as designated by the FDA and not for other biological products and biosimilars. AARDA believes that the FDA and HHS must exercise extreme caution with respect to any policy or practice that interferes with physician independent clinical judgment and treatment recommendations.

Interchangeability determination should remain an extremely high bar that cannot be cleared unless it is true and supported by meaningful and unequivocal data, that any and all patients could be expected to experience the same clinical result in response to the therapy as required by statute.

Lastly, AARDA believes that accurate tracking

and tracing of biologicals, including biosimilars in any possible future interchangeable products must be assured for the purpose of monitoring, tracking and monitoring.

As these products gain traction in their availability and use, transparency for, among and with patients and their providers is essential. Documents of any substitution that does occur should be tracked and reported to patients' providers on a timely basis via effective channels. We strongly urge the FDA to take necessary steps to monitor, evaluate and assure biologic, biosimilar and interchangeability safety and effectiveness, directly and across the healthcare ecosystem.

AARDA will submit detailed written comments per this request. It is readily available as partner and resource to continue to assist the FDA in this very important and worthwhile area.

Thank you so much.

DR. SHERMAN: Thank you for your comments. Questions from the panel? Dr. Franklin?

DR. FRANKLIN: Thanks. You emphasized the

importance of information to patients. Are there particular information resources, types of information that FDA could provide, particularly with the focus on interchangeability and providing information about interchangeability to patients?

MR. RUTTA: I think if FDA can continue to be a leader in bringing this information forward, both directly in terms of the education outreach that you support and the Agency supports, but then also to use your influence across all of the stakeholders in the system to encourage that kind of information and participation and collaboration occurs, is going to be key.

I mean, patients, particularly people with autoimmune diseases, have no greater stake than anyone in having the success of this discussion go forward and to see more of these options for their treatment move forward, but safely and with their full knowledge, so that these patients can be full participants in every step of the evolution, use and then marketing and development of new treatment, so thank you for that.

DR. SHERMAN: Other questions from the panel?

Okay. Then I have one.

Oh, you talked about for substitution that it should be tracked and reported. And we have the example from Dr. Greenspan that's going on at the VA. Tracked by whom, reported by whom, and to whom?

MR. RUTTA: Everywhere across the board as much as possible, please. I think for the purposes of patients, that tracking and reporting absolutely occurs very close to where they're seeking their treatment, so it's really that patient-physician partnership that needs to be well informed and that anywhere within the system the decisions are being made about a medication that an individual receives, particularly a change in the -- that medication's history, should be tracked. It may be at the pharmacy level. It may be at the distribution level. It may be at any level where that -- where that medicine is -- a decision about that medicine is kind of changing hands. So thank you.

DR. SHERMAN: Great. Thank you. Additional -- Dr. Kozlowski? Or no?

DR. KOZLOWSKI: So in terms of education, so I'm -- is there an interest in an education on the

power of analytics, because a lot of what you discussed were clinical evidence? And I think we've heard about small differences being measured but many cases those are small differences that don't matter, and they actually speak to the power of analytical tools to be able to really discriminate and understand these molecules.

So it would seem part of confidence in both biosimilars and interchangeable is understanding analytics and the power of analytics.

MR. RUTTA: Absolutely. I think that's going to be key for kind of a confidence level to occur across both the prescribing and the patient communities, as well as factoring in risk. You know, for a lot of autoimmune patients, they're living with such challenges day to day, that if they understand, you know, what the risks are, what the ramifications might be, what the potential benefits might be, versus some of those tradeoffs that analytics can really help us understand, that's going to be key to a more informed patient and a more informed patient community.

And groups like AARDA and other patient groups

should be considered a ready resource at every step to be a part of both the analytics component and then the interpretation of those analytics to the field.

DR. SHERMAN: Dr. Mustafa.

DR. UNLU: You said that patients and prescribers must have access to information about biosimilar that make them different -- I'm paraphrasing. Does your organization and the patients that they serve have a similar interest in knowing about differences, for example, in batch-to-batch variation in innovator products or differences that occur after manufacturing changes in innovator product?

MR. RUTTA: Absolutely. I mean, anything that's going to represent a change, both in what their understanding of a particular intervention might be or what the experience might be following the kind of scenario that you described, would be of key interest. Helping to interpret that in a way in which patients and their prescribers can understand and then put into practice, that's the challenge. But I think knowing that groups like ours are ready to be a partner in that process and that anything we can do to have a system

that's better informed at every step, will give us better results and hopefully greater efficiencies, more effective use, et cetera.

DR. UNLU: All right. So just as a follow-up, so maybe the best we can do is to put the context the variability between innovators and biosimilars, by pointing to variabilities inside innovator product, as well?

MR. RUTTA: Absolutely. That would be extremely helpful.

DR. SHERMAN: No more questions? Thank you for your comments.

MR. RUTTA: Thank you.

DR. SHERMAN: Thank you, Theresa. I missed my light. Our next speaker is Ms. Juliana Reed from the Biosimilars Forum.

MS. REED: Hi. Good morning, everyone. I am Juliana Reed. I'm the Vice President of Corporate Affairs in the Global Biosimilars Lead for Pfizer, but I am also and very proud to say I'm the President of the Biosimilars Forum.

The Biosimilars Forum is a nonprofit

organization whose mission is to advance biosimilars in the United States with the intent of expanding access to biologic medicines and improving healthcare.

The Forum works on a consensus basis to develop policy positions to ensure the United States has a competitive and sustainable biosimilars market, providing more options to patients and physicians. We appreciate the opportunity to comment today on FDA support for streamlining the development of biosimilars, enhancing the efficiency of FDA review, and providing additional scientific and regulatory clarity to stakeholders.

The Forum applauds the efforts the FDA made -- the efforts made by the FDA to facilitate greater availability of biosimilars in the marketplace and thanks the FDA for holding this public hearing. The Forum has reviewed FDA's public hearing notice and plans to submit detailed comments in the docket, and I will highlight a few of those today.

Regarding the utility of the Purple Book, we believe the FDA can and should make the Purple Book more useful for all stakeholders, by making it

available as an interactive functional and searchable database. We suggest providing an additional column for each biosimilar and interchangeable product, where the identity of the corresponding reference product is listed, along with the date of exclusivity expiration. We further encourage the FDA to provide a single product list that includes both CDER and CBER regulated products, which will assist stakeholders who may not be aware of which center regulates the product.

We strongly support FDA's ongoing stakeholder educational efforts. We encourage FDA to increase its efforts to educate pharmacists, physicians and patients, as well as to address the inaccurate perceptions.

For example, FDA can increase efforts to promote the message that the same quality standards are applied to both biosimilars and interchangeable biologics, as well as the fact that biosimilars can be given to both naïve patients, as well as to established patients, who have previously been treated with the reference product.

Furthermore, FDA should develop and offer a

continuing education program focused on biosimilar products to increase provider and pharmacist understanding of biosimilars. The forum encourages FDA to expand its educational footprint beyond its website, and place additional focus on patient and patient group educational efforts, including development of patient focused educational materials.

To further support the advancement of biosimilar programs, we urge FDA to exercise increased flexibility and clinical approaches, without sacrificing scientific rigor. We encourage FDA to exercise flexibility and reference product bridging, allowing for the use of non-U.S. referenced products, when it is scientifically justified.

FDA should also exercise flexibility regarding the structure and design of bridging studies, allowing for discussions with sponsors to determine the necessary requirements on a case-by-case basis. FDA should remain flexible regarding study end points and overall study design of the comparative clinical study or switching study.

Recent comments by Commissioner Gottlieb

suggest FDA is considering not making the naming paradigm retroactive, because of the potential high cost associated with retrospective application across the healthcare system.

The Forum is concerned that assigning suffixes to biosimilars but not to their reference products may hinder appropriate pharmacoviligance efforts and could lead to inaccurate perceptions regarding biosimilar products.

We suggest that one approach to addressing cost effectiveness is for the FDA to require application of the suffix paradigm only to biologics that are reference products.

The Forum requests FDA work collaboratively with stakeholders to find efficient means of applying suffixes to reference products.

We further support FDA's efforts to ensure reference product samples are made available to biosimilar product sponsors for development purposes. We stress the vital importance of ensuring adequate and timely access to samples of reference products in order to avoid delays and impediments to biosimilar

development.

We applaud the efforts made by the FDA to work with industry and other agencies to support market competition and increase the uptick of biosimilars. We strongly support CMS's decision to assign individual billing and payment codes to each biosimilar, reflecting the important differences FDA has acknowledged between biosimilars and small molecule generics. We further support CMS's decision to make all biosimilars eligible for pass-through payment status.

However, the Forum is concerned about advancing alternatives to current payment models, as they may stifle innovation. It is with this concern that the Forum urges the Administration to continue to examine new distribution models and options.

The Forum echoes FDA's concerns regarding the existing rebate systems for reference biologics that create and compromise the entrance of biosimilars into the U.S. marketplace. We urge the Administration to ensure rebates focus on patient access and out-of-pocket costs, and not list price.

Thank you for the opportunity to be here today and to offer comments on behalf of the Biosimilars Forum. The Forum looks forward to continuing our work with the FDA as to serve a resource and to advance biosimilars in the U.S. And I'm happy to respond to any questions.

DR. SHERMAN: Thank you very much and for remaining on time. Questions from the panel? Dr. Kozlowski?

DR. KOZLOWSKI: So you mentioned having the same quality standard for biosimilar biological products and interchangeable products, which actually is the statute, but do you think there should be a way of advancing analytical tools being considered, both for biosimilar and interchangeable biological products, that there be a fixed standard, but that standard evolves in some way?

MS. REED: Our comments are related to -- and I'll let a more scientific person answer the scientific part of the question, but our comments are related to the education piece, that the quality standards for both a biosimilar and an interchangeable biosimilar are

not different. And that's a very important piece.

You'll hear, and this is something through our experience, you'll hear folks talk about that there should be a difference between a biosimilar or an interchangeable biosimilar and perhaps that someone should expect a different clinical result. And we want and urge the FDA to simplify that, so that's what we're addressing in our response.

DR. KOZLOWSKI: Thank you.

MS. REED: Thank you.

DR. SHERMAN: Dr. Franklin.

DR. FRANKLIN: You mentioned some additional information in the -- information and formatting and kind of function of the Purple Book that would be useful. Can you provide some insight into what the utility of additional reference product or exclusivity expiration information would be, and how we might incorporate that into the Purple Book?

MS. REED: I think it's an important part. If you look back at how we're trying to figure out, and I think you guys have a requirement to establish the exclusivity piece. Looking for that within the Purple

Book, but also as the biosimilar comes on, how long did it take to get to the biosimilar to be approved to the marketplace, et cetera, and further clarity for the developers.

DR. FRANKLIN: So you're describing -- so this would be for approved biosimilar and interchangeable products, and it would show past expired exclusivity dates?

MS. REED: Yes.

DR. FRANKLIN: Okay, thanks.

DR. SHERMAN: Dr. Christl.

DR. CHRISTL: In terms of the education and outreach, you talked about FDA expanding its educational footprint beyond FDA's website. So as you know, we've done some videos. We have done a CE course and some webinars. Do you have other recommendations on, you know, all the stuff that we've done is housed on the website, so can you give a little bit more clarity about sort of your thoughts on expanding beyond the website?

MS. REED: Yeah, and first of all, thank you, because you guys are doing a great job and we

appreciate what you're doing with us at the Forum, so thank you.

This is -- our recommendation is to get it down to the patient in the physician office level. That simplicity of taking it off the website and perhaps something -- because it's the physician, as we talk about the physician confidence, in relaying confidence and using the biosimilar, having something from the Agency as you got, you know, you're the FDI and having you in that patient visit with that physician or pharmacist, to talk about it at that level is even a greater use.

DR. CHRISTL: Thank you for your comments.

MS. REED: Thank you.

DR. SHERMAN: Our next speaker is Dr. Cartier Esham from BIO.

DR. ESHAM: Okay. So on behalf of BIO I would like to thank the FDA for the opportunity to participate in today's public hearing. This is an important topic for BIO and its members.

Of particular relevance to today's hearing, BIO's membership includes all of the leading companies

on the cutting edge of biological product innovation, many of whom are also actively involved in the development and bringing to market biosimilars and interchangeable biological products.

As the FDC predicted in its 2009 reporting regarding the future development of the biosimilar marketplace in the United States, the complexity of developing and administering such product means that this marketplace is likely to take on the characteristics of a brand-to-brand competition rather than the generic competition we see under the Hatch Waxman Act of today.

This is an important and fundamental consideration to keep in mind as we discuss how best to foster a robust competitive marketplace for biological products. BIO believes that safe and effective biosimilars and interchangeable products are good for patients and good for public health, and we were a leader in developing the statutory pathway developed over a decade ago.

We are committed to helping grow a robust marketplace in which innovators and biosimilar

manufacturers can compete on a level playing field, providing a limited period of innovator exclusivity to provide the incentive necessary for companies and investors to devote the tremendous amount of resources and risk required to bring a new medicine to market.

BIO believes that robust competition at each stage of the biopharmaceutical life cycle, from other branded biological products in the same therapeutic class, to biosimilars following expiration of innovator exclusivities is the best mechanism to control cost for patients and payers, while still encouraging the continued investment in innovative treatments for cures and patients over time.

At the same time BIO believes that a level playing field requires that reference produce sponsors, biosimilar developers and the FDA work together to ensure that reasonable access to the product samples needed to safely and efficiently conduct biosimilar development programs is achieved without impeding the ongoing product operations of the reference product sponsor.

We have been a strong supporter of the

Agency's efforts to advance implementation of the BPCAA. It is through the Agency's hard work that in only eight years since the passage of this Act, 12 biosimilars for eight reference products have been approved.

By comparison, during the same initial eight years of the companion European Union process, the MA approved five unique biosimilars to two different reference products, excluding products not classified as biosimilars in the United States, such as transition products, with duplicative marketing authorization by the EMA.

There are important steps needed to be taken by FDA in order to further advance the growth of the biosimilar market, such as the current commitment and activities to educate health professionals, payers, patients and caregivers regarding the meaning, use and value of biosimilars in interchangeable products.

Additionally, the Agency has already finalized much needed guidances, including those on scientific considerations for demonstration biosimilarity, clinical, pharmacology data, and labeling of

biosimilars.

Of particular importance to BIO's members is the finalization of interchangeability guidance, which has been discussed a lot so far today. The criteria for demonstration interchangeability are legally and scientifically different from the standards for establishing biosimilarity. And consequently, demonstrating interchangeability requires additional data. FDA should ensure for products that are administered more than once that the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alteration or switching.

These additional criteria, which should me mapped through the use of clinical switching studies, are critically important to patient safety and to the Agency's faithful execution of the Act. In fact, only an interchangeable product and its reference product should be subject to pharmacy level substitution without the intervention of a healthcare practitioner

who prescribed the reference product, reference medication.

Therefore, finalization of this important guidance in its most recent form would establish how developers can meet these additional statutory requirements to demonstrate interchangeability and further promote and grow the competitive marketspace for all biological products.

BIO continues to support the FDA in its development of guidance on the analysis of analytical similarity. BIO believes that analytical similarity should be determine with the scientifically sound and evidence-based approach, and the determination of the appropriate statistical approach is best determined on a product specific basis.

FDA should work with product developers to identify scientifically appropriate ways with which to deal with changes in reference product attributes over time and how statistical methods may be used appropriately in this context.

Additionally, as FDA noted in its public hearing notice, in many cases patents or statutory

exclusivities may protect one or more conditions of use for a reference product. We are aware that biosimilar products sought licensure for less than all of the reference products conditions of use. In some instances this may be because the reference product has patented, as well as unpatented uses, or uses protected by regulatory exclusivity.

We generally support the principle that a biosimilar manufacturer should be able to sell its product for uses not protected, while the reference product holder should be able to continue to benefit from patent or regulatory exclusivity. The biosimilar label should be clear about which conditions of use are licensed. In instances where this means less than all of the reference product conditions of use, the label should be clear and should only contain information related to the approved uses, except as otherwise required.

In the same vein, supplemental and subsequent approvals of reference products for new uses, changes in product presentation and certain structural modifications of a reference product, should receive

the product's original data exclusivity, a well-established construct that is known as umbrella exclusivity. They do not receive such exclusivity, then a reference product sponsor is actually disincentivized to research and demonstrate any new uses or other improvements to the original product, since such changes would not only be not protected against immediate copying, but could also undermine the remaining data exclusivity of the original reference product.

Accordingly, applying umbrella exclusivity to such improvements is done under the Hatch Waxman Act with respect to small molecule drugs, strikes a reasonable balance.

It is critical that the FDA apply statutory exclusivities fairly and evenly, be in the context of reference products or modified reference biologics, or in the context of biologics that were approved under new drug applications prior -- prior to the -- I'm sorry, I lost my place here.

It is with this respect that BIO urges FDA to rethink its 2016 draft guidance on the application of

data exclusivity to transition biologics approved biologics under the FDCA that would be deemed licensed under the PHS on March 23rd, 2020 and could lose exclusivity protection.

As the biosimilar market continues to grow, BIO will continue to advocate for policies that encourage robust competition, protect patient access to the medicines their providers deem most appropriate for them, and ensure continued investment in innovative biological medicines.

BIO appreciates this opportunity and we will be submitting further detailed comments to the docket later this month.

DR. SHERMAN: Thank you for your comments. Questions from the panel? Dr. Kozlowski.

DR. KOZLOWSKI: So you mentioned that BIO supports access to reference products for development of biosimilars. So being a trade group for many of the companies which, in fact, can make those materials available, what is BIO planning to do to support that goal?

DR. ESHAM: I'm happy to discuss in more

detail offline, as well, and we are in the process of submitting -- developing more detailed comments, but generally speaking we are appreciative of the direction FDA is taking presently. I look forward to working out the details as it progresses.

DR. KOZLOWSKI: Thank you.

DR. UNLU: You mentioned applying exclusivity transition products in 2020, but you said -- you seemed to say that products that would be losing exclusivity on that date. Did you mean to include all transition products in your comment or just those that might have exclusivity on that date?

DR. ESHAM: I think generally speaking, and again we'll provide more details, more specific details in our comments that we submit later this month, but in its simplest terms I think what we're saying is any products that fall under that transition should not lose the exclusivities they hold due to the transition.

DR. UNLU: Thanks.

DR. SHERMAN: Any other questions from the panel? Thank you for your remarks.

DR. ESHAM: Thank you very much.

DR. SHERMAN: Our next speaker is Ms. Sarah Aoanan, Global Healthy Living Foundation.

MS. AOANAN: Good morning. My name is Sarah Aoanan. I am the Patient Advocate and Community Outreach Manager for the Global Healthy Living Foundation. I have no disclosures to make regarding my travel here today. The Global Healthy Living Foundation accepts grants and charitable contributions from pharmaceutical companies, government, private foundations and individuals.

I would like to thank the FDA for this opportunity to provide comments today. The Global Healthy Living Foundation is a 20-year-old 501(c)(3) patient advocacy organization representing chronically ill patients and their caregivers across the U.S., Western Europe, Australia and South America. We work to improve the quality of live for people living with chronic disease, by making sure their voices are heard and advocating for improved access to care at the community level.

Our patients are suffering from chronic conditions, including arthritis, psoriasis,

osteoporosis, chronic pain, cardiovascular disease and migraine, and many of them have been living with these conditions for years. Many patients in our community make sure of biological products to effectively treat their chronic disease. However, they also experience significant out-of-pocket expenses as a result of policies that shift financial burden onto the patient.

Biosimilars have the potential to drastically reduce costs for our patients and we believe in creating a system that will incentivize biosimilar manufacturing and increase competition. We are encouraged to see the steps that the Administration has taken and have outlined in the Biosimilars Action Plan, to ensure that there is an appropriate balance between innovation and competition.

We were particularly happy to see the emphasis on the importance of educating clinicians, patients and payers. We believe that the proper education of stakeholders will help to build confidence in biosimilars and ultimately increase their utilization.

GHLF has worked to harness social media, to educate patients and providers about these new

therapies and their potential to reduce the cost of care. People with autoimmune disease want to know about biosimilars. Often medical and scientific terms are not patient friendly, so we simplify them and incorporate patient lifestyle issues, using social media to reach patients through mediums they already use.

Our monthly Twitter chat averages five million impressions, which helps achieve this educational objective. Many of our patients go through years of trial and error to find a treatment plan that adequately manages their disease, making switching to a biosimilar seem daunting. We believe that education campaigns need to focus on building confidence among patients that these treatments are just as effective as innovator biologics.

GHLF also believes that in order for any educational activities to be successful they need to include robust data that showcases the safety and effectiveness of biosimilars, including those that are ultimately considered interchangeable. These include putting all clinical trials on the product label.

When it comes to demonstrating interchangeability, we have commented extensively on the importance of conducting thorough studies. It is our belief that rigorous switching studies are essential, not only to ensure patient safety, but also to build patient and provider confidence.

As we've stated in previous comments, we agree with the FDA's approach to require clinical studies for multiple switches between the biologic reference product and the proposed biosimilar. We feel that this is important as it will mimic the real world experience of patients and the insurance companies and PBM's frequent alteration to their formulary tiers from plan year to plan year.

Also needed is greater understanding and safety evidence surrounding interchangeability between biosimilars. In the near future patients will likely face switching between two different biosimilars, with or without FDA interchangeability guidance, again, because of formulary tier changes.

We also are supportive of the use of real world data to provide additional evidence on safety and

effectiveness. Patient reported outcomes should be used by the FDA to understand why a patient decides to switch from one product to another. Our 17,000 member patient registry, Arthritis Power, allows patients to actively engage in health research, while monitoring their own progress, in collaboration with their physicians.

Our primary mission is to provide patient reported data to researchers interested in understanding how patients respond to treatments over time. Often the data collected by researchers does not reflect outcomes that matter most to patients. Our patient center data points can further cement confidence in biosimilar products by providing critical usage data.

Additionally, just like generics, patients must share in biosimilar cost savings, through patients' out-of-pocket reductions. This will give patients and physicians another reason to embrace biosimilars. The price of a drug to a patient is their out-of-pocket cost, not an arbitrary list price or the price after rebates, discounts and fees, that an

insurance company, Medicare, Tricare, or a PBM pays.

Therefore, when the country talks about reducing drug prices, we think the conversation must focus on the price the patient pays. In the case of biosimilars, patients must share in the cost savings. Savings to the system, government or private, are not relevant to someone who has a multi-thousand dollar drug expense every year.

A patient's right to know is a priority for GHLF. As odd as it seems to patients they and their healthcare provider may not know what drug they are on. GHLF has successfully advocated for legislation at the State level that requires patients and providers to be notified when an interchangeable biosimilar product has been substituted in place of the innovator at the pharmacy.

These laws also require the pharmacist and the physician to keep track of these substitutions and as a result ensure that patients are aware of any changes to their patient's treatments. Patients assume this protection is baked into the system, but without legislation it is not.

Finally, GHLF feels that the responsibility for helping to build confidence around biosimilars also lies with the payers. It should be working with physicians, patients and patient groups to help them understand that these alternatives are not only just as effective in managing diseases, but will also reduce costs to patients.

GHLF looks forward to partnering with all stakeholders to continue patient education. Thank you again for the opportunity to provide comments on this issue. We will be submitting written comments to the formal docket. If you have any additional comments or questions, please reach out.

DR. SHERMAN: Thank you for your comments. Questions from the panel? Ms. Abram.

MS. ABRAM: Thank you for your comments. I'm wondering if you could expand on your comment during your remarks on the patient reported outcomes, and that the data being collected is not capturing what matters most to patients?

MS. AOANAN: There are patient powered research networks like Arthritis Power, which are a

part of PCORnet and PCORI with patient reported outcomes. I think patients need to be at the center and at the beginning of those conversations before they're collected, and I'm not always sure they are.

DR. SHERMAN: Other questions? Dr. Kozlowski.

DR. KOZLOWSKI: So this is a theme that got covered a little bit before, but you mentioned the importance of patients understanding all the clinical information, and it should be readily available. So again, a lot of the evidence for biosimilarity and interchangeability will be analytical data, which patients may not really have a sense about how to interpret, and so what are your thoughts on how education could include that, because that truly is something that's very precise and although clinical data is ground truth, analytical data is a key part of this, and really the foundation, because no matter how large the clinical studies, they will not address everything.

MS. AOANAN: Well, we initially hope that we can put clinical trials on the label and the inserts, to be as transparent and provide the maximum amount of

analytical data for the prescriber and patients.

DR. KOZLOWSKI: So by analytical data I mean, you know, laboratory data on the structure of the molecules, so not necessarily analysis of the clinical data. So again, I think that that's a harder concept for somebody to grasp, because as a patient you say well here are patients, they were treated, I can understand the outcomes. Analytical data is different and I think again I'm very interested in how that could be conveyed, because that's harder to convey, but it is a very important part of confidence around biosimilarity and interchangeability.

MS. AOANAN: I think that's working with patient groups to demystify the language, to break it down for them step by step, data point by data point. I think they can understand if you take it slowly with them, but really emphasize the educational aspect.

DR. KOZLOWSKI: Thank you.

DR. SHERMAN: Thank you for your comments.

MS. AOANAN: Thank you.

DR. SHERMAN: Our next speaker is Ms. Samantha Reid from Patients for Affordable Drugs.

MS. REID: Hi. First of all I would just like to say thank you to the FDA for having me and giving me the opportunity to speak today. My name is Samantha Reid, and I was diagnosed with Crohn's Disease in 2010.

For the first several years my disease was controlled with mesalamine but after that was no longer enough, it became clear that I needed to try biologic medication. In 2015 I went on Humira, but after nine months I stopped the drug because I wasn't seeing meaningful improvement.

I'd like to share my story with you to underscore the importance of enhancing competition and innovation in the biological products marketplace for people like me.

In late 2015 I became so ill that I was admitted to the hospital. From then on my journey with Crohn's proceeded on a downward spiral. I had to move back home with my parents, go on a high dose of steroids with terrible side effects, like insomnia and hair loss, and I couldn't eat solid foods.

When I could sleep, I was sleeping upwards of 16 hours a day. Life was pretty untenable for a 24-

year-old who was just trying to support herself and start her career.

In the spring of 2016 I was started on the biologic drug Entyvio. While I have faced other health hurdles since, Entyvio has controlled by Crohn's Disease well over the last few years. I regained a basic qualify of life that I didn't have before. I can exercise, travel and even eat out at restaurants, which probably doesn't sound like much but it was a basic luxury that my disease was preventing me from before. But Entyvio and biologics in general are expensive. I am painfully aware of how dependent I am on Entyvio's Connect Program in affording my drugs, and how capricious it is for my life and health to go on at the whim of a pharmaceutical company.

I don't have the same flexibility and opportunities as my health peers, because access to quality health insurance is always at the top of my mind. I know there's no way I could afford the list prices of my drugs if it came to that. I live in fear of losing access to the medications that have given me my life back.

I grew up in a middle-class family. We didn't take lavish vacations, and I bought my first car, which was a 1998 Ford Escort, with $2,000 that I saved up from working shifts at Applebee's. I afforded college largely on a scholarship. I don't have a huge safety net to fall back on. All I want is for me and for patients like me to be able to afford the medication we physically need to go forward living our lives. I don't want to spend the rest of my life in debt, simply because I was unlucky enough to inherit an incurable disease.

That's why I know how important access to cheaper biosimilars would be for patients. Another patient who could benefit from faster access to biosimilars is a friend of mine, Stacey Ransom. She is a mom to an eight-month-old son from Southern California and she also lives with Crohn's Disease.

Humira, a blockbuster anti-inflammatory drug, for which there is no generic or biosimilar, has given her her life back, but it is draining her family's bank account. Because AbbVie is making delay deals that will maintain the company's monopoly, the Ransoms will

be forced to pay $15,000 for Humira through 2023, money that could instead be saved, used for retirement or put in her son's college fund.

In light of patient experiences with biosimilar drugs in competition or lack thereof, we would like to offer comments in three primary areas. The FDA should seriously reconsider whether biosimilars found to be interchangeable, safe and effective, should be required to perform switching studies, or if the scope of these studies could be limited. We believe that biosimilars should be regulated in this regard as closely as possible to generics.

Switching trials at high costs, which drive up prices and delay biosimilar market entry. If the biosimilar has demonstrated effectiveness and safety, we prefer to minimize time and expense to market in order to capture the greatest possible savings. We believe that labeling conventions should be the same as for generic drugs. The biosimilars should be able to rely on brand biologically bling to ensure that professionals and patients understand clearly that the two drugs are interchangeable and have no clinically

meaningful differences.

One goal of biosimilars should be to encourage substitution at the pharmacy counter for patients first starting on a biologic or biosimilar. Manufacturers say they would benefit from greater regulatory clarity in this regard. And there should be a clear direction from the FDA to states in favor of substitution, provided that safety and efficacy have been demonstrated. But we do not support forced switching of patients currently on a biologic, especially for complex diseases, switching should only be by informed choice for those patients.

Drugs don't work if people can't afford them and access to treatment shouldn't depend on your socioeconomic status. If young people like me have access to affordable biosimilars, we give them the chance to enter the work world on a level playing field. Without cheaper options than these $25,000 per dose medications, young people like me are entering adulthood at a deficit that is going to be nearly impossible to climb out of.

I thank you for giving me the opportunity to

speak today.

DR. SHERMAN: Thank you for sharing your story with us. Questions? Dr. Franklin?

DR. FRANKLIN: Thanks. You mentioned that for substitution at the pharmacy counter is important and also that patients should be involved in the decisions to switch if they are already established on a biologic. Those two concepts are compatible from your perspective, and how does that work when the patient interacts with the pharmacist?

MS. REID: So they are. I know it's a very specific circumstance but I think that if you are on a biologic that's working for you and you are stable on that biologic, switching should not occur unless it is you and your doctor's decision to do so, because it is such a precarious situation for patients on biologics to find one that works for them and to stay on it.

But I think if, for example, you're like me, where I was on mesalamine first and then just entering the biologic market, I think that it should be an option for -- and it should be encouraged for interchangeability from the pharmacy counter for

patients to -- if, you know, they've been started on biologics and should be on Remicade, to be offered the biosimilar of Remicade, for that first entrance into biologics, but I think from there it should be very dependent on what is working for the patient and what the medical provider and the patient think.

DR. FRANKLIN: And just as a follow-up, so if the -- if interchangeability of that designation by FDA results from a showing that the product has met the requirements for interchangeability, is there -- do you think that there needs to be more understanding of the -- what those interchangeable products are required to show to get approval by FDA, to enhance the confidence of -- regarding substitution among patients?

MS. REID: Absolutely. Absolutely. I think that there's some skepticism from patients on biosimilars, truly because they just don't know enough, and because of what you all were talking about earlier in terms of analytical data being more difficult than clinical data for patients to understand. And so I think that the more information you could put out there, the better, and not just from FDA websites but

on the ground floor from patient visits with providers and getting in there, because not all patients are going to have the knowledge base to go out there and seek out that information themselves. It needs to be brought to them from the very beginning.

DR. SHERMAN: Other questions? I have one. From a patient's perspective, labeling, because I think we heard slightly different things this morning, putting aside interchangeability for a moment, what do you think should be reflected in the labeling? What would be most useful to a patient in terms of what kind of -- how much information other than the fact that it is a biosimilar, be communicated?

MS. REID: I think that, like I said, it is a scary prospect for a patient switching to any new medication, let alone a biosimilar, and because there isn't as much information, people tend to get a little nervous about making that switch. So I think that making the labeling as close as possible to generic labeling is key in creating that confidence in patients that it really is interchangeable, and that's if the FDA has proven that it is and has shown that it is and

has approved it as such. It should be labeled as such, because I think any other type of labeling just leads to more uncertainty from patients.

DR. SHERMAN: Thank you. Any other questions? Thank you. We are a little ahead of schedule but not enough ahead to squeeze another speaker, so do any of the panelists have questions for any of the previous speakers? Dr. Kozlowski.

DR. KOZLOWSKI: So to go back to the original presentation, I think by Janssen, where we talked about switching between biosimilars and the difference between switching between different anti-TNF's in the class, so I was kind of curious what you think is a higher risk, switching between a different anti-TNF in the class or switching between a biosimilar?

DR. SHERMAN: Please do. Thank you.

DR. GREENSPAN: So as you may be familiar, some of the drugs within the TNF class have different indications. For example, etarnecept Enbrel has not been shown to be effective in IBD, so those would be obvious examples of how the molecules are so different enough that some of them don't seem to work in

indications where some of the other drugs do work.

DR. KOZLOWSKI: Right. But if they were switched sort of, again, it's not substituted, it's switched, obviously it's by a healthcare provider and it's for an appropriate indication.

DR. GREENSPAN: Yeah.

DR. KOZLOWSKI: Because you mentioned some risks about that, even in the context -- same indications, so I'm sort of curious what do you think is a higher risk?

DR. GREENSPAN: I think it's fair to say the similarities between an innovator and a biosimilar are closer than two different molecules within the TNF class, but just to highlight, the absence of data on biosimilar switching is a real concern for prescribers, and I think having some data around that, whether it be postmark and commitment safety data, I think would be valuable and increase the confidence of prescribers on this issue.

DR. FRANKLIN: Thank you.

DR. SHERMAN: Thank you. Any other questions from any of the speakers? Okay.

Then we will take our break and we will start promptly at 10:26. Thank you.

(Break, 10:14 a.m. until 10:24 a.m.)

DR. SHERMAN: Just one announcement. Linsey Mayor has now joined us from OMA. Linsey, can you just wave, if any members of the press need to contact? Thank you.

Okay, our next speaker, first speaker after the break is Nathan Doty from AbbVie.

MR. DOTY: Good morning. My name is Nathan Doty and I work on Bara Therapeutics Regulatory Matters at AbbVie. AbbVie is encouraged that FDA is holding this Part 15 hearing today to collect important feedback from all stakeholders.

We agree with FDA that we will eventually see multiple biosimilar products approved as interchangeable with a single reference product. We urge FDA to respond with science-based policies that will provide clarity to stakeholders.

Today I will discuss the issue of automatic substitution between two biosimilars, each found interchangeable with a single reference product. I

will present three points for FDA to consider.

First, the likelihood of automatic substitution between two interchangeable biosimilars of the same reference.

Second, the lack of scientific evidence to support such substitution.

And third, some proposed actions the Agency can take to address the challenges of automatic substitution in a complex environment.

So first let's look at the likelihood of automatic substitution between interchangeable biosimilars of the same reference product. Consider the following situation. Three medicines are approved to treat a chronic condition. We have a reference product A and two biosimilar products, B and C. B is interchangeable with reference A, and so is C.

Now let's imagine you're a patient with that chronic condition. You go to the doctor and she prescribes you reference A. You take that prescription to your pharmacist. She knows that there are interchangeable products approved for reference A, and she appropriately substitutes interchangeable B.

The next month you need a refill. You go back to your pharmacist or maybe you're changing pharmacies, again carrying a prescription for reference A. This time your pharmacist automatically substitutes interchangeable C for the prescribed reference A, and this substitution seems consistent with the interchangeability determination for interchangeable C.

So what just happened? You were switched from interchangeable B to interchangeable C without the intervention of your doctor, an automatic substitution. Yet these two products have not been determined interchangeable with one another. You can imagine these substitutions happening again and again over the course of your treatment. And the issue is compounded as more interchangeable products become available.

But your pharmacist did what she was supposed to do. And such cross-substitution feels appropriate and familiar. After all, A-rated generic drugs of the same reference are substituted all the time.

And that bring us to our second point. We don't have the clinical data needed to scientifically justify the automatic substitution we've just

described. We can't use the generic paradigm for interchangeable biosimilars. For generics generally active ingredients are chemically synthesized to be structurally identical to the reference. That means that two generics of the same reference contain the same active ingredient.

But that's not true for biologics. Even biologics demonstrated to be biosimilar to one another will have structural differences. Plus biologics that are interchangeable with the same reference will have differences from one another.

We might like to assume that the structural differences between two interchangeable biosimilars of the same reference would be relatively subtle. Even so, as FDA recognized in the draft interchangeability guidance published last year, subtle differences matter. I'm quoting from the draft guidance here. "With switching multiple exposures to each product can prime the immune system to recognize subtle differences in structural features between products, and the overall immune response could be increased under these conditions."

Now, FDA has made clear that this immune response in patients cannot be fully predicted from structural comparisons or pre-clinical data. An interchangeability application doesn't include analytical structural comparisons between two different interchangeable biosimilars of the same reference. More importantly that interchangeability application doesn't include clinical, multiple switch studies between two biosimilars. That's to say it doesn't include the clinical studies that FDA asks for in making statutory interchangeability assessments.

So we can see these issues present a real challenge and here's my third point. How do we respond to that challenge? In navigating complex healthcare environments, we all count on guidance from you. The key role for FDA in addressing the issues we're raising, is to educate stakeholders on the scope of FDA's interchangeability determinations.

All stakeholders need to understand that interchangeable biosimilars of the same reference are not themselves automatically substitutable with one another. A pharmacist who understands this issue would

more carefully examine a patient's medication history when deciding which interchangeable product to dispense.

Efforts to educate stakeholders on the scope of FDA interchangeability determinations can take a number of forms. It should be included in the planned ramp-up and education efforts as described in the Biosimilars Action Plan. It should be included in the labeling of all approved interchangeable products. And most importantly, it should be included in the Purpose Book.

At a minimum there should be a statement in the Purple Book making clear that an FDA interchangeability determination does not imply interchangeability with other interchangeable biosimilars of that reference.

The Orange Book primarily serves as guidance to the states regarding pharmacy dispensing practices. The Purple Book should play that same role. Many states have already developed laws, guidance, rules and practices around automatic substitution of biosimilars. Other states are still working on this issue.

Importantly, the states need good guidance that will clarify the relationship between biologics and clarify the scope of FDA interchangeability determinations.

Like the Orange Book the Purple Book can give them that guidance.

Let's put this altogether. A complex biosimilars world is coming, a world with multiple interchangeable biosimilars approved for a single reference. Science must drive the policies needed to navigate the coming complex environment. And we need to educate stakeholders on those policies.

I'd like to thank you again for the opportunity to provide input and look forward to any questions that you might have.

DR. SHERMAN: Thank you for your comments. Questions from the panel? Dr. Kozlowski.

DR. KOZLOWSKI: So obviously the FDA draft guidance recognizes such a possible risk, but do you think that the residual risk is the same after two products have already undergone switching studies with a potentially subtly different reference product and

not had differences, that that risk is the same as if none of those studies were done, or in fact does that reduce the residual uncertainty?

MR. DOTY: Thank you for the question. I think what we would identify is that we have subtle differences between those two products, and those differences could be differences in degree or differences in kind between the differences that were evaluated between the interchangeable products and the reference.

What we're asking is that FDA think about the scientific evidence that was needed to demonstrate interchangeability between the reference and the interchangeable product. Think about whether that similar evidence is needed to make a determination between interchangeable products of the reference. There could be subtle differences that could matter.

DR. KOZLOWSKI: Yeah, but I think the question though is there's always some level of uncertainty as you look at things. The question I would ask is does having two products with two switching studies already with a reference product and not having an issue, does

that change your starting point? In other words, is that a different place in risk that you're starting from than if you were de novo with no experience in switching at all?

MR. DOTY: I think the reason that the Agency does clinical switching studies and asks for those studies and the reason the BPCIA asks for the Agency to look at those issues is because we can't predict in advance what differences between products might prompt a response in the immune system.

And so what we're asking the Agency to do is to think about the importance of that scientific evidence and what that scientific evidence is showing us and why we need to collect that evidence before we can make a determination that those two products would be interchangeable with one another.

I think the key takeaway that I would give here is that we need to understand that there are fundamental differences here between biologics and generics, and that we can't just port the A rated generic model onto the interchangeable biosimilar model, and we need to understand that that's going to

be a different market and we need to educate stakeholders about that different market and explain to them those differences?

DR. KOZLOWSKI: Thank you.

DR. SHERMAN: Dr. Unlu?

DR. UNLU: To kind of build upon your example, manufacturer of reference product A makes a manufacturing change that results in a subtly different reference product, let's call that A prime. And the patient goes to the pharmacy and gets dispensed with A prime, so she just got switched from A to A prime. What do you think is the amount of scientific evidence we should be asking for to justify that kind of switching?

MR. DOTY: So it's an interesting question. I think I would just say that we have to focus really clearly on the standards that are set out in the statute and the evidence that FDA is asked to collect as a result of that. And so there's the specific standards set out for interchangeable biosimilars and the kind of data that needs to be collected to support that. And it's collected because there is a concern

about the switching back and forth between two products, and in my view it's a recognition of some of the complexities that we're talking about here.

Where FDA is looking for that specific evidence to make a determination about immunogenicity risks between a reference product and an interchangeable product, it makes sense that that same data would be collected to demonstrate interchangeability between two interchangeable biosimilars.

DR. SHERMAN: Great. Thank you for your comments.

MR. DOTY: Thank you.

DR. SHERMAN: Our next speaker is Dr. Steven Lucio from Vizient.

DR. LUCIO: Good morning. My name is Steven Lucio and I am speaking today on behalf of Vizient, the largest member group in healthcare performance improvement company in the United States. Vizient provides innovative day-to-day solutions, expertise and collaborative opportunities that lead to improved patient outcomes and lower costs.

We would like to express our appreciation to FDA, not only for this public forum, but also for its continued efforts to establish, implement and enhance the biosimilar approval process. We fully endorse the scientific principles of biosimilarity and the biosimilar approval pathway.

Part of Vizient's core capabilities is our sourcing services represents over 100 billion in annual healthcare expenditures, much of it associated with pharmaceuticals. Give the size and the diversity of our membership, we are critically akin to all strategies, managing, increasing drugs costs.

Since 2010 Vizient has provided ongoing training and education on the biosimilar paradigm in the form of over 200 in-person presentations and web conferences, and have displaced clinical resources to support formulary evaluations of biosimilars and ongoing contractual relationships with biosimilar manufacturers to maximize the value and cost savings of our membership.

We have over 50 pharmacists and other subject matter experts that are currently facilitating

appropriate biosimilar adoption and documenting the value and sustained high quality of care these products provide.

Based upon our experiences and more importantly that of the endorsed membership of leading academic medical centers, pediatric facilities, community hospitals, integrated health networks and critical access providers, we would like to share our insight of our experiences with the biosimilar paradigm in the form of these full-in recommendations.

Our first recommendation is that FDA should provided increased detail concerning aspects of biological drug approvals to address the continued hesitancy some clinicians still possess regarding biosimilar safety and efficacy.

We applaud FDA's efforts at enhancing the educational information available on its website. Still the disclosure and ease of accessibility of two additional data sources would further facilitate understanding of biosimilars.

First we encourage FDA to publish a summary review documents for all biosimilar approvals at the

time of initial approval, regardless of whether or not a biosimilar was subject to an advisory committee discussion. While a concept such as totality of the evidence can be well articulated in principle, documentation of those precepts and practice greatly enhances clinicians' understanding.

We've witnessed the impact, the availability of this information or its absence has had on biosimilar uptick. Whereas member formulary reviews of infliximab DYYB were enabled by the availability of the summary review information, the consideration of infliximab ABDA has been hindered by its absence. The availability of this documentation increases awareness of the value, relevance and importance of analytical data in the characterization of a biosimilar.

Second, we request that FDA publish information concerning the history and timing of manufacturing changes for originator biologics. Few practitioners are cognizant of these changes that occur throughout the life cycle of an originator and view the role of analytical characterization as something novel to the biosimilarity determination experience.

Information on manufacturing changes, such as the content disclosed by the European Medicines Agency, has been incredibly beneficial in explaining the variability of originators as evidenced by the comment that you see from one of our member clinical pharmacy experts. If FDA were to disclose this information about originator changes to the originator biologic, which are measured and monitored via analytical techniques, the validity of these studies would find greater acceptance within the discussion of biosimilars.

Recommendation number two, the FDA should revise and expand the content in the Purple Book, as well as increase the ease of data review and interpretation. Information in the Purpose Book ideally would reflect a more user friendly, searchable database that would clearly represent the relationship between originator reference biologics and any associated biosimilar and/or interchangeable product.

When searching for a biosimilar, a user should be able to see quickly to what extent a products label matches that of the originator reference product and

what absent indications is a result of various exclusivity, such as orphan exclusivity.

Third, the Purple Book would be an excellent place for the previously requested information such as the links to the summary review documentation for approved biosimilars and information concerning the manufacturing changes of originator reference biologics.

Recommendation three, FDA should finalize the interchangeability guidance to maximize the efficiency of approval of interchangeable biologics and to further clarify the utility and relevance of the interchangeability designation.

Our members understand that final guidance on this issue remains pending and that no formal trials to assess interchangeability have been completed; however, in addition to the absence of this information, there remains a lack of understanding regarding the utility of this specification beyond the overt definition in the Biologics Price Competition and Innovation Act. Our members continue to struggle with the long-term impact of interchangeability designation, particularly

given the wealth of clinical data already present for approved, non-interchangeable agents.

As seen above, our members even reference the Agency's website, detail of the assurance of comparable safety efficacy of non-interchangeable biosimilars, further calling into question the extent to which an interchangeable biologic would be further differentiated.

To the extent to which both biosimilar suppliers and the FDA itself should invest substantially in this designation remains an uncertainty among many clinicians themselves and requires additional clarification.

Recommendation number four, FDA should review its decision on the devoid of meaning suffix, when it comes to biologic nomenclature. Vizient continues to receive numerous comments from its membership regarding the devoid of meaning suffix, and its utility and clinical practice. Our members understand the significance of pharmacovigilance for all pharmaceuticals. Still our clinicians continue to question whether or not the current application of this

strategy is most useful or whether this differentiates or actually conveys that a biosimilar is, in fact, not similar to an originator.

Vizient and its membership agree that the documentation of safety and efficacy of biosimilars will increase the level of acceptance of these products. In addition, we believe there are multiple options to make an identifier approach more effective and efficient.

Option one, you could be utilizing the serialization strategy of the Drug Quality and Security Act to promote improved monitoring pharmacovigilance of all medications. One alternative to the devoid of meaning suffix is the tracking and monitoring of the unique serialization requirements established by DQSA. The unique designation at a product level would enable tracking not just a version of the biologic, but the specific law providing the higher level of specificity.

Option two, the FDA considers modification of the proper name to include the separate identifier as a necessary element. Vizient recommends using a meaningful differentiator to convey useful information

about the product, such as whether it is an originator or a biosimilar, whether or not it's interchangeable, the extent of indication coverage.

And option three, if FDA maintains the approach of the devoid of meaning suffix, we recommend the application of this standard to all biologics, originators and biosimilars. This approach would address the aforementioned member concern that biosimilars are in some way meaningfully different from originators.

Vizient affirms the important of the biosimilar approval pathway and the absolute necessity of creating a sustainable market of competing biologics and we appreciate FDA's willingness to review and revise the approval process and to call attention to other factors that affect the uptick of biosimilar, even those outside of the Agency's scope.

Such efforts will enable us to achieve that virtuous cycle of innovation and competition that benefits patients and the healthcare community as a whole.

In closing, we would like to highlight that

the success of biosimilars is more than simply whether or not we can support competing biologics, but if we can achieve a more stable, predictable and value-based approach to medication supply and management. We will be submitting written comments and I now look forward to entertaining your questions.

DR. SHERMAN: Thank you for your comments. Questions from the panel? Dr. Franklin.

DR. FRANKLIN: Hi. On the recommendations for the Purple Book, I think could you clarify a little bit or expound upon the -- some of the recommendations that you have, including the inclusion of information about manufacturing changes? Is that intended to be useful to providers or to some other group. Could you clarify a little bit?

DR. LUCIO: Absolutely. Thank you for the question. Yes, we -- that information has been very helpful. What has been available either directly from EMA or in some of the other clinical literature that has been published, helping them to understand the paradigm of originator biologic variability. That has kind of demystified some of the concern and made it not

quite as novel of an experience, but still even with the information that, you know, our organization provided, others have provided FDA, there's still a lot more education that could take place. And so making that easily accessible would be very helpful.

DR. SHERMAN: Dr. Kozlowski.

DR. KOZLOWSKI: So in terms of making manufacturing changes public, kind of, one assuming that there was a legal framework to do that, which there may not be, there are many, many, many manufacturing changes. Some of them are very small, right. Some of them are very, very large. Do you have any sense about what would be looked for to be public?

DR. LUCIO: I think even just the number of manufacturing changes and that gradation of whether they are more complex, whether simple, and even helping the public to understand what the differentiation of those types of changes happen to be, would be very instrumental, so even if the number could be per molecule of what has transpired, even that is informative and maybe even over a certain timeframe that would be very useful.

DR. KOZLOWSKI: Okay, thank you.

DR. LUCIO: Sure.

DR. SHERMAN: Other questions? Thank you for your comments.

DR. LUCIO: Thank you.

DR. SHERMAN: Our next speaker is Kathleen Arnsten from Lupus and Allied Diseases Association.

MS. ARNTSEN: I am Kathleen Arnsten, President, CEO, of Lupus and Allied Diseases Association. Good morning and thank you for the opportunity to provide my unique patient perspective.

Biosimilars hold tremendous promise and therapeutic advantages for people like me, just as biologics have revolutionized treatment for millions of individuals. As more biosimilars become available in the United States, we want to ensure they are safe, efficacious, accessible and affordable. We must remain vigilant in protecting patient safety while promoting unfettered access to vital treatments.

Lupus is an extremely complex, chronic, inflammatory autoimmune disease affecting virtually any organ system of the body, with few approved drugs, no

known cause or cure, and a challenge to live with and treat. Besides Lupus I struggle with several other autoimmune disorders and comorbid conditions. I take 46 drugs a day and have a paralyzed GI tract and am blind in my right eye.

I have allergies and sensitivities to both active and inactive ingredients in drugs and I recently developed a cardiac complication after using an eyedrop for only four weeks.

There is no cookie-cutter approach to treat intricate patients like me. Our immune response to drugs is unique, contrary and at times adverse. Due to the heterogenous nature of autoimmune diseases, no two patients are alike and treatment is highly individualized. Effectively treating us requires thinking outside the box and media access to the entire arsenal of treatments and open and transparent communication between us and our providers. They know best what therapies to use.

In response to Question 3, it is essential that the intricacy and vulnerability of the patient populations is taken into consideration when dealing

with biosimilars, especially since the performance may not be equivalent in every population, resulting in unexpected effects.

Patients like me are so hypersensitive that even the slightest change in manufacturing dose or delivery method, as well as switching between drugs, can provoke immunogenicity.

In order to be designated as interchangeable, biosimilars must unequivocally produce the same clinical result in any given patient and each condition for which the biologic reference product was approved, rigorous criteria including sufficient proof of clinical efficacy, safety, purity, potency and tolerability must be provided for each population, even if they are small studies, not just projected clinical safety, and any product that is deemed as such must be shown to be safe and effective in a marketplace, where one originator will have multiple biosimilars and interchangeable products, which will lead to patients being switched multiple times.

We urge you to finalize guidance on interchangeability and keep in mind atypical patients

like me, who do not fit the norm, and the importance of safety as you consider ways to increase confidence in these products. We also ask that you include clarification on the potential substitution of two biosimilars that are deemed interchangeable with the same reference product but not considered interchangeable with each other.

We applaud you for instituting guidance for distinguishable suffixes, and support the establishment of a policy that includes unique nonproprietary names with meaningful suffixes, for future interchangeable biosimilars in order to assure patient safety and provide transparency and from collegians processes.

Utilizing discernable names is necessary to identify exactly which medicine was received, if an adverse event does occur, since all biologics will be administered to individuals suffering from serious diseases, who also take multiple medications and do not participate in a controlled study. This will increase patient provider confidence, which will foster market uptick, while enhancing industrial competitiveness.

The regulatory process must also evaluate

biosimilars through post-marketing surveillance in order to not diminish product efficacy and be detrimental to patient safety. Preapproval, non-clinical and clinical testing will establish that there are no meaningful differences in safety, efficacy or mechanism of action comparability. But only real world evidence will demonstrate this.

We suggest that you consider adopting innovative methods, such as aps on electronic devices and patient reported outcomes to monitor real world events. Pharmacovigilance is essential for all biologics, as they pay produce immunogenic reactions in patients who may also be hypersensitive to changes in production methods or impurities. Adverse effects are difficult to predict and may only occur after many years of treatment. And due to the abbreviated review process, you must do more to implement comprehensive post-market tracking and reporting to detect safety problems. Developing an aggressive tracking system will also help to guarantee stakeholder confidence and facilitate market uptick while establishing a longitudinal electronic medical record.

In response to Question 9, one of the biggest impediments to the advancement of innovative therapies is the overabundance of egregious payer utilization management policies, such as step therapy and non-medical switching protocols. These cost containment measures pose an ethical dilemma for healthcare professionals by requiring the provider to follow a set course of care, regardless of their best personal judgment. They are not based on a person's specific medical profile or the physician's assessment of the best treatment option for an individual's condition and certainly do not apply to an atypical patient like me, who is excluded from the cited clinical studies the insurer uses as justification.

As an individual who is harmed by step therapy protocol, I am concerned that patients who are stable on a biologic will be switched for non-medical reasons to a biosimilar that has not been determined to be interchangeable. We urge you to establish robust patient safeguards by applying strong scientific safety standards, as stating the switching of stable patients should only be determined by the treating provider and

patient and facilitating dialogue among multi stakeholders, including payers.

These practices do not keep pace with biomedical innovation and nothing is being done to modernize the process. We must act now or payers will continue to manipulate research to their benefit in order to justify preferred treatments. You must reach out to other federal agencies and work with them to develop sound policies that address access issues. We feel that biosimilars have the potential to promote greater competition among biological products and hope that they are more affordable and accessible for individuals struggling to manage life-diminishing diseases. There are many Americans who struggle to get through each day with some semblance of dignity and tact, who have little or no treatments. It is the promise of research and development to discover better treatments and the belief that a regulatory system should deliver them, that motivates us to keep going, but it's time to finalize all biosimilars guidances and execute your action plan and get back to regulating and advancing all drugs and devices for those who

desperately need them. Regulatory policy must keep pace with innovation.

In closing I want to reiterate that I am unwavering in my belief in the sanctity of the doctor-patient relationship and that only providers who are familiar with an individual's personal medical history should be making treatment decisions. Patient's safety must be first and foremost in choosing the most appropriate therapies for any person with complex medical conditions.

I have faith that we can advance biosimilars while still allowing physicians to make decisions in the best interest of their patients. I believe in the FDA and our regulatory process. There are millions of people who could benefit from access to innovative therapies now and many more in the future who are yet to be diagnosed. United we can achieve the promise of biological medicines for them. We need to work together to make that happen.

I thank you for the opportunity to share my perspective and I applaud the FDA for continually recognizing the importance of the patient voice during

the regulatory process, and we will be submitting comprehensive written comments. Thank you.

DR. SHERMAN: Thank you for your comments. Questions from the panel? Ms. Maloney?

DR. MALONEY: Yes. Could you just, point of clarification, you spoke about post-market surveillance for biosimilars but were you suggesting it should be different than for the originator?

MS. ARNTSEN: No. I think that all drugs and devices should have robust pharmacovigilance. I believe that with the advent of electronic health records that it's very easy to track and trace through electronic systems. I recently had surgery and I have several devices planted in my body, and they all have serial numbers. They're all part of my EHR, and f anything was to happen, it would be very easy to track them and trace them.

DR. SHERMAN: Other questions? Thank you for your comments.

MS. ARNTSEN: Thank you.

DR. SHERMAN: Our next speaker is Dr. Richard Markus from Amgen.

DR. MARKUS: Thank you. My name is Richard Markus and I'm Vice President of Development at Amgen for Biosimilars Division, and as you know Amgen is a developer and manufacturer of both originator products, as well as biosimilars.

I will present thoughts on four of the questions asked, as listed here, as well as some additional recommendations.

The FDA has been effective in reviewing and approval of biosimilars, with the first approval in 2015. FDA has approved a total of 12 different biosimilars to eight reference products, and they have been meeting the timelines as outlined in both PPCIA agreements. We can compare that to the EMA, which has also been effective, though they started six years earlier with a legal basis for approval, and hence it's understandable that more applications have been approved in that region.

But if comparing the eight years of the PPCIA pathway in the U.S. to the first eight years of having a pathway, the EU approved five unique biosimilars to two reference products compared to the FDA's 12

biosimilars to eight reference products. Our experience working with both agencies is that the requirements and expectations are generally consistent and the FDA has been very flexible while maintaining scientific integrity.

We hear a lot of discussion about the U.S. Market and questioning why it's different than Europe or elsewhere, and I suspect that's a major reason we are all here today. We believe the current U.S. landscape is set up for significant competition that will lower costs to healthcare systems.

In the U.S. there so far has been two originator biologics to face biosimilar competition, and two more just recently launched. The first approved biosimilar, which competes with Filgrastim, has rapidly obtained substantial market share and market uptick over the first three years was comparable to its uptick in Europe.

The second product with competition is infliximab and those biosimilars have struggled but there are multiple reasons as to why those may have struggled, and we don't believe this is indicative of

the market behavior as a whole.

A key aspect for evolving the biosimilar landscape is through education. We believe that the current FDA requirements are appropriate to ensure confidence in biosimilars and with that the requirements and scientific standards should be shared and understood by the stakeholders, so they are well informed, and this can facilitate their acceptance and confidence in this new type of biologic.

Amgen's caution with standardization in order to maintain regulatory flexibility within the scientific approach.

I will now address Question 4 with consideration for testing the reference product lots. First, based on our experience, developing biosimilars, the cost of procuring the reference product used for analytical characterization and analytical similarity testing is generally less than five percent of the process development and preapproval manufacturing costs. Therefore, limiting the number of reference product lots will only minimally decrease costs. However, it may add risk as the sampling of fewer lots

may not provide a true range of product attributes.

Additionally, if this approach is employed by multiple sponsors, this increases the likelihood of greater differences between two biosimilars or between two interchangeable products. This concept is illustrated in the figure on the right, where one sponsor may randomly acquire the lot circled in blue and a second sponsor may randomly acquire the lot circled in green.

Both sponsors would believe they have a representative sample of the reference product, as well as a good estimate of the mean for the attribute, when in fact they don't, and the two would differ in their product design targets.

Ultimately, the number of lots tested should be appropriate to characterize the variability of critical attributes in the reference product.

Question 5 is regarding the potential use of non-U.S. license comparator. We believe such an option may be appropriate and this includes potentially being appropriate for development of interchangeable biologics. However, bridging of non-U.S. product to

that of the U.S. product is still important and a flexible science-based approach to bridging is recommended.

Incentivizing innovation is clearly a key consideration in the ideal healthcare environment. Developing new medicines is high risk, where many programs ultimately do not show clinical benefit. So to make such risky investments worthwhile, there has to be confidence the intellectual property created will be maintained and supported, and that the appropriate patent protection and regulatory exclusivity will be awarded for biotechnology innovations.

Amgen believes that umbrella exclusivity preserves critical incentives for continued development and innovation that can improve patient outcomes.

I'd like to spend a moment addressing perspectives on interchangeability, since there's been some rhetoric about how critical this is for competition. First, the U.S. is the only highly regulated jurisdiction with a defined pathway for health agency determination that facilitates pharmacy substitution of biologics. For example, this doesn't

exist in Europe and that market is very competitive.

Another point is that only ten percent of biologics that are reported to lose exclusivity in the U.S. through 2023 are primarily distributed through a retail pharmacy, where substitution can occur. And, therefore, the function of pharmacy substitution likely will offer little contribution to the marketplace for 90 percent of these products.

For the ten percent of products for which interchangeability could be relevant, Amgen feels that the FDA draft guidance on interchangeability outlined appropriate science-based standards and allowed the appropriate degree of regulatory flexibility.

We, therefore, urge the Agency to finalize the draft guidance without significant revision. However, it would be beneficial if the FDA clarifies in this or other guidance how proposed interchangeable products can address potential life cycle management by the reference product, including those listed on the slide, such as changes in formulation, updated devices and new indications.

In my last couple of minutes I'd like to make

a few suggestions to FDA, including circumstances when expedited review could be available, with some suggestions listed on the slide.

Regarding manufacturing plant inspections, the expectations of GMP manufacturing are and should be the same for originators and biosimilars, as there should only be one GMP standard of what is appropriate for biologic manufacturing. Therefore, these recommendations apply to both originator and biosimilar approvals. Conducting preapproval inspections earlier in the review process and more communication about potential findings could provide more time to address the concerns, potentially facilitating approvals.

With regard to labeling changes, we know there are many times a biosimilar will be licensed without all the indications of the reference product, when scientifically appropriate and when the patent or regulatory exclusivity ends, then an expeditor review to add the additional indications should be considered.

In conclusion, the FDA has been very effective with regard to meeting the review timelines outlined in both PPCIA agreements. And there are now two products

with biosimilar competition of more than a year and two more just launched, so it's early as there are many more expected to launch in the near future, and the market will likely evolve quickly.

What can FDA do? We have outlined some points that may be helpful. Importantly, the FDA can partner with medical societies and patient groups in outreach and education and we recommend maintaining flexibility and current regulatory standards that are consistent with other ICH agencies, as this will maintain confidence in this class of products.

Thank you.

DR. SHERMAN: Thank you for your comments. Questions from the panel? Dr. Kozlowski.

DR. KOZLOWSKI: So you mentioned the cost of acquiring reference product lots is not prohibitive but it may not just be the cost, it may be availability and access to them. You know, what actually is the challenge in terms of accessing reference product lots?

DR. MARKUS: Thanks. We have ten programs in development so this is a spanning experience of many different types of products, and we haven't actually

had great challenge, only in the case, I think, where there's restricted distribution, such through REMS would there be challenges with access to these products. The others we have not had challenges.

DR. KOZLOWSKI: And then you comment on reference product lots. Do you have any comments on the number of biosimilar product lots?

DR. MARKUS: Can you clarify what you're asking?

DR. KOZLOWSKI: Candidate product, how many lots need to be generated?

DR. MARKUS: So that's -- talking about sampling of the reference. I think that is an area that also the manufacturer having more experience with -- definitely provides more confidence with regards to control of their process, and I think importantly those have to be at scale and in the, you know, at full scale basically in the commercial -- to the commercial process as opposed to the process changes during the development.

DR. KOZLOWSKI: And one last other question. You made a recommendation about facility issues in a

more rapid timeline. Were you referring to all products? Were you referring to biosimilar products? What's the scope of that suggestion?

DR. MARKUS: Of which suggestion?

DR. KOZLOWSKI: You know, you suggested expedited manufacturing plant inspections.

DR. MARKUS: Uh-huh.

DR. KOZLOWSKI: Three-month clock instead of a six-month.

DR. MARKUS: So the scope of that suggestion?

DR. KOZLOWSKI: Yes, the scope of that suggestion.

DR. MARKUS: Yeah, I think the -- if there's potential challenges in the inspection, then -- and that's the only remaining element is in essence clarifying questions, are you going back and forth with questions and answers, then that circumstance and the rest of the file, for example, has been deemed acceptable, then that would be in general the scope, where --

DR. KOZLOWSKI: General scope, not just biosimilars?

DR. MARKUS: No, in general -- I think the scope is as I said for originator and biosimilars, that that should be an opportunity to facilitate approvals.

DR. KOZLOWSKI: Thank you.

DR. SHERMAN: Additional questions?

DR. UNLU: Your caution against standardization of requirements, can you explain a little more what kind of standardization did you have in mind?

DR. MARKUS: Yes. The aspect of maintaining flexibility, because each development program, including each from an analytical perspective as well as choices that the manufacturer may choose to make in clinical development, could be different, and I think from a development perspective I'd like the flexibility and not a one -- only one development pathway is what exists for each product, and so I think in many ways that flexibility with scientific backing and integrity is what is most appropriate and provides for the targeted approach and step-wise approach, so that again if there is -- where there is residual uncertainty, is where then the rest of the experiments would lie.

MS. ABRAM: Your presentation touches upon the number of products approved, and then those that have actually entered the market, and others today have touched upon that with the 12 approvals, and yet only a handful are actually in market. What do you see as kind of the driving factors for that difference between the number approved and the ones that are actually available to patients on market today?

DR. MARKUS: So I cannot speak for other companies that also have products approved and launched, but I can tell you from Amgen's view there is still intellectual property that's still standing. If we have two products approved in the U.S., neither have launched yet, due to intellectual property that still stands, but we respect the intellectual property. We think that's a key aspect of innovation, and so that's -- we by design would get the products approved and go through the intellectual property exchange, and then be available once the intellectual property is expired, if that's the right word.

DR. SHERMAN: Joe, do you have a quick question?

DR. FRANKLIN: We'll stop there.

DR. SHERMAN: Okay, great. We're at a time -- if I could just ask in your comments, if you could address two things. One that caught my eye, hasty policy changes on Slide 4, if you could just let us know in your comments what you meant by that. And you talked about that only ten percent are at a retail pharmacy, but we've heard some discussion this morning about substitution, written substitution, whatever you want to call it, at the formulary level, if you could discuss that in your comments?

DR. MARKUS: Yes. I think interchangeability -- quick, I'm sure -- or you don't want me to --

DR. SHERMAN: No, if you could just address them in the written comments, that would be great.

DR. MARKUS: In the written comments, sure.

DR. SHERMAN: Thank you very much for your comments.

DR. MARKUS: Thank you.

DR. SHERMAN: If I get us late, then I'm in true trouble.

Our next speaker is Dr. Harry Gewanter.

DR. GEWANTER: Got.

DR. SHERMAN: Thank you. From Medical Home Plus.

DR. GEWANTER: Good morning and thank you for the opportunity to speak. My name is Harry Gewanter. I'm a pediatric rheumatologist, and Medical Director of Medical Home Plus. This is a nonprofit that works with families of children with any kind of chronic or disabling condition, and try to help them, provide them with information, support and resources.

I'm both a prescriber and someone who has benefitted from biologic therapies through members of my family, and I want to really thank the FDA for all they've done to get these wonderful, wonderful products on the market.

I do want to remind everybody that this is Rheumatic Disease Awareness Month, through the American College of Rheumatology and for everyone to take advantage of that.

I also want to, you know, sort of disclaimer in advance. I'm a very concrete pediatrician with ADHD, and so I'm going to go through questions

specifically as I go through these, with some comments for you, looking at it from really both a prescriber and patient/family perspective.

I think with respect to Question 1, how do we get more biosimilars out? I think you all need more help and more bodies to be able to expedite the processes, both in terms of valuation and as was mentioned, in terms of plant monitoring and so on. I think we really need to help have therapeutic choices for everybody, and my pie in the sky would be that we eliminate formularies.

If you want true market competition, let's let me have availability of all the products out there. Let me know what the costs are to the patient, as was mentioned earlier, the out-of-pocket costs, and let me and the patient decide what to do and not have these decisions made by anybody else.

With respect to the Purple Book, most folks don't even know it exists, and I think you've got, you know, some education to do with that. I think perhaps having a Cliff's Note version or something similar for prescribers to be able to access it when they launch

and perhaps have it in the electronic health records or so on, but I think other people have really addressed the question of other ways to improve the Purple Book.

With respect to the biosimilar marketplace, approval and interchangeability does not equal access, and we need to have an equal playing field for all options. The current systems of formularies and decisions made by someone other than a patient and the prescriber goes against what we're all supposed to do as physicians, and it goes against the patient's ability to make rationale and appropriate decisions for themselves.

Open formularies with transparent pricing would help make a true marketplace, and you know, I'm not sure that's under your legal purview, but I think it ought to be. I mean, if you are going to be in charge of ensuring that medications are safe, efficacious and available, then the post-approval process is an important aspect that needs to be addressed, because many of us view that as a current limiting factor.

In terms of Question 4 about biosimilar

development, keep up your scientific rigor. Even if it takes longer to get the drugs to the market, having any lack of confidence in your approval process, is going to be detrimental both in the short and the long term, and you know, I think that we need to maintain that at all cost.

It's already been mentioned, I think having adequate samples for biosimilar manufacturers, so that things that can be -- processes that can be created are the most flexible as possible but certainly be very helpful.

With respect to multi-national development, I think whatever the FDA can do to work with WHO and other nations to have a global harmonization of naming both -- of all biologics, both originators and references are absolutely crucial. I'll give a nod to Gail Attara, who is a Canadian involved with their Crohn's Agency, talked about having identical twins and they have the same genes, but they are different and you have to have two different names for the twins, and I think the same is true for these products. We need to have identifiable names so that we know everything

about which medicine is being given.

We need to harmonize our criteria so that products can be utilized both in the U.S. and elsewhere, and that we be able to use those comparators and again going back to Question 1, where how do we get biosimilars to market more quickly, if we can show that a non-U.S. comparator is sufficiently close, I think that that would be one way of improving access.

With regard to Question 7, Dr. Kozlowski keeps coming back to the analytics and I think it's an important thing that we have to, you know, teach all of us that it's about the molecules. As physicians we're trained that to look at clinical studies, and we're not as used to looking at analytics, but talking about this in terms of the molecules, I think would help with that.

I think the other thing has been mentioned before is using patient report outcomes, real world evidence and registries. I give a nod to the American College of Rheumatology's Rise Registry, where we now have over a million patients with rheumatoid arthritis being tabulated through physicians' offices and

extractions from the electronic records.

Those kinds of information would be extraordinarily helpful moving forward, so that we can know what is the real work effects. You know, we worry about the down side of biosimilars but we haven't thought much about the potential upsides, that there may be with genetic variabilities certain biosimilars or certain glycosylations or whatever that are going to work out better for some individuals than others, and unless we can monitor and track these changes, both good and bad, we're never going to know.

I'm fine with Question 9. The challenge is, again, from a practical standpoint, the administrative barriers and the pricing is just a huge problem, and I think that that is really one of the biggest issues you have right now. As was mentioned, I think having out-of-pocket costs are really what matter.

We are as patients the ultimate payers, not the insurers, not the PBM's. It's coming out of our checkbooks and those need to be addressed that way. I think as was mentioned, having testing of biosimilars against biosimilars and the active pharmacovigilance is

absolutely critical.

And thank you. Appreciate the time.

DR. SHERMAN: Thank you for your comments. Questions from the panel? Dr. Kozlowski.

DR. KOZLOWSKI: So clarifying your comment about harmonizing criteria, so do you mean that there should be standards like the International Council of Harmonization has standards that many regions accept or are you talking about something more than that in terms of --

DR. GEWANTER: No, I think it would be, you know, as you've gone through biosimilar approvals, you know, saying you have to use an EMA approved lot versus a U.S. approved lot, I think if we can have some standards where those are sufficiently close, that that would allow us to be able to expand access a lot quicker.

DR. KOZLOWSKI: So currently we have bridging, scientific bridging, which allows use of the XUS material, so are you thinking about something broader than that? In other words, because that's an individual comparison for each product that's brought

as a candidate.

DR. GEWANTER: No. No, I think that really I was thinking about this thing how do we get more, you know, medications to market or if there's manufacturing problems or things like that, and we can show that a non-U.S. -- that the bridging standards have shown sufficiently that the medications are close, that we can use them that way.

DR. KOZLOWSKI: Oh, so you mean to actually bring them to market as opposed to use them in studies?

DR. GEWANTER: Yeah, or both.

DR. KOZLOWSKI: Okay, that's --

DR. GEWANTER: I look at life as an "and" not an "or."

DR. KOZLOWSKI: Okay. And in addressing Question 9, you talk about encourage testing of biosimilars versus biosimilars. So I wondered what sort of testing? Was that analytical testing? Was that clinical testing? What were you thinking of by that?

DR. GEWANTER: I was thinking about clinical testing. I think it has been, you know, talked about

before, the range of differences between two potential biosimilars could be sufficient that -- for patients there would be -- even though they are interchangeable with the originator, they may not be interchangeable with each other, and I mean, a personal experience with chemical medicines has been patients with duloxetine that went from brand to one of generics had significant problems, and another one went from one generic to another generic, and also had significant problems.

And if you're going to have those kinds of differences with chemical medications, you know, even though they're both within the range, you know, they're not -- you know, their ranges are apart from each other, so I think that that's something that we need to have that evidence. I'm not sure it's necessary to prevent them coming to market, but I think being -- again, this perhaps where pharmacovigilance can come in, we need to be able to know as much as we can about these molecules, and how well they're going to work or not work for individuals.

DR. KOZLOWSKI: Thank you.

DR. SHERMAN: Thank you for your comments.

DR. GEWANTER: Sure.

DR. SHERMAN: Our next speaker is Bruce Leicher from Momenta.

MR. LEICHER: Good morning. I'm Bruce Leicher, Senior Vice President and General Counsel at Momenta Pharmaceuticals. Momenta is a biotechnology company engaged in the development of biosimilar and interchangeable biologics, as well as complex generics and novel products. We innovate to develop biosimilars and new cures for patients. Thank you from holding this important meeting.

The Biosimilars Action Plan evidences strong leadership by the Agency to support biosimilars. It recognizes the primary goals of the Biologics Price Competition and Innovation Act, to unleash competition and innovation to provide access to biosimilars and interchangeable biologics.

We offer seven steps the Agency can take to enhance competition and innovation, competition to drive affordability and access and innovation to reduce the cost to biosimilar development and accelerate biosimilar approval. Each are necessary to deliver

lifesaving biosimilar medicines to patients.

First, access to reference product for biosimilar development is necessary for competition. For over 30 years reference product access was unrestricted and considered a condition of originator product approval. It was available promptly on commercially reasonable terms for testing under the regulatory supervision of the Agency. When access to originator products is blocked or delayed, biosimilar development is not possible.

Similarly, the misuse of REMS programs to block access and approval of biosimilar compounds this problem. The Commissioner's decision to publish a list of restricted access abusers is a valuable first step but some brand companies still simply refuse to sell their products for biosimilar development.

The FDA should issue a policy confirming the commercially reasonable access to reference products as a condition of approval under Hatch Waxman and the BPCIA. FDA should also work with CMS to condition CMS reimbursement on compliance with these supply obligations.

In parallel, the Agency should provide assurance to Congress that a supervision of biosimilar development ensures patients are protected and assist Congress in ensuring any legislation actually fixes the problem as the CREATES Act would.

Second, the Agency should continue to lead the world in promoting innovative biosimilar regulatory science. Advances in the United States made it possible to develop highly complex generics without clinical studies. These advances in analytical science also paved the way for development of biosimilars with targeted clinical trials. We now need to continue to use innovation to develop more affordable interchangeable biologics. Continuing to hire scientists with analytical expertise and encouraging a science-driven flexible approach to biosimilar review is essential. Highly talented and engaged staff are key for industry to attract investment, take risk and use innovation to make medicine more affordable.

Federal characterization of biologics and biosimilars makes it possible to prove fingerprint-like similarity. This reduces residual uncertainty.

Further advances should enable targeting clinical trials for both biosimilars and interchangeable biologics. Receptivity and clear guidance that new ideas and innovation are desirable is necessary to encourage private investment.

Over-reliance on clinical data will discourage innovation and raise the cost of seeking interchangeability too high. Let's drive innovation, not limit its use.

Third, issue an explicit policy statement in the Purple Book that an interchangeable biologic is therapeutically equivalent to the reference product. This policy is present for interchangeable drugs in the Orange Book and necessary to enable substitution at the pharmacy, but currently absent from the Purple Book. CMS relies on this statement in the Orange Book to provide favorable reimbursement for drugs. CMS is awaiting guidance from the FDA for interchangeable biologics.

Pharmacy substitution drives savings and affordability by reducing the need for marketing and promotion. Without it, affordable interchangeable

biologics will be an unattractive investment.

Fourth, level the playing field for biologic naming, ensure biosimilars do not look different or inferior by requiring originator products to also have proper name suffixes. Today only some originator products have suffixes. This is very confusing to physicians and patients and creates an additional barrier to biosimilar competition. Pharmacy computer systems will not be reprogrammed to accommodate a suffix unless all biologics must comply.

In addition, provide that interchangeable biologics have the same proper name as the reference product to ensure pharmacy substitution is instead implemented, as it is with interchangeable generic drugs.

Fifth, publish a policy that states substitution laws not conflict with the substitution of interchangeable biologics authorized under the BPCIA. A patchwork of state substitution laws, some of which facilitate substitution and some of which might not, also deters investment in interchangeable biologics. An explicit policy will provide certainty and eliminate

this barrier by rendering conflicting laws unenforceable.

Sixth, allow scarce application -- I'm sorry, allocate scarce application resources toward truly novel cures and biosimilars. Reduce resources assigned to incremental life extension products. Routine formulation changes or convenience devices set the stage for abusive behaviors, such as product hopping, patent misuse and citizen petition abuse. Given their pricing they do not warrant the same research priority as new cures or affordable medicine that actually address urgent patient needs. Incremental changes can come later.

In addition, promptly deny citizen petitions that seek to delay or prevent biosimilar approvals. As noted by Carrier and Midea, citizen petitions are rarely granted, are mostly filed at the end of a product's life cycle and delay the approval of affordable medicine.

Seventh, continue to call our companies that game the system to block competition. Work with CMS to end rebate abuse and contracting practices that make it

economically infeasible to launch a more affordable biologic.

The rebate trap is but one example. As shown by Aaron Hakim, the rebate trap can undermine competition by making the cost of market entry so high for a biosimilar that sales are unprofitable. Even with a substantially less expensive biosimilar, the pair will spend more if it buys the less expensive biosimilar product than if it remains exclusively with the originator product. Unless these issues are addressed, the goal of competition, affordability and innovation will be thwarted.

We should ask why is it the 12 biosimilars have been approved but less than half that number have been launched? Why is it that biosimilar market access is slower than expected? Is it because federal policy inadvertently provides protection for incumbent products over new competitive entrance?

We believe these seven steps could help address these questions and thank you for the opportunity to address the panel today.

DR. SHERMAN: Thank you for your comments.

Questions from the panel? Dr. Franklin.

DR. FRANKLIN: You mentioned that there are a couple things FDA might do to encourage access to reference product samples by similar developers. And you mentioned I think specifically that FDA should issue a statement that it would be a condition of approval I guess for the reference product that samples be provided. From your perspective is this something FDA could do under its current statutory authorities or would additional authorities be needed?

MR. LEICHER: We believe it's authorized under the current law. I mean, the practice for years was the understanding that when you were approved, when the whole underlying premise of Hatch Waxman was that the reference product had to be available. So we believe it's implicit in the statute and you can read it into the existing authority in both statutes.

DR. SHERMAN: Dr. Kozlowski.

DR. KOZLOWSKI: So we heard from Amgen that accessing reference product was not necessarily that much of a challenge. So what do you think the difference is in the experience you had and that of

certain other companies?

MR. LEICHER: Well, it's interesting. We have both kinds of experiences, so when we're both a novel company as well as biosimilar company. We've been doing competitive studies in our novel product trials. Never an issue purchasing product from a manufacturer when we're doing the comparative study. But when we go to purchase product from a wholesaler for the biosimilar company for a biosimilar program, the first question we're asked is is it for biosimilar study and we're often told -- once we were told there's a REMS program in place, we looked it up. There was no REMS program in place. They then said well, we're not allowed to sell it to you.

So what happens is you go through a two to three, four month, delay. You may ultimately be able to purchase it, and there are products that we have not put into development because it was just too hard to buy.

DR. KOZLOWSKI: Thank you.

MS. ABRAM: I'm curious, going back to your remarks on the citizen petition process, if you have

anything to expand on those remarks or if you have specific suggestions that might be considered with respect to potential reforms in that area?

MR. LEICHER: Well, you know, looking at the article that was published, I think the risk is that you have to look at not just the citizen petition, but you have to look at examples of product hopping and examples of life extension, incremental changes to products. If there's an opportunity to delay the approval of a biosimilar or a generic through a citizen petition review process, and it slows down the review, it creates the setting in which minor changes can be introduced, you know, and planned as a way to switch the market to a new -- a question was raised earlier how is it going to affect interchangeability if there's a new presentation or a new convenience device, and all of those things are barriers to entry for biosimilars and potentially for interchangeable products in the future, and we ought to ask what is -- you know, what's in the interest of patients? Is it to get the new competitive product out or to get the new incremental improvement out?

DR. SHERMAN: Thank you for your comments. Our next speaker is Dr. Lisa Skeens from Pfizer.

DR. SKEENS: Good morning. I'm Lisa Skeens, Vice President of Global Regulatory Affairs for Pfizer Essential Health.

I'm here today to share with you Pfizer's recommendations on the steps necessary to ensure a robust biosimilars marketplace in the United States that has the potential to provide patients with greater access to these important medicines while lowering healthcare costs.

Pfizer has a long heritage in developing both originator biologics and biosimilars. We have more than 30 years of expertise in the development of biologics and more than ten years in market experience of biosimilars in Europe.

We are the leading company worldwide by revenue. We market three biosimilars globally, Inflectra, infliximab, Retacrit, epoetin, and Nivestim, filgrastim.

We have a strong and exciting pipeline, which demonstrates our continued commitment to the success of

biosimilars worldwide.

Pfizer's experience shows that one of the greatest hurdles to biosimilar success is market access. Here is the example of the infliximab market. The originator molecule of Remicade in the green line has 95 percent market share, one-and-a-half years after the introduction of infliximab biosimilars. Even though the average sale price of Pfizer's biosimilar, Infectra, the orange line, is 24 percent less than that of Remicade as shown in the smaller graph.

There could be savings up to half a billion dollars a year for commercial payers and Medicare, according to one study, just by increasing the use of infliximab biosimilars to 50 percent. In order for patients to benefit for the U.S. healthcare system to realize cost savings, for the biosimilars pathway to be successful, and for companies to continue to commit to this important area of drug development, work needs to be done to ensure that all of these important biosimilar medicines have the potential to reach patients as quickly and efficiently as possible.

The biosimilars marketplace in the U.S. is at

a critical juncture and more needs to be done to ensure its success. Opportunities to further advance biosimilars go beyond FDA working alone. For a successful biosimilars marketplace that will expand access to patients, for these important medicines and bring lower costs to the healthcare system, it's important that multiple federal agencies and state agencies work both individually and collectively to implement policies that will remove barriers and support biosimilars uptick.

Today we will highlight several opportunities to take action now to support a successful biosimilars pathway and marketplace. There are three key areas that will take biosimilars to the next level and ensure continued commitment and success. They are optimization of biosimilar development, proactively combatting misinformation and instilling confidence in both prescribing and using biosimilars, and expediting market access to biosimilars.

Now I will share our recommendations for each of these in a little more detail.

Pfizer fully supports the rigorous evaluation

standards that FDA applies to all products, including biosimilars, so that patients can be assured of the quality, safety and efficacy of these products. There are opportunities to further optimize the development of biosimilars without compromising these scientific standards. Pfizer recommends several key actions the FDA can take to build efficiencies and to biosimilar development programs.

First, FDA should consider flexibility in bridging expectations and acceptance of non-U.S. licensed comparator data that would enable efficient development and minimize redundant work.

Second, FDA should be flexible in their willingness to consider alternative comparative clinical study and switching studies statistical approaches, study end points and overall study design, when sponsors have alternative approaches supported by scientific justification, that meet the standard for demonstrating there are not clinically meaningful differences between the proposed biosimilar and its reference product.

Third, FDA should maximize review efficiencies

by ensuring there is appropriate allocation of resources and timely implementation of the GDUFA INSPECTION goals, particularly hiring goals.

It's also essential that the FDA work to ensure there is clear and consistent communication of application expectations relating not only to demonstration of biosimilarity but also to biotherapeutic manufacturing standards in general.

Finally, FDA should develop a seamless process for biosimilar sponsors to add indications post-approval. Currently FDA is suggesting a prior approval supplement process to add indications. However, as sponsors have already scientifically justified extrapolation of the indication they propose to add, the Agency should consider a CBE-0 submission to prevent unnecessary delays in patient access to biosimilars.

In addition to optimization of development of a biosimilar through the regulatory pathway, it is of the utmost importance for multiple agencies and stakeholders to combat misinformation and instill confidence in biosimilars to support the development of

a robust and accessible biosimilar marketplace. More must be done to combat false and misleading marketing practices that create confusion and undermine efforts to enhance stakeholder confidence in biosimilars.

The FDA, FTC, as well as other agencies need to take an active role to ensure the information regarding biosimilars and interchangeable biologic products is represented in a way that is complete, truthful and non-misleading.

Pfizer has filed a citizens petition with FDA asking the Agency to issue guidance outlining the kind of reference product communication surrounding the safety and efficacy of biosimilars, including interchangeability and switching, that would be truthful and non-misleading. This is another step to combat the behavior by certain originator companies that could build barriers or block access to the use of biosimilars in the United States.

While not sufficient on its own, ongoing education is also necessary and it should be created in a manner to facilitate a conversation between a healthcare provider and their patient.

Pfizer appreciates the steps FDA has taken in this area and urges the Agency to expand in their efforts.

Finally, in our experience without market access, an approved lower cost biosimilar will not be successful in the U.S. We need to implement policies that will proactively remove barriers and advance the uptick of biosimilars. Support is needed from the FDA and other agencies, such as the FTC and CMS, as well as stakeholders such as commercial payers and purchasers. First and foremost the U.S. Government should enforce antitrust laws to prevent anti-competitive practices by reference biologic manufacturers that use exclusionary contracts to create access barriers.

Contracts that require patients to fail first on a reference biologic before they can access a biosimilar are preventing access to biosimilars. CMS should do more to proactively support uptick of biosimilars such as publicly track, update, uptick, expand balance incentives to drive uptick at the hospital and provider level, such as the 340b pass through and work with state and Medicaid agencies to

ensure biosimilars are available to Medicaid patients.

We call upon all stakeholders to engage in driving uptick of biosimilars and we thank the FDA for their support in hosting this important public meeting.

Thank you.

DR. SHERMAN: Thank you for your comments. Any questions from the panel? Dr. Kozlowski.

DR. KOZLOWSKI: So you mentioned manufacturing guidance for biological products in general, so I would hope in comment to the docket you are a bit more specific about what would be particularly helpful.

DR. SKEENS: We do. We've seen additional requests in some of our biosimilar FDA's during review that are more typically handed through prior approval inspections or other means, and so if there is new expectations, then we really need to call that out in guidance instead of during review and it should be applicable to all BLA's, not just biosimilar BLA's.

DR. KOZLOWSKI: Okay. Well, clearly sharing that would be of use to us. Thank you.

DR. SKEENS: Thank you.

DR. SHERMAN: Other questions? Thank you for

your comments.

DR. SKEENS: Thank you.

DR. SHERMAN: Our last speaker before lunch is Dr. Richard Dolinar from the Heartland Institute.

DR. DOLINAR: You had to put in lunch to remind everybody they're hungry.

My name is Dr. Richard Dolinar. I am a clinical endocrinologist in private practice in Phoenix, Arizona. In our group we have 12 endocrinologists. We see over 200 endocrine patients a day so it's quite a busy practice.

Let me get this organized here. I'm also a senior fellow on healthcare policy for the Heartland Institute and I was a member of the National Legislative and Regulatory Committee as listed there for 15 years, but since this slide was made, I've moved over to the Socioeconomics Committee, where we focus on healthcare economics.

I'm also a member of the Editorial Advisory Board of Endocrine Today and the Journal of American Physicians and Surgeons.

I was the first Chairman of the Alliance for

Safe Biologic Medicines, and I'm quite proud of what ASBM has one over the years in the world of biologics and biosimilars. I think it's been very helpful for everybody.

I should also add that in my experience when I was in the Air Force, I was able to travel to many parts of the world and see healthcare systems and see how other countries have their healthcare set up, so it's allowed me to compare and contrast our system with theirs. I'm also a retired Air Force Colonel.

The first item I'd like to get into today involves the transition products and as you know, those are the products that meet the FDA's definition of a biologic, but currently are approved under Section 505 of the Food Drug and Cosmetic Act.

The Biologics Price Competition and Innovation Act of 2009 provides that on March 23rd, 2020, these products will transition and become deemed -- that's a legal term, not a medical term -- deemed as approved products under Section 351 of the Public Health Service Act, and potentially under Section 351(k) as a biosimilar.

This transition raises a number of regulatory and also process questions that impact the continued development of biologics and follow-on biologics. For example, Basaglar. Basaglar is a glargine insulin. In my practice I focus primarily on diabetes, and so I do use many of -- in fact, I use all of the diabetic drugs. But let me focus on Basaglar. It was approved by the FDA as a follow-on biologic under Section 505(b)(2) of the Food Drug and Cosmetic Act.

It's been designated as a transition product and, therefore, will become a Public Health Service Act approved product as of March 23rd, 2020. The FDA has not yet decided how Basaglar and similarly situated products will be classified, whether as a standalone biologic under Section 351(a) of the Public Health Service Act, or a biosimilar under Section 351(k).

In March of 2016 the FDA issued a draft guidance on this topic entitled Implementation of the Deemed to be a Licensed Provision of the Biologic Price Competition and Innovation Act of 2009. However, key questions, including how products such as Basaglar will be classified have not yet been addressed.

I urge the FDA to finalize its guidance on this transition and these transition products in order to offer more clarity and promote a robust biosimilar and biologic market.

Naming. Let me go on to naming. Naming is absolutely critical and I think the FDA is correct in using a suffix to differentiate these products. But the current names used in the suffixes -- the suffixes are non-sensical. They're difficult to pronounce, if you can pronounce them at all, and these suffixes are untethered to anything. So they're difficult to remember. So we have a situation where we have a name that a doctor can't pronounce or is very difficult to pronounce, and if you have words that you can't pronounce, you're not going to remember them. And if you don't remember the name of that drug, you won't order it, and if you don't order the drug, the patient won't have access to that drug.

So our recommendation is that we allow for more memorable and meaningful names in brand names, and especially in the design of the suffixes that are being used. And I encourage the FDA to work with WHO to

advance the use of distinct naming systems worldwide.

More education. It's been touched upon by others. Doctors need to be educated on biologics and biosimilars and follow-on biologics. That's a major issue. That could potentially block bringing these drugs to their patients, so I'd strongly encourage education for the physicians. Most doctors don't even know a Purple Book exists. We've got to get word out to them and got to get them educated.

We need to educate the public too about biologics and biosimilars. I think there's a role for direct to consumer advertising. I think the FDA could advertise and alert the public to this issue, and I think the companies could also do that.

Remember, the purpose of advertising is not only to inform and educate but to persuade, educate the public regarding biologics and follow-on biologics and biosimilars, and persuade them that these are safe, effective, they're cheap, they're beneficial, so I think that that word needs to get out.

Data over time builds confidence. As the others here have said, I thank the FDA for maintaining

their high standards. I think that's critically important. Recommend that clinical studies should be done in every indication. Switching studies will help physicians feel comfortable switching their patients. This will all help to have a robust active market.

Extrapolation will be a problem with treating physicians. They'll be reluctant to accept that and that's why I encourage the clinical studies. We practice evidence-based medicine, so that's what we'll want to see, the evidence, rather than the extrapolation.

Analytical studies are needed, as the others have stated. I won't spend time on that.

PBM's. This is a real problem. On Mondays I see the patients. I make my decisions. I use my best medical judgment, and then on Tuesday I'm back peddling because I'm being told the formulary no longer covers this, although it covered it maybe the month before, and now I'm in a situation where I'm using my second, third or fourth best medical judgment. PBM's in certain cases set up obstacles to me giving my best medication for my patient.

They call it a walk-away rate. Walk-away rates can be as high as 65 percent, meaning only 35 percent of the time is the patient getting the drug that we ordered, the drug that we thought was best for them. So I think there's a lot needs to be done regarding PBM's. I think the incentives are misaligned. They're paid on a basis of a percent of the initial list price, and I think that's problematic.

I will just finish by reiterating that the importance of naming -- if the doc cannot remember the name because he can't pronounce it, he won't be using that drug. And if he doesn't use that drug, not ordering it, the patient won't have access to it, so all these hurdles that we talked about today, you may surmount all of them, but the final one with the physician, we've got a problem.

So thank you. Thank you for this morning.

DR. SHERMAN: Thank you for your remarks. Any questions from the panel? I guess everybody is hungry. Thank you for your remarks. Well, for the speakers this morning, we heard a lot about the Purple Book, but I think very differing ideas of the intended audience,

so anything you can do to elaborate in your comments would be much appreciated.

And on that note, we'll -- it's lunch, and we'll be back. We'll start promptly at 12:45. Thank you.

(Lunch break from 11:41 a.m. until 12:45 p.m.)

DR. SHERMAN: Hi. I think we're going to get started. Good afternoon. It's my pleasure to announce the first speaker of the afternoon is Commissioner Gottlieb.

COMMISSIONER GOTTLIEB: Thanks, Rachel, for that warm and detailed introduction.

DR. SHERMAN: Should I try a do-over?

COMMISSIONER GOTTLIEB: Moving. I want to thank you all for being here today and I want to thank you for the opportunity to join you for a short period of time.

This meeting is really important to us. The information that we gather here today that's submitted to us is part of the docket. It's going to help FDA as we continue to work to foster the competitive marketplace for safe and effective biologic products.

We're committed to this work at FDA. We have a vital role to play in supporting innovation and ingenuity that provides patients will novel therapeutic options, while also helping encourage a competitive marketplace that can make these therapies more affordable and more accessible to patients. And while FDA isn't directly involved in the pricing of drugs or biologics, we know that we play an important role to play in these issues, applying science-based policies to help facilitate greater access to affordable new drugs.

Biologics, as all of you I'm sure share, have become crucial in the treatment of many serious and life-threatening diseases. But the high costs of biologics are likely familiar to you, as well. Almost 40 percent of total prescription drug spending is on biologics and biologics represents 70 percent of the growth in drug spending between 2010 and 2015.

We know it's going to take more work to achieve a vibrant and competitive marketplace for biologics, and today's public dialogue is an important part of that process for us.

Congress, through the Biologics Price Competition and Innovation Act gave FDA the authority to implement a pathway for approval of biosimilars and interchangeable products, and to balance innovation and competition when it came to this category of drugs.

In the past several years there has been substantial efforts vested to make this pathway successful by many people here at FDA, many of whom are with us today. FDA has developed the scientific and regulatory framework for the review, marketing applications for biosimilars products, incorporating feedback from many diverse stakeholders, some of whom are also here with us today.

Manufacturers have also invested a lot of money in developing biosimilar products and the information needed to support approval, and this work has yielded some concrete results. We've seen 12 biosimilar products approved, including six approvals in the last year alone.

But as I've said before, I'm not satisfied with the current state of the biologics market, and biosimilars in particular. Even as we meet to discuss

these important issues today, not even half of the biosimilars approved by the FDA have entered the market.

Each approved biosimilar product that is not yet marketed means a lot of loss, potential cost savings, from a biosimilar that meets FDA's rigorous standards but is not yet available to patients and not yet available to increased competition with the referenced product.

I have expressed concerns in the past that biosimilars are not being developed or submitted for approval because of marketplace dynamics that are viewed as unfavorable to biosimilars, and I know you've discussed some of these here today, including the challenges that biosimilar manufacturers face in getting access to the doses that they need in order to run their studies.

Another one that I've talked about is the consolidation of supply chain that can work in favor of incumbent reference biologics and discourage adoption of biosimilar competitors.

We know there is more work to do at FDA to

advance the science and policies to make the development of biosimilars more efficient, to increase the acceptance of biosimilars and to avoid the regulatory gaming that can deter competition in this space. That's why earlier this year we announced the Biosimilars Action Plan, working with the staff of the group in CEDR that's charged in reviewing and approving these products, and we announced that a little over a month ago now.

To formulate this plan FDA looked at how we could adapt the lessons learned from our regulation of generic drugs. We looked to what we had already learned from our interactions with biosimilar sponsors, as well, during the product development and application review process.

And we looked to how we could modernize our policies on the development of biosimilars to improve the efficiency and increase regulatory certainty, without compromising safety and effectiveness and we evaluated input from various stakeholders such as professional societies and patient organizations.

Under that plan not only are we making the

biosimilar development and review process more efficient and predictable, we're also taking new steps to communicate with patients and payers and providers to improve the understanding of biosimilars and interchangeable products. And we'll act, where appropriate, to deter the gaming of FDA requirements that unfairly delay competition among biologics.

The Federal Trade Commission is a vital part in this work, and we look forward to continue coordination with them to address anti-competitive behavior in drugs and biologics marketplace, and we'll be taking some steps in conjunction with them in the coming months to work more closely with them in all of these efforts.

Our action plan is dynamic, and we continue to evaluate additional FDA actions that are needed to strike the appropriate balance between encouraging ongoing innovation and biologics, while also facilitating the robust competition that we know can reduce costs and help increase access for patients.

And so a key element of FDA's Biosimilars Action Plan is to learn from stakeholders in today's

public hearing. It's encouraging to see such a diverse group of perspectives here. And in announcing today's hearing FDA solicited input from the public on a broad set of questions about how we should address complex and challenging issues related to the biosimilars marketplace, including interchangeable products, taking steps to try to encourage competition, while also supporting innovation and striking other important balances.

We asked about other areas where we see real potential to make the development and review of biosimilars more efficient, and where we can clarify regulatory requirements for stakeholders. And so I'd like to thank you all for joining us here today. The feedback from today's meeting is very important to us. We learn a lot from these Part 15 hearings, but also the information that we get submitted to the docket is equally important. So I hope you all take the opportunity to not just share comments today but also think about information that you can submit to our docket to help us, as we think about how to improve this marketplace going forward.

Thanks a lot. Thanks for having me here today.

DR. SHERMAN: Thank you, and I appreciate that you stayed on time. Does the panel have any questions for Dr. Gottlieb? All right.

Our second speaker of the afternoon will be Dr. Mariana Socal from the Johns Hopkins Bloomberg School of Public Health.

DR. SOCAL: Good afternoon. My name is Mariana Socal. I'm a medical doctor and I have a Ph.D. in health systems from Johns Hopkins and a master's in public policy from Princeton University.

I currently work as an assistant scientist at Johns Hopkins School for Public Health. My research focuses on ways to provide the best appropriate pharmaceutical coverage for people who need drugs in order to improve their health and their quality of life.

I would like to thank today the Laura and John Arnold Foundation, who support my research in Johns Hopkins. However, I'm speaking here today on my own behalf and neither of the institutions have had any

role in preparing my remarks today.

So I would like to provide commentary on how the FDA could improve information availability and accessibility in the Purple Book. And I'm going to be focusing on competition. I already understood that there's also interest in hearing about other stakeholders use of Purple Book, and I'm going to address that in the written remarks.

So the information currently available in the Purple Book is limited to drug proprietary and non-proprietary name, biologic license application number, BLA, and licensing date. Reference products may also have information on date of first licensure and exclusivity expire date. Although this information is available for a small number of products, any potential 351(k) applicant who wishes to obtain more information on a particular product must spend considerable time and financial resources running independent search.

These searches may add cost and delay biosimilar development. The uncertainty generated by the lack of readily available information may also prevent investors and manufacturers from considering

becoming 351(k) applicants in the first place.

Improving information availability and accessibility in the Purple Book would increase transparency and decrease uncertainty in the market, contributing to decreasing barriers to entry and increasing competition.

So three pieces of information should be added to the Purple Book. First, drug identification information should be expanded to include information such as manufacturer's name, the drug's route of administration, dosage form, strength and others, so drug identification is key to allow potential 351(k) applicants to easily identify products that exists in the marketplace corresponding to each of the FDA licensed biologics.

Also the biosimilars should be identified by the name of their main active ingredient, and the four letter suffix should be presented in a separate field to increase clarity.

Okay. Second, all unexpired exclusivity periods should be published in the Purple Book. Potential 351(k) applicants and the investors gain

greater clarity when exclusivity information is transparent and readily available. This means that first the FDA should make a determination on the date of first licensure for all licensed biologics. And for those found to be eligible to the 12-year reference product exclusivity under the BPCIA, the exclusivity expiration date should also be determined and made available in the Purple Book.

Currently the policy appears to be that the FDA determines first licensure dates only in cases of regulatory necessity or on the wishes of the reference product license holder. This policy is in my view misguided.

A better policy where the FDA would automatically make and publish determinations for all drugs would significantly promote competition.

The FDA has issued guidance on reference product exclusivity and in particularly the limitations on exclusivity set forth by the Public Health Service Act. With this guidance document in hand, FDA should be in a position to modify its policy and make determinations on date of first licensure and reference

product exclusivity on all drugs.

In addition, many biologics also have other FDA granted market exclusivities, such as pediatric use or orphan status. All biologics with unexpired FDA granted exclusivities should have the exclusivity description and the expiration date listed in the Purple Book.

The FDA already makes this information publicly available through the orphan drug database in the pediatric exclusivity list, for example.

Third, the Purple Book should contain information on all unexpired patents that the BLA licensee reasonably believes protect their biologic product. Licensees should be requires to submit patent information as part of a BLA, and to update this information in keeping current after licensing. Including patent information in the Purple Book is critical to increased competition in the biologics marketplace.

Absent readily available information, a potential new market entrant must engage a scientific expert or a patent attorney or both to sift through

hundreds and hundreds of complex pharmaceutical patents. Also, even in this case, it's easy to miss a key patent.

Patents are public information. If a BLA applicant or licensee reasonably believes that its product is protected by one or more patents, then it should be required to provide the FDA within information on those patents and the FDA should list those patents in the Purple Book.

Requiring BLA's to include relevant information on patents would require the FDA to amend its existing regulation, which the FDA is authorized to do under the Public Health Service Act. The amended regulation should apply to all BLA licensees current and future. The FDA should adopt some reasonable timeframe for BLA licensees to comply with this new requirement.

A final note is that the ideal format of the Purple Book would combine the CDER and CBER lists, would be searchable online, and potential link to the products' corresponding indices. The FDA has expressed their commitment to helping facilitate competition in

the biosimilar marketplace. Increasing transparency and reducing uncertainty are important to building blocks of this effort.

Thank you so much.

DR. SHERMAN: Thank you for your comments. Any questions from the panel?

DR. UNLU: So let's say we had the regulation that said you need to list all patents you believe reasonably protect your product, and then it turns out that the manufacturer made a mistake or forgot to list a patent and they wanted to assert that in litigation against the biosimilars applicants, what would the remedy be?

DR. SOCAL: So it would depend on how exactly the new amended regulation would frame it, because if it frames it as a requirement for the FDA to approve the biosimilar, only for those patents that are listed in the Purple Book, then litigation could be a questionable pathway. It depends on what the actual language would be.

DR. UNLU: But we don't approve biosimilars for uses listed in patents. I mean, that doesn't have

anything to do with our approval.

DR. SOCAL: I agree. But if that -- it depends on what the language of the regulation would be. If you made one thing a requirement to the other, then it might change the remedies that are available from a legal perspective.

DR. SHERMAN: Dr. Franklin.

DR. FRANKLIN: Right. I guess to follow up a little bit more specifically, have you looked at the potential interaction between this proposal to provide -- to require that 351(a) applicants provide patent information, if I'm characterizing that accurately, interaction between that and the patent exchange provisions under Section 351(l) of the --

DR. SOCAL: So let me first make a clarification about my previous answer, and I just assume -- I'm assuming we're thinking the same, we are seeing things from the same perspective. And what I was referring to is in the small molecule space in the Orange Book, if a patent is unexpired and it's published in the Orange Book, then the FDA should not approve a generic, if that information is there. And

I'm thinking that if the same language would be available for biologics and biosimilars, then we would incur the same provisions. That's just clarifying my thought before.

And so in response to your current question about how would that change patent exchange information, that wouldn't necessarily change but it wouldn't necessarily change the implications of it, but given that most patents will become publicly available, then it might not be even necessary.

DR. KOZLOWSKI: So clarification, because as now other than the patent exchange, a patent doesn't really withhold the Agency from making a decision, so you're referring to something that would actually have the Agency not approve something based on the existence of a patent. So is that what you're suggesting?

DR. SOCAL: It would be an option, yes. It depend on the willingness of the Agency to update its regulations. In my opinion, my main suggestion is publishing the patents and that's important for transparency.

DR. KOZLOWSKI: So publishing the patents

helps transparency but limiting the Agency's ability to approve is different than transparency.

DR. SOCAL: Correct.

DR. KOZLOWSKI: So you think the only way to have one is to have both?

DR. SOCAL: No, not necessarily. Yeah, that's why I mentioned the Orange Book, so it's an option. That's not necessarily what I'm proposing today. I'm proposing effort for transparency first and foremost.

DR. KOZLOWSKI: Just as a comment I would encourage you to provide even more detail about these recommendations, because I think as a lot of folks have recognized today, we're looking at ways to increase the utility of the information in the Purple Book and so the more detailed the proposals we can receive on that, the better.

DR. SOCAL: Perfect. Thank you.

DR. SHERMAN: Thank you for your comments. The next speaker is Michelle Cope from National Association of Chain Drug Stores.

MS. COPE: Thank you for the opportunity to share the perspectives of chain pharmacy on ways to

promote biosimilars uptick and facilitate competition and innovation in the biological products market.

I'm Michelle Cope, Director of Federal and State Public Policy for the National Association of Chain Drug Stores. And ACDS represents traditional drug stores, supermarkets and mass merchants with pharmacies. Chains operate over 40,000 pharmacies and our members operate nearly 100 chain member companies, including regional chains with a minimum of four stores and national companies.

And ACDS strongly supports policies that will lead to growth in the biosimilars market and promote use of a more affordable biological medications. In that vein I am here today to speak to the following issues and questions that FDA raised in the Federal Register.

Number one, improving the utility of the Purple Book. Number two, cultivating a robust biosimilar market and promoting stakeholder confidence in these products. And finally, increasing healthcare provider and patient understanding of biological products, including biosimilar and interchangeable

products.

We thank FDA for the chance to speak to these issues today. Regarding ways to improve the utility of the Purple Book, to enable pharmacists to substitute more affordable therapeutic alternative biological products, it is critical that FDA provide tools and resources like the Purple Book to support such dispensing. To this end we recommend the following revisions to the Purple Book to facilitate this.

The format of the Purple Book should be designed to clearly group and identify both therapeutic alternative biosimilars and interchangeable biological products with their respective reference products. This is especially important given that there are unlikely to be a significant number of interchangeables on the market for years due to various market disincentives.

Accordingly, pharmacists will need to know which products relate to a specific reference product and may, therefore, be appropriate for therapeutic interchange. Additionally, we believe that the terms describing biosimilars in the Purple Book and elsewhere

are confusing to most laypersons.

To address this we recommend that FDA use the simplified term "clinically equivalent" to mean no clinically meaningful differences.

Number two, regarding cultivating a robust biosimilars market and promoting confidence in these products. With respect to the question of what more FDA can do to facilitate the evolution of the biosimilar and interchangeable product market, we encourage the Agency to prioritize efforts to expedite the availability of interchangeable biosimilars, recognizing that it may not be cost effective for many biosimilar manufacturers to perform the studies necessary to demonstrate interchangeability, we encourage FDA to work with Congress and AHRQ to explore new approaches to facilitate the performance of the required interchangeability studies.

FDA could achieve this by securing federal funding for interchangeability studies of approved biosimilars, or by accepting studies performed by health systems or other private entities that demonstrate interchangeability.

Additionally, in the meantime, we urge the Agency to encourage federal and private programs to recognize the benefit of therapeutic interchange for biosimilars as a cost-savings measure.

With respect to what more the Agency can do to ensure patients and healthcare providers' competence in biosimilar products, we urge the Agency to update its recent naming policies for biological products to align with the naming practices for small molecule drugs. FDA's new naming practice for biosimilars that tacks on a non-sensical four-letter suffix deviates from historical naming conventions. We have ongoing concerns that this nomenclature can lead to general confusion relative to the appropriate use, safety and efficacy of these medications, as well as therapeutic duplication that would be detrimental to patients' health.

Moreover, naming practices for biological and biosimilar products that are different from other medications undermines healthcare provider and patient confidence in these medications and perpetuates the notions that biosimilars are not comparable to the

innovator product. This must be remedied.

All biological medications regardless of whether the product is an innovator, a biosimilar, or a biosimilar that has been deemed interchangeable, should be assigned the same non-proprietary name. This naming paradigm is familiar to healthcare providers and patients alike, and promotes confidence in use of these products.

Finally, relating to healthcare provider and patient education opportunities, physician and patient confidence in biosimilar and interchangeable products is critical to increased market acceptance of these products. NACDS supports the education and outreach efforts to physicians, patients and other healthcare providers to facilitate awareness, understanding and adoption of biosimilars. We encourage FDA to continue efforts to educate healthcare providers and the public about biosimilar mediations.

Initiatives such as CE programs designed to familiarize healthcare providers with biosimilar mediations and multi-media public awareness campaigns can be useful to promote further understanding and

adoption of biosimilar medications. Specifically biosimilar education should stress that biosimilars are designed to match the structure and function of the reference biological product.

Patients should be assured that FDA approved biosimilars have the same safety and efficacy as their reference products. Moreover, FDA should convey that the Agency approves biosimilars utilizing the same high standards for manufacturing and quality that apply to all biological products.

The Administration should educate that the availability of biosimilars is anticipated to lower cost burdens for the U.S. healthcare system.

We thank you again for the opportunity to speak and I will be submitting our statement to the public docket, so thanks.

DR. SHERMAN: Thank you for your comments. Questions from the panel? Dr. Kozlowski?

DR. KOZLOWSKI: So you referred to third party or outside groups helping smaller entities meet interchangeability expectations. So you mentioned health system studies, so were you thinking of real

world evidence? What type of evidence were you thinking about?

MS. COPE: Well, currently, I mean, where in the United States you're seeing any sort of switching from one to another, it would be formulary driven. So that being the case, this is just one potential avenue to pursue where you have patients that have been potentially been switched from the innovator to a biosimilar, and that's when -- you know, as times goes on, you may compile the data. We were just trying to kind of think outside of the box so --

DR. KOZLOWSKI: Okay, thank you.

MS. COPE: mm-hmm.

DR. SHERMAN: Other questions? Thank you for your comments.

MS. COPE: Thank you.

DR. SHERMAN: Our next speaker is Christine Simmon, Biosimilars Council, Division of the Association for Accessible Medicine.

MS. SIMMON: Thank you. On behalf of AAM and its Biosimilars Council, we want to thank the Agency for its tremendous leadership on biosimilars.

As policy makers from the President on down to State Governors, grapple with high drug prices, biosimilars represent new savings and access for patients and payers. Unfortunately, the biosimilars face marketplace challenges, as we just heard Commissioner Gottlieb reinforce.

And Dr. Gottlieb has previously remarked that had all of the FDA biosimilars that were approved in 2017, FDA approved in 2017, been successfully marketed, Americans could have saved more than $4.5 billion last year alone.

This illustrates the unfortunate truth that FDA approval of a more affordable medicine does not guarantee the medicines get into the hands of patients, and it doesn't guarantee that the savings accrue to the health system. So what's standing in the way?

Three of the biggest obstacles are reimbursement issues in Medicare, patent tactics to extend monopolies, and unwarranted restricted access to reference products. So you might believe I just named three things that the Agency can't do anything about. But we would disagree.

The Agency is more than the regulator of biosimilars. FDA is the most credible federal resource on biosimilars. It makes you all a key influencer. You're well positioned to collaborate within HHS with CMS, and with other agencies, such as USTR and PTO, as well as Congress, to advance biosimilar competition, and we applaud that you are having an ongoing collaboration with the FTC, and that's fantastic to hear.

So clearly much of what is holding back biosimilars from patients requires policy makers to build on actions the FDA already has taken or will be taking under the Biosimilars Action Plan. As the Administration continues to implement its blueprint on lowering drug prices, FDA is the engine that can drive policy makers on biosimilars opportunities.

Let's start with those issues where FDA's credibility and influence can drive policy wins for patients.

Reimbursement. A sustainable biosimilars market depends on well-designed FDA regulations combined with market incentives, created by CMS payment

and formulary review policies. Predictable reimbursement and market access is critically important. Would-be biosimilar manufacturers can't justify allocating significant capital into development programs without a reasonable potential for commercial success.

CMS has taken important steps to support biosimilars, but rebate traps, exclusionary contracting and a lack of reimbursement incentives remain barriers. We encourage FDA to work with HHS and CMS to ensure that Medicare reimbursement and formulary design prioritize utilization of these lower lost lifesaving medicines.

Patent tactics or shenanigans. AAM and the Biosimilars Council strongly support innovation. That said, efforts by some brand new pharmaceutical manufacturers to manipulate the patent system through patent thickets that extend their market exclusivity beyond Congressional intent are a primary reason FDA biosimilars cannot timely enter the marketplace and get into the hands of patients.

These patent thickets not only delay entry,

they chill competition overall because of the exorbitant cost of litigating meritless patents. We urge FDA to work with the patent trademark office to stem the issuance of non-innovative patents and support the use of inter partes review or IPR. IPR provides biosimilars manufacturers an earlier and more accurate picture of the patent landscape in a timely and less expensive manner.

We are also deeply concerned that the recently announced U.S. Mexico trade understanding to extend brand name biologic data protection to ten years will harm patients and the biosimilar industry. We believe USTR's efforts actually undermine both the President's blueprint and the biosimilar action plan. We encourage FDA to work with USTR, advocate for rejection of these provisions.

Finally, we appreciate the FDA's commitment to naming the companies seeking to block competitor acquisition of reference product samples via restricted distribution schemes to try to deter such conduct. However, a study released today by Matrix Global Advisors reveals the growing cost of these abuses, with

annual loss savings exceeding $13 billion. This is nearly triple the annual loss savings number of just four years ago.

The bipartisan CREATES Act would prohibit brand pharmaceutical companies from restricting access to samples to delay biosimilar competition. We are not aware of any companies who have changed their practices as a result of FDA's naming and shaming. Congress needs to act, and we urge FDA to work with Congress and help it pass this important legislation.

I will now touch on some of the questions in the hearing notice or the topics.

Education. We applaud FDA's introduction of provider education materials about biosimilars. As I say, you're the single-most credible resource for stakeholders, especially patients and healthcare providers, seeking information about biosimilars. We urge you to expand your efforts to promote and instill confidence in biosimilar safety, efficacy and quality. This should include using understandable terminology and prioritizing efforts toward those stakeholders who stand to benefit most.

We also agree with those urging the FDA via the citizen petition process to address misinformation campaigns that are damaging marketing confidence in biosimilars. We believe this includes statements around so-called non-medical switching. In fact, patients are routinely switched from one biologic to another, if the treating physician deems such a change as the appropriate course of treatment.

In Europe physician-led switching from a brand biologic to a biosimilar is common, and extensive data shows that a one-time switch for a brand biologic to a biosimilar does not carry increased risk of an adverse event. This is one way false and misleading information undermines public confidence in the safety and efficacy of biosimilars.

Also, it's important for the FDA to continue to make clear that an interchangeability designation does not indicate a better biosimilar than one approved absent that designation. It's not a superiority designation.

We believe this misperception is gaining traction among payers and delaying biosimilar update.

You've heard a lot about the Purple Book today, so I'm going to kind of skip over some of that, except to say we agree with many of the stakeholders here today, we want the Purple Book to list which products have been determined not to have exclusivity and those that are still subject to pending decisions.

We also applaud FDA allowing biosimilar manufacturers to carve out specific indications protected by patents from their label, and we would like you to continue your current policy around that.

In terms of facilitating development, AAM strongly supports eliminating the requirement for sponsors to conduct expensive and unnecessary bridging studies when using non-U.S. licensed reference product. We are concerned that some aspects of the draft guidance on interchangeability impose unnecessarily burdensome scientific standards on interchangeability determinations or may be inconsistent with statutory requirements.

If finalized, these requirements not only will create significant disincentives for sponsors to develop interchangeable biologics, but more importantly

will also significantly affect patient access.

We look forward to submitting our written comments and am happy to take your questions. Thank you.

DR. SHERMAN: Thank you for your comments. Questions from the panel? Dr. Franklin.

DR. FRANKLIN: You mentioned some of these very important but -- very important concerns that may be in some ways or in many ways peripheral to FDA authorities, but when it comes to one -- when it comes to intellectual property and some of -- and the patent thickets as you described them, are there actions FDA can take? You mentioned patent carve-outs from labeling. Are there other actions FDA can take to help out from your perspective in this area?

MS. SIMMON: Well, we appreciate what you have done. We appreciate Dr. Gottlieb, you know, that term patent thicket is his. He's called this out himself using that exact language, and so we do understand that PTO and FDA are separate agencies. But we do think that first of all some of the Purple Book that I kind of glossed over, but some Purple Book improvements

would also help alleviate this by clarifying, you know, which products have been determined not to have exclusivity. That way -- and maybe allowing exclusivity determination requests, you know, to come from biosimilar applicants and not just the BLA holder.

So those are some ways of getting at it. But again, we really encourage you to continue to use your bully pull pit, that the Commission has, to influence other agencies, because you've taken us all very far in biosimilars, but you need the assistance of your compadres in the Federal Government to get us across the finish line.

DR. SHERMAN: Dr. Kozlowski.

DR. KOZLOWSKI: So you mentioned that we should work on making scientific bridging less burdensome. So were you focused on PK, BPK aspect of bridging or the analytical part of bridging?

MS. SIMMON: I will be focused on asking our Senior Vice President of Science and Regulatory to embellish on that in our written submission.

DR. KOZLOWSKI: Okay, thank you.

DR. SHERMAN: Any other questions? I have

one. We saw this morning the difference in update from (indiscernible). Do you have any thoughts on why that might be?

MS. SIMMON: Well, some of what I mentioned, but a lot of it too is these rebate traps that happen in the commercial payer side of the equation. I think several speakers have touched on this today and that is a lot of it. I was fascinated by the new data that Pfizer and that the Pacific Research Institute will be highlighting today, and I think that's really very telling. That charge is very telling, and it just shows that, again, FDA approval is super important obviously. It's critical, but it's insufficient.

DR. SHERMAN: Great. Thank you very much for your comments.

MS. SIMMON: Thank you.

DR. SHERMAN: Our next speaker is Dr. Meni Melek from Novartis.

DR. MELEK: Thank you and good afternoon. My name is Meni Melek and I'm the Global Head of Regulatory Affairs at Sandoz Biopharmaceutical.

Sandoz is a division of Novartis and today I'm

representing Novartis. We think FDA for organizing this hearing and for their recent actions to improve biosimilar development and ultimately access for U.S. patients.

We believe that the Agency has adequately identified a number of important topics in the biosimilar action plan, that if addressed have the potential for substantial positive impact on biosimilars.

We, therefore, urge the Agency to continue its efforts and identify actionable solutions to these topics. Novartis will comment to the questions raised by the Agency in writing.

For today's hearing we'll focus on selecting topics listed here, where we believe the FDA can either take rapid action or those which could have a longer-term significant impact on biosimilar development.

So Novartis is in a unique position, where for decades we've been the global leader, serving patients with treatment options across a full spectrum, from generics to breakthrough innovative biologics, to biosimilars and others.

We have the fortune to recognize the value that each of these can bring to the U.S. healthcare system. At Novartis we've been a biosimilar pioneer launching the first biosimilar, Omnitrope, in Europe in 2006, and in receiving the first U.S. FDA biosimilar approval with Zarxio in 2015.

Through our multiple sources and projections supporting the value of biosimilar, not only to the individual patient but also to the healthcare system more broadly, Novartis would like to reaffirm its conviction that biosimilars can play a critical role to the U.S. healthcare system to ensure sustainability of the system and to expand access to these important medicines.

As such, we support FDA's renewed efforts to foster biosimilar approvals and uptick in the U.S., while at the same time ensuring the balance in order to support continued innovation in diseases and sub-populations that remain underserved.

The first item we'd like to address is staffing in the Agency. FDA has made a number of commitments as part of the BsUFA II process as well as

in the biosimilar action plan with identified priority deliverables. At the same time the Agency has had continued difficulties to deliver guidance documents and/or meet some of its BsUFA goals. We, therefore, strongly support the continued efforts from the Agency on its organization, including the establishment of the Office of Therapeutic Biologics and Biosimilars and full recruitment of open positions through their recently announced streamlined hiring program.

Adequate staffing is a cornerstone of the Agency's ability to deliver effectively on its commitments.

Within the biosimilar action plan FDA has taken the action to explore the potential for increased use of non-U.S. licensed comparator product for certain biosimilar studies. And thereby streamlining related bridging requirements.

Novartis fully supports the Agency efforts and also acknowledges that challenges need to be addressed before implementation could occur. We look forward to continued dialogue to define the framework for implementation and believe this could provide

significant benefit, not only to biosimilar development but also for innovative biologics where comparative studies may be needed.

Analytical similarity assessment is at the foundation of biosimilar development, and the key focus during review and registration. However, as the Agency noted in the biosimilar action plan, this can represent a hurdle for efficient development of biosimilars for two reasons.

The first one is when defining the reference product range, which is typically established quite early in development, and is then set for the duration of development.

The second hurdle is in regards to aiming the biosimilar at a moving target. During the life cycle of biologics, changes to analytical characteristics may occur, changes that are detectable with newer advanced analytic tools, but they have also been shown by the sponsor not to impact efficacy or safety.

To address these issues we do look forward to continued engagement with the Agency on the new statistical guidance and any other guidance documents

or tools which FDA has referenced in the biosimilar action plan. We hope these actions will put more emphasis on the totality of evidence over statistical analyses of single attributes.

As recognized by the Agency and the biosimilar action plan, a sponsor may need to revise a product label to remove indications or related information protected by IP rights, before an approved product can be launched. A biosimilar label is always based on the reference product's label, and in these instances changes are a result of either removing and/or anonymizing information related to information covered by patent.

Alternatively the biosimilar sponsor may re-introduce the approved wording contained in the reference product. In this context we recommend that FDA develop streamlined and pragmatic review processes to allow for simplified and timely implementation of these changes.

We have included some suggestions on this slide as an example. We believe that this topic which is one which the Agency could address relatively

rapidly.

Education is an important consideration for the efficient uptick of biosimilars in the U.S. An understanding of biosimilars, what they are, what they can bring to the U.S. healthcare system, not only to patients but also to providers, and to payers is paramount to the acceptance of their use.

The FDA, as a trusted government agency, has a key role to play in this regard. We welcome the Agency's initiatives here and encourage continued outreach. We believe it could be useful for the Agency to more actively monitor information in the public domain to target education efforts on topics that remain misunderstood, to address misinformation and to engage in an educational campaign on the basics of biosimilars.

The last topic we would like to address is FDA's biologic's naming policy. At the July Brookings event the Commissioner emphasized the Agency's belief in the value of this naming approach for biologics. Novartis respectfully disagrees and believes that experience gathered to date, especially in regions

where biosimilars have been accessible for over a decade, does not support the hypothetical concerns that the naming policy was intended to address.

Novartis has a sizeable pharmacovigilance database with Zarzio in the U.S. Our experience shows that the suffix is not being used in PV reporting. But more importantly, that it has not impacted the reporting of these cases. In fact, the naming policy has created a distortion in the marketplace, where reference products do not have suffixes, where biosimilars do.

Connected to the previous slide on education efforts, we would like to draw attention to the fact that some FDA decision and actions, such as this one, may indirectly contribute to misperceptions about biosimilars in the community and consequently hamper uptick in access.

And with that I'd like to close and open for questions.

DR. SHERMAN: Thank you for your remarks. Questions from the panel? Dr. Christl.

DR. CHRISTL: Just a point of clarification.

In terms of the biosimilar labeling, question seven, you had given some points initially about enabling scientific review for all indications that are not covered by regulatory exclusivity, but then talk about re-introduction of an indication that was left out initially. Do you envision from your perspective some difference maybe in regulatory approach between, again distinguishing initial review of things that weren't covered by exclusivity, if you made a decision to leave something out for, you know, non-exclusivity reasons, if the Agency had already reviewed that information from a scientific standpoint versus adding in indications that weren't previously reviewed?

DR. MELEK: So we had considered all different scenarios and we'll go into detail in our written response, but I think we can all agree that if you have seen and reviewed something previously and were pulling something in or pulling out, that could be -- I think that would be a foundation for something streamlined and pragmatic, where if there, for example, if there's a new indication from the innovator and you're reviewing something de novo, it would likely have a

different type of pathway, but we'll provide this in more detail.

DR. CHRISTL: Yeah, it would be very helpful to sort of parse that out in terms of what you think the approach should look like. And also in your comments if you could give some more meat around this connection between streamlining bridging requirements versus circumstances where maybe bridging studies could be waived or not needed, you acknowledge the challenges that might exist, it would be helpful to us to have your approach about how to address those challenges, versus just pointing out that there could be challenges, so that the more information you can give us in the comments, the more helpful that will be.

DR. MELEK: Yeah, we'll do our best to provide as much detail and direction as we can.

DR. SHERMAN: Dr. Kozlowski.

DR. KOZLOWSKI: So you referred to a global reference standard, sort of continuing this lack of need for bridging. So what do you envision that means? Does that just mean a set of material from different regions all could be equally used as reference product?

Do you mean a third party holding, for instance, some sort of reference material? What is your intent by global reference product?

DR. MELEK: So just to clarify, when non-U.S. approved product -- and I think it depends. It's on a case-by-case basis, depending on the publicly available information. In some cases it's quite transparent based on EPAR's in Europe or summary based approval in the U.S. that you indeed have the same product in the U.S. and in Europe, and so that's one extreme case.

We could also imagine a scenario where there is analytical data and maybe that would suffice to show that the products are the same, but what we're looking to is to find scientific and credible ways to provide what's needed, no more, no less.

DR. KOZLOWSKI: Thank you.

DR. SHERMAN: Any other questions? Thank you for your comments.

DR. MELEK: Sure.

DR. SHERMAN: Our next speaker is Andrew Spiegel from the Global Colon Cancer Association.

MR. SPIEGEL: Good afternoon and thank you for

allowing me to speak on behalf of the patient community today. My name is Andrew Spiegel, representing the Global Colon Cancer Association. I've been a patient advocate for nearly 20 years now, having founded the U.S. based Colon Cancer Alliance back in the late 90's, and now I run an international colon cancer organization called the Global Colon Cancer Association.

I think I've seen all of your in the past from earlier testimony that I have given on biosimilars and so I won't spend much more time getting involved with why I'm here. I lost both of my parents back in the late 90's to cancer, two days apart, and since then have been full time a patient advocate.

I'm immediate past chair of the Digestive Disease National Coalition and I was just elected as incoming Chair Elect of the International Alliance of Patient Organizations, but most relevant for today is that as many of you know, almost a decade ago we started the Alliance for Safe Biologic Medicines, which is a patient and physician led group to put together to ensure that biosimilar regulatory policy benefits

patients.

So colon cancer affects a lot of people in this world. Actually this is old data. It's now over 1.4 million people who are diagnosed with colon cancer. That number is expected to double over the next 17 years, so it is a rapidly growing cancer worldwide, and we have been advocating now for six years on a regional and international basis for a number of policies to help colon cancer and regular patients.

And like I said, in late 2010 we co-founded ASBM, the Alliance for Safe Biologic Medicines, to bring our perspective to this exact discussion.

We know that about 800 million patients worldwide have benefitted from biosimilar medicines and we often know that patients like Kathleen, who testified earlier, sometimes may take years to find the right medicine or the right cocktail, I would say, for them and as a result we don't want to expose patients like Kathleen to serious or more serious concerns, because we've messed with her cocktail.

But biologic medicines have had a tremendous impact in the colorectal cancer community. I remember

the days when there was only one drug, when my mom was diagnosed with colon cancer in the late 90's, which was highly ineffective and now we're knocking on the door of almost 15 approved drugs and more than half of those are biologics. And the data that's come from that is that the average life expectancy of the metastatic patient has tripled from less than a year to now knocking on the door of three years, and there's very other few cancers that can say they have measured success like that in such a short time.

So the colon cancer community does have a vested interest in biologics, and has a great interest in getting biosimilar medicines to market. We're excited about biosimilars. We want them to come to the market. We understand the many benefits that biosimilars promise, which is greater access. And this is especially true worldwide, where I do most of my work, where other countries -- they simply cannot afford the expense of originator biologics and biosimilars really do hold promise to not only provide for cheaper medicines for the payers but an increased pool of patients who will then benefit from that

treatment because of the lower price.

But we want to make sure that policies like the FDA and the WHO put forward, put patients first and, therefore, we've developed about six recommendations that I'll run through quickly.

So obviously patients have to be the focal point of all biosimilar regulatory policies, not potential cost savings. We would ask that the regulators do not consider costs when determining biosimilar policy considerations and always keep the patient as the forefront of their objectives, because we're all going to be patients some day.

Number two, there should be no sacrifice on quality, safety or efficacy. Patients have the right to expect access to biosimilars and assurances that they are approved based upon the same high standards the FDA has always had for other types of reference medicines.

And third, we want robust data collection. We want data that shows that if a patient like Kathleen who has autoimmune disease is switching between a product time after time again, that that switch is

going to be safe, and that that drug is going to remain effective and she's not going to be made worse, and the only way we could really know that is with data, and so we know that Europe has biosimilars now for ten to 12 years, and just a couple of years with monoclonal antibodies but I would say and I have said that I believe that the experience in Europe has been a missed opportunity rather than an opportunity which is helping patients, and that missed opportunity is the failure to collect post-marketing data once these biosimilars have put to market.

And I think the real proof of that is the uptick that has not happened in Europe. You would think 12 years after biosimilars have taken over, they would do like the generics did and own most of the market, and that simply has not been the case and when you look at the survey data as to why that is, it's a lack of confidence from the physicians and the patients because of the lack of data.

Treatment choices should be made. This is number four, by the patient and the patient's healthcare team, not by third party such as payers and

governments, who are looking to save money. The decision between whether to switch a patient to an -- from an originator product to a biosimilar has to be made by the patient and by the healthcare provider, not by the payer.

And fifth, we want robust pharmacovigilance. The biosimilars that have been approved, we expect good tracking, good pharmacovigilance. We want to make sure that the FDA continues its use of non-proprietary names, unique but nonproprietary names on all biologics, not just biosimilars, but all biologics. Contrary to what an earlier speaker said, I feel that the nonproprietary names is a critical, critical element to continuing post-market data collection and pharmacovigilance, and I know that the FDA already agrees with me, because I've attended meetings in the recent months where FDA has absolutely credibly defended its use of unique nonproprietary names in biosimilars, and we would ask that all biologics have those unique names.

So the last thing I want to focus on is probably something you won't hear from other speakers

today. I literally came here from the ICDRA meeting in Dublin, which is the International Conference of Drug Regulators, which takes place every two years, and I've participated in a pre-ICDRA panel yesterday, with senior leadership from the WHO and other patient groups, and the issue that -- one of the issues that we discussed with senior leadership of WHO, and this is leadership within the naming division, were a global system for pharmacovigilance, such as unique naming, like the FDA has here in America.

And what I'm asking of the FDA, because the FDA is truly respected all over the world, when I meet with other regulators and I don't mean Health Canada and the TGA. I'm talking about other smaller regulators from around the world. They truly look to the FDA for guidance on how to conduct themselves and how to approve drugs, and the FDA has to use its leadership position to push the WHO and to get other regulators together to push the WHO on a universal, global naming policy, and that's my ask of the WHO today, to use its gravitas as perhaps the leading regulator in the world, to help all of the other

regulators by combining efforts and pressuring the WHO to move forward with the unique naming proposal.

With that I will close and take any questions you all may have.

DR. SHERMAN: Thank you for your comments. Questions from the panel? Dr. Kozlowski.

DR. KOZLOWSKI: So you mentioned there was a missed opportunity in all the years of biosimilar use in Europe, so what sorts of data were you thinking could have been collected that were not?

MR. SPIEGEL: Well, because of the lack of mandatory post-data marketing collection or post-marketing data collection, we don't have data that says multiple switches from one biologic to a biosimilar to another biosimilar, which we certainly will be -- we will see happening soon enough, is safe and is effective. And as I've said before and other regulators have said before, lack of data is not data. So for you to say there hasn't been any major safety concerns, there hasn't been any major things that have happened from biosimilars to date, that's great, so we know that they're not going to kill all of us, but if

we had data that we could present to the physician community and the patient community to say look, we switched thousands of patients from this drug to this drug, and then this drug to this drug, and this drug to this drug, and there's been no adverse events, and the drugs are still safe and effective, then I think physicians would be much more apt to prescribe biosimilars, and the patient community would be much more apt to take biosimilars. And I think it's that missed opportunity with the lack of data that's been collected from drug manufacturers that has led to the lack of confidence and I believe has led to the lack of uptick.

DR. KOZLOWSKI: So there is adverse event reporting. So you're talking about something beyond that, in terms of claims data, if there's national healthcare, that sort of data, because it would seem that data probably exists for a lot of this.

MR. SPIEGEL: I'm talking about real world data. I'm talking about the fact that when prescribed a medicine in Europe, there may -- I'm sorry. What was the first part of your question?

DR. KOZLOWSKI: So in other words, that there is adverse event reporting. So you're asking for more than that. And so there are in different countries in Europe, national healthcare, other things where presumably there are data sets, so is the question that that data exists and nobody is actually mining it?

MR. SPIEGEL: Well, if the data existed and I've asked for it for almost a decade now, I think it would have come forward. I think if the EMA has data, that they've been collecting, post-marketing -- post-marketing data, they would have shared it by now. With the number of people that have expressed concerns about the lack of post-marketing data, wouldn't you think they'd say sure, we have the data, here it is. Well, they don’t have the data and they don't have it because they haven't mandated collecting it.

And if we look at real world, what percentage of European physicians do you think actually do adverse event reporting and take that a little step further, is loss of efficacy. We did a survey of -- from 11 countries and asked physicians is loss of efficacy an adverse event? Would you report that? And the vast

majority said no. So the fact is there's no international standards. There's no European standards for when these physicians should be reporting, and I've heard data that says physician reporting of adverse events is actually under five percent in Europe.

So I think that's not the kind of date the FDA relies upon. It's not the kind of data that WHO should rely upon. And again, we would ask that the FDA take that leadership position to push the rest of the world to have these high safety standards, just like we have here in America.

Thank you.

DR. KOZLOWSKI: Thank you.

DR. SHERMAN: Any other questions? Thank you for your comments.

MR. SPIEGEL: Thank you.

DR. SHERMAN: Our next speaker is Dr. Soumi Saha from the Premier Health Alliance.

DR. SAHA: Thank you. Premier Healthcare Alliance thanks the FDA for the opportunity to provide comments on the FDA's approach to enhancing competition and innovation in the biological products marketplace,

including by facilitating greater availability of biosimilar interchangeable products.

My name is Soumi Saha and I am the Senior Director of Advocacy at Premier.

Premier is a leading healthcare improvement company uniting an alliance of more than 4,000 U.S. hospitals and health systems and approximately 165,000 other providers and organizations to transform healthcare through integrated data and analytics, collaboratives, supply chain solutions and consulting and other services.

Premier plays a critical role in the rapidly evolving healthcare industry, collaborating with members to co-develop long-term innovations that reinvent and improve the way care is delivered to patients nationwide.

A key component of our alliance is the Premier pharmacy program, which combines essential clinical data with purchasing power to deliver reduced costs, improve quality and safety, and increase knowledge sharing with other healthcare providers.

Premier views the accessibility of biosimilars

as a key element in creating a more competitive drug marketplace in the United States, and has been a leader in promoting a competitive biosimilars marketplace through our supply chain, clinical support, education, advocacy and thought leadership efforts. Premier currently has all marketed biosimilars on contract, and employees dedicated biosimilars team, that works with biosimilars manufacturers through a products life cycle from pre to post-launch, to ensure continued access to biosimilars.

Clinically Premier develops value analysis toolkits, provides product-specific information, including clinical and financial considerations, and supports its members with reimbursement considerations for biosimilars within the Medicare and 340(b) programs.

In regard to education, Premier maintains a dedicated website on biosimilars for health system pharmacy members that provides factual and unbiased information on biologics and biosimilars. In addition, Premier has developed several continuing education programs for healthcare providers and biosimilars and

outreaches to health system stakeholders to educate and promote the adoption of biosimilars.

From an advocacy perspective, Premier has been actively engaged in ongoing effort to Congress, FDA, CMS, and other stakeholders to ensure that the pathway to market for biosimilars prioritizes patient access and safety and encourages the development of these cost-saving medications.

And finally, Premier has authored several pier-reviewed journal articles, white papers and blog posts discussing the current biosimilars landscapes and encouraging adoption, as well as serving on the Advisory Board for the Center of Biosimilars.

So the Biosimilars Action Plan. Premier applauds the FDA for recognizing the value of biosimilars and its important role in minimizing the time and cost to develop biosimilars and in promoting effective communication. We further applaud the FDA for releasing the Biosimilars Action Plan to outline the Agency's approach to striking the appropriate balance between innovation, access and competition.

Premier offers the following comments on

elements of the action plan that it believes can be enhanced to further promote a robust biosimilars marketplace.

So one, to improve the efficiency of biosimilar interchangeability product development and approval, as an over-arching principle, FDA should permit a designation of biosimilarity parallel to granting an interchangeability designation, if the applicant seeks both. The FDA has previously advised that applicant should seek designation of biosimilars first and then subsequently seek interchangeability designation. A bifurcated process that creates procedural inefficiency and potentially delays the introduction of interchangeable biosimilars to the marketplace.

Therefore, Premier recommends that FDA create a parallel review process to permit applicants to seek a simultaneous designation of biosimilarity and interchangeability to create procedural efficiencies and improve access to interchangeable biosimilars.

Two, to maximize scientific and regulatory clarity for biosimilar manufacturers, Premier supports

FDA's intent to improve regulatory predictability, harmonize international regulation of biosimilars, and the acceptance of non-U.S. comparator products, and the use of real work evidence in supporting regulatory decision making.

One area to note, however, regarding harmonization and the acceptance of non-U.S. comparator products, is that the FDA's draft interchangeability guidance released in January, 2017, states that the use of a U.S. license reference product is required. Therefore, Premier urges the FDA to revise this requirement when issuing final interchangeability guidance to permit the use of non-U.S. comparators when seeking interchangeability designation.

Three, to improve the understanding of biosimilars, Premier agrees that it's critical to educate healthcare professionals and other stakeholders and applauds the FDA on their efforts thus far with the biosimilar education outreach campaign, and the FDA's commitment to creating additional innovative educational materials.

As the FDA looks to develop these innovative

educational materials, Premier suggests that FDA work with private partners who have already created these type of materials to adapt existing factual and unbiased educational materials to help speed the availability of these educational materials.

And four, to support market competition Premier agrees that it is necessary to reduce the gaming of FDA requirements, other attempts to unfairly delay competition. Premier offers two specific recommendations to help improve market competition.

First, some manufacturers restrict access to samples for biosimilar manufacturers by setting compliance with limited distribution or REM's requirements. This practice inhibits the ability of biosimilar manufacturers to demonstrate bioequivalence and thereby delays the ability -- I'm sorry, and thereby delays the availability of biosimilars in the marketplace.

Now, the FDA has acted in this regard and has begun on their website listing manufacturers that the FDA is aware of that is abusing these requirements; however, more needs to be done to actually prevent

these practices. And, therefore, Premier recommends that FDA work with Congress to prevent access restrictions to product samples needed for bioequivalence testing for biosimilar development.

Second, there's been an increase in patent disputes and settlements between biologic and biosimilar manufacturers, delaying the availability of biosimilar in the marketplace beyond market exclusivity granted under the BPCIA.

Currently this process is not transparent, as biological and biosimilar manufacturers do not have to report patent settlements to the Federal Trade Commission in the same manner that brand and generic manufacturers must. A process that is considered a deterrent for brand manufacturers to enter into patent settlements.

Therefore, Premier recommends that FDA work with Congress and the FTC to require biological and biosimilar manufacturers to report patent settlements to the FTC.

Finally, one additional area not included in the action plan that Premier would like to raise is the

naming convention for biosimilars. Current naming convention finalized by the FDA in January of 2017 adds complexity to the healthcare system, which could lead to errors in prescribing medications and pose a risk to patient safety, hampers clinical decision making and the ability to identify lower cost therapeutic alternatives, and causes unnecessary confusion amongst patients and providers, all issues that do not lend themselves to increasing the adoption of biosimilars.

Therefore, Premier urges the FDA to rescind the current naming guidance and reissue guidance that uses the same international non-proprietary name for biosimilars as the reference product.

So in summary, Premier encourages the FDA to permit a parallel designation of biosimilarity to interchangeability, harmonize international regulation of biosimilars and the acceptance of non-U.S. comparitors to demonstrate interchangeability, work with private partners to adopt existing factual and unbiased educational materials, work with Congress and the FTC to address anti-competitive practices and revise the naming guidance to use the same INN for

biosimilars as the reference product.

Again, I'd like to thank the FDA for the opportunity and I'm happy to take any questions that you may have.

DR. SHERMAN: Thank you for your remarks. Questions? Dr. Franklin.

DR. FRANKLIN: Thank you. I think many of your comments focus on interchangeability. We obviously agree that interchangeability is a very important concept and I think one of the questions that I had is for an organization entity like Premier, can you give some examples of how interchangeability is -- do you think is going to play an important role in the uptick of these products?

DR. SAHA: Absolutely. So you know, our health systems and hospitals are frequently using biosimilars and biologics, and what we think is happening right now is the more interchangeable products that we can get to market, the easier it will be to substitute an interchangeable product for a biologic, thereby reducing healthcare costs to the overall health systems. And that's one of our utmost

goals.

DR. FRANKLIN: Okay. And so you're primarily looking at pharmacy substitution?

DR. SAHA: Correct.

DR. FRANKLIN: I just wanted to clarify one thing, which is that you stated that the draft interchangeability guidance describes a requirement to use the U.S. license product as a comparator. I believe it just states that that is strongly recommended. Again, that's just draft guidance, but I just want to make that clarification.

DR. SAHA: I will double check but I believe it was a requirement and not a strong suggestion, but we will absolutely double check.

DR. SHERMAN: Ms. Abram, Anna.

MS. ABRAM: Not so much a question but more a request for when you submit comments in to the docket.

DR. SAHA: Absolutely.

MS. ABRAM: Under your bucket that denotes supporting market competition by reducing gaming, and you touched upon restrictions in the distribution and access to the samples, to the extent that you think

that there are other actions the Agency might consider under its existing authorities, I would just encourage you to denote that in your comments.

DR. SAHA: Absolutely.

DR. SHERMAN: Dr. Kozlowski.

DR. KOZLOWSKI: So you mention real world evidence as something that should be used more. So from your Alliance, based on your description of the breadth of this organization, clearly has access to a lot of information on patients and patient records, so are you taking on an attempt to at least explore the idea of real world evidence and what it can show you about these products?

DR. SAHA: Absolutely. So Premier currently has access to over one-third of hospital discharge patients and we are looking at an opportunity to utilize our robust data infrastructure to look at biosimilar safety and efficacy in the marketplace in the real world.

DR. KOZLOWSKI: Thank you.

DR. SAHA: You're welcome.

DR. SHERMAN: Diane.

DR. MALONEY: Just a request that you clarify or provide more explanation of your comment that we should improve regulatory predictability. You know, if you have examples. Thanks.

DR. SAHA: Right. And I think the goal there is we support everything that's in the Biosimilars Action Plan in regards to improving predictability for a biosimilar manufacturer coming into the marketplace and we are continuously happy to work with the FDA to come up with any additional solutions that may bridge beyond the action plan, but it is a concept that we are extremely supportive of.

DR. SHERMAN: Any other questions? Thank you for your remarks.

DR. SAHA: Thank you.

DR. SHERMAN: Our next speaker is Dr. Madelaine Feldman from the Alliance for Safe Biologic Medicines.

DR. FELDMAN: Well, I too thank the FDA for holding this public forum on promoting biosimilar development uptick and access.

I'm Dr. Madelaine Feldman and I've been in

practice in rheumatology for 30 years now, and have a pretty good idea of what encourages physicians to write prescriptions and what sort of engenders confidence in new drugs that come to market.

I wear a lot of hats. Today I'm here as the Chair of the Alliance for Safe Biologic Medicine.

So a little bit about it. We've had a few speakers that talked to the beginnings of ASBM about ten years ago, and we have over 135 members. And as you can see, our steering committee is comprised only of physician and patient groups.

We've participated in the past ten WHO INN consultations and on July 12th we had a second in a series of meetings with various regulators from around the world, including the FDA. Oh, another thing that we're pretty active in is in education, particularly with pharmacists. We have CE programs that we offer around the states, as well as patient organization education.

And we also conduct surveys around the world in terms of adverse event reporting and how physicians view biologic naming, et cetera. So we have sort of a

wide breadth of what we do.

You know, we look at access and uptick. Uptick I think is based on access and confidence, but access is actually based on availability and affordability. So all of these attributes go into what makes a biosimilar available, what gives the confidence and thus leading to update, and I think the FDA is on the right track, certainly in terms of availability and providing rapid approval and getting them out there.

As you can see, we're really not far behind Europe. It was only two-and-a-half years after the EMA that we approved the first monoclonal antibody, so we're not really slow in our ability to approve these drugs, and I think they're getting out on the fast track and perhaps we may actually even overtake Europe in terms of approvals.

So the speed with which it's -- I don't think we should try to enhance the speed by reducing safety and lowering standards. I think we're on the right track with that, because we do have the biosimilars out there, so I don't think we necessarily have to increase the speed.

But one of the things we have to do is build confidence so that the drugs that are out there will be prescribed, and as you know there's two different pathways for the originator and the biosimilars, and with the reduction of regulatory emphasis on clinical studies, I think physicians would like to see real world evidence, and we're talking about RWE over and over again, and organizations like Premier perhaps can help us with real world evidence to engender this confidence to see that analytics are applicable and enough to demonstrate biosimilarity and efficacy and safety.

But convincing physicians of that is something else, and that's where education is going to come in, and we do need to have increased pharmacovigilance because that also will increase confidence from physicians.

So building this confidence. Education, as we've stated, is extremely important and ASBM is very active in that, particularly with pharmacists, physicians and patient groups.

So some of the thing that have been mentioned

in terms of whether it's naming or the ability to increase the rapidity of approvals, I think those -- some of those comments actually -- I would submit that not having unique naming decreases confidence. It doesn't increase confidence.

As a physician, I would like to know in terms of adverse reporting the exact drug that we're using. Unfortunately, in some of the surveys that we've done, up to a third of physicians worldwide and in the United States use only the non-proprietary name, when reporting adverse events. So, of course, that can lead to mis-attributing adverse events to the wrong or perhaps to the reference product or do a biosimilar that it really shouldn't be attributed to.

So I think we really need to continue with educating physicians and patients and that will increase confidence.

Of course, I have to bring this up. We keep talking about the transitive property with interchangeability of biosimilar A's. Interchangeable with reference product and biosimilar B, but they're not interchangeable to each other. And we feel that

that is an important guidance that the FDA needs to emphasize in their final guidance.

Okay, getting back to naming. Here is where we talk about nearly 70 percent of physicians and pharmacists in the United States support the FDA in terms of distinct, non-proprietary names. And we've held a number of meetings with regulators from around the world in terms of supporting distinct naming and international harmonization as with what Andy Spiegel had talked about, and I think that as much as the FDA can encourage regulators from around the world to harmonize a global system, particularly for pharmacovigilance, I think it would be a good thing.

So I'm going to get to the part that everyone else has been talking about. The bottleneck in access is really happening after the FDA approval, and that is why despite 12 approvals, we only have four that are available to patients. Dr. Gottlieb has observed this in terms of barriers to access are not scientific but commercial. Yes, there is patent litigation but I think one of the main things is formulary access, because competition alone does not lower price.

And if you look at the list price of the reference products, even if they were offered at 40 percent off, patients could not afford them if they're not on the formulary. And I mean, the first question that I ask after I go through diagnosing a patient and we come to what the patient can take is what's your insurance.

So how do they determine what is on the preferred? We'd like to think that the more competition there is, the lower the price goes. So there's two different ways that competition can drive price.

When you're building a house, the more competition, the lower the price. When you're selling your house, competition actually drives up the price, and unfortunately that's the -- our drug distribution system as it stands. So it does create a perverse incentive for a higher priced medicine. Rebates based on the list price, present discount and market share. Biosimilars have no market share and a lower price so they're behind the eight ball to begin with.

So we really need to penetrate the formulary

wall and whatever the FDA can do, whether it is joining up with the Federal Trade Commission, whether it is CMS, Congress, and even the Department of Justice has taken over looking at vertical integration with PBM's and plans. So I think this has to be sort of a global approach. PhRMA, PCMA, everyone has to get in here to turn around this formulary wall, so biosimilars can actually be prescribed and taken by patients.

So overall we encourage the FDA to continue with its rigorous standards and because of the way biosimilars are approved, real world evidence is important, and the approach to distinct naming, we support you on that, and in general doing the right thing.

So thank you. I'll take any questions.

DR. SHERMAN: thank you for your comments. Questions from the panel? Joe.

DR. FRANKLIN: Thank you. I have a question about your slide four, and this a point that's been reiterated by a few commenters, but you point out that FDA may make a designation of interchangeability between a reference product and product A and --

interchangeable product A and interchangeable product B. This is something we pointed out in our notice we wanted to ask about, ask for comments on, this kind of scenario, because we expect there would be different perspectives on it.

And you have lines connecting the reference product with the two interchangeables that are both green and then a big red line, not interchangeable, between biosimilar A and biosimilar B or interchangeable A and interchangeable B. And say that this is an important policy point which FDA should emphasize in guidance. I just want to clarify. When you say that we should clarify that point or the non-interchangeability between those products and guidance, are you talking about doing so without specific information about safety or efficacy problems, so this would be something proactive, it would be general, and would not be based on any kind of specific information that would demonstrate a lack of interchangeability between those products?

DR. FELDMAN: I think in terms of education, what interchangeability means, whether it's to the

pharmacies, to physicians, so that they understand that when a product is interchangeable and they write the prescription, that they don't -- that it doesn't fall into the trap of what was spoke to earlier, I believe by the AbbVie representative. So I think it's more of an educational thing and in listening to Dr. Christl at the DIA meeting recently, she reiterated that this is the way it's going to be.

Now, I don't know if there's going to be a change in that, but if that is the final guidance, I think it needs to have a little bit more PR behind it.

DR. FRANKLIN: Okay. So just to clarify, you're proposing that we would just clarify the -- what FDA's policy is with respect to the alternating or switching between products.

DR. FELDMAN: Yes. The biosimilar A and B would not be interchangeable with each other, even though they're both interchangeable with the reference product.

DR. FRANKLIN: Okay. Thanks.

DR. SHERMAN: Other questions?

DR. CHRISTL: Just possibly a point of

clarification, maybe for written comment if it's too much to get into, but there's been a lot of conversation about the value of real world evidence that, you know, could help to, you know, give confidence to prescribers and inpatients about scenarios that might come in opposed to approval setting, where patients are switched, things like that, and I'm struck a little bit that the more that I listen to it during the day about the chicken and egg scenario maybe here, you know, that in order to collect that information you have to have uptick and use of these products, and there's a little bit of conversation I think about sort of validating the pathway and validating the data asks through this real world evidence of showing, you know, there's not issues or problems.

And so I don't know if you have thoughts of perspectives about how to balance that in terms of the ability to collect that information versus having the products, you know, be approved based on the FDA standards and the statutory standards and then this requirement for this data to be collected to sort of

support uptick in use, but again, as I said, to get that data you have to have uptick in use.

DR. FELDMAN: It's difficult. So in the United States with 80 percent of the patients having their formularies controlled by three entities, it's going to be difficult to get real world evidence if the patients can't get the biosimilars to begin with, but as I look back over the years, there are I would say a good 30 to 40 percent of physicians that I know would wait until a drug was out three or four years, you know. They would talk to their peers about how the drug worked, and then that would give them the confidence.

So I think we have to break that wall to allow biosimilars to be used in order to get the real world evidence or from companies like Premier that have perhaps more evidence because they have a better controlled formulary that is allowing biosimilars or Europe.

DR. SHERMAN: Any other questions? Maybe in your comments if you could also address the uptick issue for (indiscernible) versus infliximab and I guess

for all the speakers, when we talk about RWE, it can be lots of different things. Are we talking about rear adverse events? Are we talking about outcomes? What is it that you're all thinking that we might be able to get?

DR. FELDMAN: Thank you.

DR. SHERMAN: All right. As I mentioned, we are running ahead in large part thanks to Dr. Gottlieb. Someone should tell him I said something nice about him, please. So we're going to take our break on time, which means we're ready for our next speaker, Dr. Wayne Winegarden. Great, you're here. Thank you. From Pacific Research Institute.

DR. WINEGARDEN: Good afternoon and thank you very much for giving me the opportunity to present to you here today. I'm Wayne Winegarden, a senior fellow with the Pacific Research Institute. One of my areas I concentrate on is pharmaceutical economics.

And we've spent some time trying to evaluate kind of what's the dollar value of the savings and try to put that into the context of what you're doing here. I should apologize up front, being an economist, there

are many numbers and I apologize up front for all of those.

What we had found that in effect the savings do exist. I'll kind of just flip to the conclusion and start with that, that there are significant savings. We examined one specific originator of biologic versus the biosimilars and infliximab. We wanted to evaluate -- are the savings that we believe existing, do they exist, and then if they do, then kind of how can we connect that to the obstacles that we've been talking about over and over here today?

When we were looking at the savings, we found that in a commercial market you could save about 50 percent market share, you could save $278 million if you had 50 percent biosimilar market share, and almost $150 million in savings for Medicare. So the savings are very significant and so the obstacles that we've been talking about today, buy and bill, fail first, the PBM's that Dr. Feldman just mentioned, all of these are very, very important to kind of obstructions that need to be addressed, and I think it's important to state right up front that some of these are outside of your

control.

But the regulatory clarity and especially the interchangeability designation, that is within your control. And while that may not be sufficient in terms of getting a biosimilars market similar to generics here, at 90 percent, it is necessary, and so we need to see these types of reforms if we're going to actually get the savings that we've estimated here.

So I wanted to just very quickly kind of walk you through what we did so you can kind of see where these savings are coming from and the importance of the regulatory clarity.

Again, we looked at infliximab, because there's a well-developed market. We have one originator, a biologic, two biosimilars. We based the analysis on the CMS Medicare payment data that was effective between April and June, annualizing that, so we're trying to use the most kind of -- most recent data available. And then we broke the markets into our employer sponsored market and the Medicare market.

And so we broke out the average sales price, the ASP, from the Medicare payments data, and then we

said okay, at the kind of commercial kind of price, you're going to have different markups. Zero to six percent, ten, 15 and 20, kind of based on that kind of cost plus pricing scenario.

And then Medicare was, in fact, statutory with the current sequester, you're talking about 4.3 percent increase over ASP's are the prices that are being paid. And so we wanted to see what the potential savings are on both a per patient and an aggregate savings basis.

This is diverse of -- far too many numbers. But on a per patient basis what we looked at is what would be the prescribed maintenance dosage for infliximab for the five common kind of autoimmune disorders that it treats. You can see across the board.

And then based on that we looked at what would be kind of the annual cost of administering infliximab versus Renflexis versus Remicade. And then obviously on a per patient basis the savings is simply just the difference between -- I think the most important one is the average biosimilar price compared to the biologic price. And what you can see, and this is with respect

to the Medicare market, you can see that there is about $2100 to $3600 per patient of savings that's possible if we can actually increase our use of the biosimilar versions of infliximab.

In the commercial market -- I skipped one -- we'll just leave this one up. In the commercial market, again, it was the same process but what you saw was -- oh, here it is. One more. One more down. It should be slide five. Perfect, thank you. Sorry about that.

We look at a per patient basis for the commercial market. You can see again it's a savings of $2100 all the way up to $4400, with a potential savings, depending upon the condition that's being treated, and of course depending upon the markup. Obviously, simple arithmetic, the markup savings increase as the percentage markup rises, as well.

If we then look at it from an aggregate basis, and we say okay, we can see there's large per patient savings that are available, what about for the entire market? And so what we did is we created a scenario. We said imagine the entire market was based on the

biologic. Right, the originated biologic is the entire market, and that's that first number in the top row, the $1.9 billion.

How much savings can we get under alternative scenarios? Kind of going by tens, all the way up to the current generic market share, how much potential savings are out there? And this is for the Medicare program. You can see, taking about a 50 percent market share, you're talking about eight percent cut in costs or about $150 million in savings, just from infliximab.

Now, I don't think it can be the same share as the generics because they're fundamentally different, but using that as a benchmark, you're talking about almost a 15 percent savings to Medicare in its expenditures on infliximab that biosimilars can create. And the savings are very similar if you look at the employer sponsor market.

Again, depending upon the markup, the savings are going to vary, but at a 50 percent market share, you have somewhere between 260 and 300 million dollars in annual savings that's available from greater use of biosimilars.

And so kind of the whole point in presenting terms -- you're talking a bit over eight percent, and so the whole point of kind of going through this exercise and why we went through it is, you know, one possible explanation in terms of why biosimilars haven't developed is that the savings are a ruse, right? The savings aren't really available. We only think they are.

But when you look at the actual pricing data that's out there, in one of the more developed markets, that's not the case, right. The savings are there and so both the market barriers, right, the fail first policies, which required it to fail first and the originator, before you can go to a biosimilar, or the whole buy and bill, networks off of the PBM problem, right, where all of a sudden there's an incentive to use higher prices.

And one of the things that's kind of very important in terms of just economics, particularly healthcare economics, is that you've got to get the incentives correct, and so we need to address those market disincentives to biosimilars in order to get to

the market shares that we're talking about, but from an FDA perspective the interchangeability guidelines is very important, and ideas such as kind of having the dual efficiencies so that we don't have to have separate tracks to speed up the cost. That's going to reduce your cost of development, reduced cost is going to increase the outcome.

So I think it's that kind of combination of market changes, as well as regulatory changes which is what we need to work toward to kind of get the savings that are potentially out there.

So thank you for the opportunity and I'm certainly happy to take any questions.

DR. SHERMAN: Thank you for your remarks. Any questions from the panel?

DR. UNLU: So your study was based on reference product and two biosimilars that are not interchangeable. From your last slide can we understand that if they were designated interchangeable, they would be prescribed more? Is that what your first bullet point, is that what that's supposed to mean?

DR. WINEGARDEN: I don't think you should take it that cause and effect, because -- and that's what I was trying to very carefully talk about other factors that are involved, as well, and I think it's -- they work with each other, right, the lack of interchangeability works with the BPM's, works with the, you know, the other obstructions and so just pulling on one isn't going to solve it. But you need to address all of them to get the environment kind of -- in effect you want to properly incent the biosimilars, right. We don't want to over-incent, so the patient that should be on the originator are not able to get that medicine, but the incentives shouldn't be discriminating against the biosimilar, and kind of the whole environment that they can kind of exist in, that's a discriminatory environment, and that's the problem.

DR. UNLU: So as a follow-up, on your second bullet you're saying that current regulations need to be clearer. Can you be more specific, either here or in your written comments, about what kind of uncertainties you're detecting and how they can be made

more clear?

DR. WINEGARDEN: In the written comments I'll be much more explicit about that.

DR. FRANKLIN: Yes. Following on my colleagues comments, you know, I think it would be useful from an economics perspective to look at -- undoubtedly the role of guidance is importance enough to stress the importance of finalizing the interchangeability guidance, but we've also heard from at least one other commenter today that overly prescriptive recommendations from FDA can limit the flexibility in the context of particular development programs. It would be useful to look at whether there's any way to kind of model the benefit versus cost of different levels of detail in FDA recommendations when it comes to product development, if there's any possibility. That's -- I guess that's more of a comment.

But the question I have is infliximab a useful case study? Is it representative of other product classes that may have different pricing considerations or pricing results?

DR. WINEGARDEN: I think so. Part of the problem is we don't have enough data out there to know for sure, so I think it's an important case because of the lack of data that's out there and it's something we can kind of plan to flag, and I think it warrants a lot more research to be sure.

DR. SHERMAN: Steve.

DR. KOZLOWSKI: Following up on the interchangeability comment and bullet you have, so you note that interchangeability can be used as an excuse not to prescribe.

DR. WINEGARDEN: Right.

DR. KOZLOWSKI: Is that actually saying that just the existence of the standard of interchangeability discourages biosimilarity or discourages biosimilar use?

DR. WINEGARDEN: Again, I don't think it's just the existence. I think it's the existence in the current environment. Right. So when you have -- and you have to be very careful, because I don't mean to assign any adverse kind of intentions on anyone's part, but what you're looking at is a very complex issue, and

then at the same time when you're saying this is very complex, you're not sure which is the right way to go, but hey, you're going to make more money if you go on this side, which is the safer side. You're now biasing the environment towards one versus the other, as opposed to having a neutral environment.

And so when you're establishing the incentives, in terms of between the different products, you need to make sure that that's neutral. I mean, that's not what we have now, so I wouldn't say by itself, no. And I wouldn't want to comment -- I think I'd be out over my skies to say whether or not it's medically viable. That's not my area. I wouldn't want to comment on that, but from an incentive perspective, how do we get the right system? It's interacting inappropriately.

DR. KOZLOWSKI: Thank you.

DR. SHERMAN: Okay. We'll now take a ten-minute break. Thank you for your comments. And we'll resume at 2:31.

(Off the record from 2:21 p.m. until 2:33 p.m.)

DR. SHERMAN: All right, our panel is assembled. And we're going to move forward with our next speaker, Molly Burich, Boehringer Ingelheim Pharmaceuticals. Thank you.

MS. BURICH: Well, thank you on behalf of Boehringer Ingelheim. My name is Molly Burich and we, of course, as all other speakers have echoed, want to thank the FDA for allowing for this hearing and listening to our feedback and comments.

Boehringer Ingelheim is a global innovative biopharmaceutical manufacturer, and one of the largest producers of biological medicines in the word.

As a pioneer in the production of biologics with more than 35 years of experience, Boehringer Ingelheim is developing its own and has manufactured more than 25 biologics for 15 of the top 20 global pharmaceutical companies. We've also strongly invested in the development of biosimilars, which as you know represent an opportunity to help improve patient access and drive down costs of biologics by introducing high quality, lower cost options.

Boehringer Ingelheim currently has one

approved biosimilar, Cyltezo, a biosimilar to Humira. It was FDA approved in August of 2017, but has yet to commercially launch due to ongoing litigation. Noteably, Humira biosimilars are anticipated to launch outside of the U.S. market later this year.

We are committed to bringing such a biosimilar to U.S. patients as soon as possible and certainly before 2023, when companies that settled their lawsuits will be able to launch their biosimilars.

Our presentation today is going to focus on questions one, two, three and nine.

So question one. As I go throughout, we strongly support and appreciate the continued advocacy and commentary by Commissioner Gottlieb and others sitting up here, highlighting the existing challenges in commercially launching a biosimilar.

A new white paper called Steps to Reducing Barriers to Biosimilars in the U.S. by Matrix Global Advisors echoes the challenges recognized by Commissioner Gottlieb and your Agency's recent report.

In particular the white paper cites unjustified late stage patents acquired by reference

product companies with a goal of obstructing or delaying competition. To be clear, we strongly support legitimate exclusivity for true innovation as contemplated by the patent system, but we also believe that when exclusivity is up, the system must allow for prompt market-based competition.

Current many biosimilars are facing multiple year litigation based delays before we can launch. With the average cost to develop a biosimilar at two hundred to three hundred million, it's untenable to have multiple years of delays before being able to launch a product after clinical development.

If this pattern continues, this may have a significant impact on investment in future biosimilar development, if not addressed, and could have a negative impact on patient access and affordability to all biologics in the future.

Question two, improvements to the Purple Book. We, like many others, consider the Purple Book a valuable tool for all stakeholders, not just pharmacists, but also other healthcare providers, patients and others. As such, we are concerned that

other stakeholders may request changes to the Purple Book to describe what biosimilars are, but also what they are not, or more accurately, what listed products have not applied to be, which is inconsistent with the Purple Book's purpose.

For example, any addition to the Purple Book that would list all biosimilars as quote, "not interchangeable," end quote, is grossly misleading, that it implies the biosimilar has aske the FDA for an interchangeable designation and failed to obtain one. Hence, it is only appropriate to list approved interchangeables and remain silent on those that have not pursued or been reviewed for interchangeability. Anything else we believe risks the perception of less quality, efficacy or other concerns, and could certainly generate stakeholder confusion.

In a time when the Agency recognized the myriad of misunderstandings surrounding biosimilars, and interchangeables, and is taking action to educate the public, we urge the Agency to be ever vigilant regarding additions to the Purple Book that would serve to undermine the proven safety, efficacy and quality of

biosimilars.

We would also ask the Agency to -- that a statement of interchangeability is equivalent to a description of suitable generics, namely, therapeutic equivalence and A rating. This will help build physician confidence and understanding and follow the themes of what we've seen in generic medicine.

Lastly, as previously outlined, the number of pens held by reference product companies pose numerous challenges for biosimilar companies, and we feel there's an opportunity for improvement via the Purple Book. Therefore, we would suggest that all process and product patents for a given reference product be listed in a manner already established by the Orange Book. This would help improve the ability of potential biosimilar manufacturers to identify which patents are relevant to a particular product.

Question three, interchangeability. As the only company to have publicly announced the initiation of an interchangeability clinical trial for an approved biosimilar, we believe the FDA outlined an appropriately high bar to establish interchangeability.

This high bar builds confidence in the interchangeable biologic pathway and is important to ensure these products will enjoy significant uptick in the market once they are available. We firmly believe the FDA should finalize the guidance and not lower the requirements, as this could have a negative effect on the value of interchangeability to providers and patients.

We would, however, encourage the Agency to consider some flexibility based on the nuances of a given product, and the most appropriate requirements for that specific situation. However, as I said, in general we support the draft guidance and would like to see it finalized.

We would also encourage the Agency to be aware of reference company tactics to undermine the designation by developing alternate formulations or other product variations that do not impact the fundamental components of the product. We implore the Agency to support the durability of the designation and grant interchangeability to products as appropriately outlined in your guidance and sustain that designation

against tactics that would seek to thwart competition.

Interchangeability should be a designation that a given biosimilar should only need to obtain one time in their development. It is not something that should have to be chased based on anti-competitive action by the reference product manufacturer.

Question nine, continued FDA activity to address market challenges. We are very supportive of the excellent education materials the Agency has developed for biosimilars. The marketplace is unfortunately overflowing with misinformation and misleading messaging surrounding biosimilar and interchangeable biologics which has generated the perception of risk for switching to a bio. This is unwarranted and notably does not apply to reference products undergoing manufacturing changes as those are de facto invisible to patients and providers in the U.S.

We greatly appreciate the FDA's efforts to combat misinformation with its education initiatives. Such primary resources are invaluable to a multiple of stakeholders interested in insuring biosimilars and

interchangeable biologics can compete and provide increased access and affordability to these medicines. As such, we encourage the continued development of more materials aimed at healthcare professionals and would recommend the Agency consider the development of materials specifically aimed at switching and transitioning patients to biosimilars and interchangeables. There continued to be the proliferation of misleading terms across the landscape, like non-medical switching, which we believe scientifically does not apply to biosimilars, because clinically biosimilars are the same therapeutic protein as the originator, and does not constitute a therapeutic switch to the patient.

Non-medical switching is being used to dissuade the use of biosimilars via state legislation designed to block and materials being developed by those wishing to thwart biosimilar competition. As such, we would ask the Agency to specifically develop materials that can provide appropriate education and tools on patient transition to biosimilars and interchangeables for both healthcare professionals and

patients alike.

Boehringer Ingelheim appreciates the opportunity to present to you today and the continued support by the Agency on the biosimilar pathway. We look forward to continued engagement on creating competition to allow for a vibrant and sustainable U.S. biosimilar market. We will also be submitted our comments in further detail via comment letter. I'm happy to take any questions.

DR. SHERMAN: Thank you for your comments. Questions?

DR. FRANKLIN: I'd just ask you about something that other have also commented on today, which is the idea of listing patents in the -- or listing information about certain patents in the Purple Book, and would just encourage you to provide more detail about this. I think previously today we talked about the -- whether or not this is something FDA has within its current authorities.

MS. BURICH: Mm-hmm.

DR. FRANKLIN: Also I think, you know, it would be useful for any commenters to consider the

relative benefits of this information from the biosimilar products development perspective, in addition to the cost of providing that information. So I think more of a comment to provide more clarity on that in your comments, if possible.

MS. BURICH: Happy to do that, absolutely.

DR. SHERMAN: Steve.

DR. KOZLOWSKI: So you mentioned strategies like formulation changes and other things meant to serve as barriers. So obviously improving products and innovating originator products over time is an important thing. So do you have thoughts about how you could separate out, you know, improvements that are meant to say a convenience and increase compliance, versus those that are potentially blocking in some way, and not really a benefit to patients?

MS. BURICH: Yeah, it's a great point and I think that from our perspective, that's particularly important from an interchangeability standpoint, so if the fundamental components of the product don't change, e.g., don't warrant a brand new BLA, then we feel like if a company is pursuing or has pursued

interchangeability and obtained that designation, then there shouldn't be a need to continue to chase that because of improvements that don't warrant a brand new BLA.

DR. KOZLOWSKI: Okay, thank you.

MS. BURICH: Yeah.

DR. SHERMAN: Other questions? This would also be for your written comments, if you could expand a little bit and all speakers on we talked about the flexibility and interchangeability. Dr. Kozlowski earlier had asked if we have let's say five or six or seven -- pick your number, of products, biosimilars, demonstrated to be interchangeable with the reference product, do we have more confidence about that universe?

MS. BURICH: Great, thanks, will do.

DR. SHERMAN: Thank you again. Our next speaker is David Korn from PhRMA.

Mr. KORN: Thank you for holding this hearing and inviting the views of the public. I am David Korn, Vice President, Intellectual Property and Law at Pharmaceutical Research and Manufacturers of America.

PhRMA represents leading innovative biopharmaceutical companies who research and develop new and improved medicines for patients and includes companies making biosimilar products, as well as reference products.

We appreciate the Administration and FDA's effort to maintain the intended balance between innovation and competition in America's healthcare system, and specifically the marketplace for biological products. PhRMA supported the enactment of the BPCIA, has actively participated in FDA's implementation activities and supports continued development of the biosimilar pathway.

As America's heathcare system evolves, biosimilars are anticipated to play a critical role in constraining prescription drug costs by reducing spending on biologics. This is on top of the cost savings from generics, which now represent 90 percent of all medicines given to patients.

PhRMA urges FDA to do what it can under the law to foster a scientifically rigorous regulatory policy for biosimilar products that can bring these important medications to patients and maintain

incentives for innovation, and we look forward to working with the Administration and FDA as additional guidance documents are released.

While there have been many proposals discussed today and included in the Biosimilars Action Plan and FDA's meeting notice, today I will focus on five key areas. We also plan to submit written comments to the docket.

First, we strongly support FDA's application of an umbrella exclusivity policy for biologics, as FDA already does for small molecule products. With an umbrella policy the approval of a supplement or new application that does not receive its own period of reference product exclusivity, would not compromise already earned exclusivity for the first license product. Instead, the period of remaining exclusivity would cover the innovation reflected in the new application. Importantly, am umbrella policy would not extend exclusivity beyond the original period.

Am umbrella policy is central to preserve the value of reference product exclusivity and encourage the R&D investments needed to support the development

of continued improvements to biologics to meet patient needs. Without an umbrella policy, a product change that doesn't result in new reference product exclusivity, for example, a new indication or root of administration, would have no exclusivity. A biosimilar applicant could immediately obtain approval for that changed product or new use even before it could obtain approval of a biosimilar of the original product.

This would effectively eviscerate the exclusivity for the first license product, as the biosimilar would be relying on the original approval. Failure to apply am umbrella policy would serve to disincentivize additional R&D investments that lead to the development of new indications and otherwise improve biologics and expand treatment options for patients.

Second, PhRMA supports FDA's use of appropriate data sharing agreements to expedite biosimilar development by facilitating harmonized development advice. Further, we support the adoption of analogous bridging study standards when non-U.S.

license comparators are used in innovator and biosimilar development programs.

PhRMA is concerned, however, with proposals to waive bridging study requirements based on non-public information where a non-U.S. comparator is produced at the same facility as the reference product. PhRMA does not object to waiving bridging study requirements if the biosimilar applicant can demonstrate through publicly available information that the non-U.S. product has the same drug substance, dosage form and root of administration as the U.S. reference product and is produced by the same manufacturer in the same plant, using the same sell line.

But in cases where this information is trade secret, FDA reliance on these trade secrets or disclosure of them to the biosimilar developer, either explicitly or implicitly through waiver of a bridging study requirement, would raise serious issues under federal law, and the takings clause.

Third, PhRMA seeks clarification of the plans for implementing the transition provisions of the BPCIA under which approved NDA's for biological products will

be deemed BLA's in March, 2020.

In comments on FDA's draft guidance we expressed concern with the proposal to extinguish unexpired Hatch Waxman and pediatric exclusivity for transitioning NDA's and deny them any reference product exclusivity. This proposal is inconsistent with the BPCIA, raises serious issues under the takings clause, and would significantly harm incentives for innovation.

We noted that the statute allows FDA to adopt an alternative approach in which granted exclusivity would remain in place and the Hatch Waxman patent provisions would apply through the term of the last expiring Orange Book listed patent.

This approach would be consistent with the statutory provision allowing sponsors of innovative transition products to choose between the NDA and BLA pathways, and their corresponding rights until the transition date.

Further, to increase efficiency and reduce regulatory burden, rather than requiring pending transitional applications be withdrawn and resubmitted as BLA's, FDA should allow these applications to retain

their status until final approval, when they will be deemed to be BLA's.

The transition date is just 18 months away and we urge FDA to provide prompt clarity on these issues so sponsors can prepare.

Fourth, PhRMA urges FDA to state in the Purple Book the Agency's commitment to publish prompt reference product exclusivity decisions at the time of BLA approval. This approach will give both innovators and biosimilar developers information they need to inform investment decisions.

We also recommend that the Purple Book state that an interchangeable determination reflects the Agency's judgment that an interchangeable biosimilar product may be substituted for the reference product, not another biosimilar product.

It's important for FDA to convey clear meaning of an interchangeability determination to avoid inadvertent substitution of products not demonstrated to be interchangeable with one another, and to promote prescriber confidence in interchangeable products. Individual interchangeable biosimilar products could

have differences and the potential immunogenetic effects of alternating or switching between them will not have been evaluated by FDA.

Finally, FDA's notice asked for input regarding a situation where a biosimilar applicant did not initially seek approval of a reference product condition of use due to patent or exclusivity protection, that protection expires and the applicant subsequently desires to seek approval for the condition of use. In such cases PhRMA supports approval of the conditions of use for the biosimilar based on clinical data or scientifically justified extrapolation.

We also support adoption of a clear process that enables the biosimilar applicant to obtain the approval of the new condition of use promptly upon expiration of the protection. Before the protection expires, however, FDA should not publicly discuss whether the product is biosimilar to the reference product with respect to the protected conditions of use, particularly for orphan protected uses, as this could undermine incentives to develop biologics for new indications.

In conclusion, we agree with FDA on the importance of fostering greater competition in the healthcare marketplace. As noted in the Biosimilars Action Plan, biosimilars have a crucial role to play in delivering new options to patients and in constraining prescription drug cost growth.

PhRMA looks forward to working with FDA on the continued implementation of the BPCIA in a way that encourages additional biosimilar competition, while protecting incentives for innovation.

DR. SHERMAN: Thank you for your comments. Questions? Joe.

DR. FRANKLIN: Thank you for the comments on these various issues. In our hearing notice we -- in our question about umbrella exclusivity, I'll just read it. We asked, "What is the relevance and significance, if any, of the patent scheme in considering this issue?" And I'm wondering if either today or in your written comments you can provide some insight to the significance in relationship of patents to the exclusivity questions that we highlighted in that notice.

Mr. KORN: We can address that in our written comments, but they are separate issues.

DR. FRANKLIN: Thanks.

DR. CHRISTL: Just a point of clarification, you had talked about FDA shouldn't be discussing in the review prior to exclusivity expiring, you know, where there's something that may be covered. Is it PhRMA's position that in an original 321 KBLA an applicant could submit data and information to support approval of conditions of use that would be covered by exclusivity for the reference product and just somehow redact that from the reviews, or are you talking about a process where it couldn't be included in the original 321 KBLA and it would just have to be addressed once that exclusivity expired?

Mr. KORN: Well, for example, on orphan, people do submit before the time is up, but if someone is not currently seeking approval for an indication, then the process shouldn't be the public process about whether it's biosimilar for that indication, and we can address that further.

DR. CHRISTL: Thanks.

DR. SHERMAN: Other questions? Thank you. Our last scheduled speaker is Chrys Kokino from Mylan.

MR. KOKINO: Good afternoon, everyone. My name is Chrys Kokino. I'm the head of Biologics for North America. But that's not the most important thing today. The most important thing today is that some of you, I've been told, this is the first day of school for your preschoolers and your other kids. So congratulations, big moment for all of you. Now, I do have to ask the question, at least my kids in New Jersey, look forward to snow days to get off of school. So are we going to have scorch days where kids don't go to school anymore? Just a thought.

So some of you may already know that Mylan has a very robust portfolio of about 20 biosimilars in our pipeline. We have now launched and commercialized a number of those products in rest of world markets, and here specifically in the United States we have two biosimilars that have already been approved by the FDA, so thank you for that.

The first, of course, is our tras 2 bara give (phonetic) product. The second product most recently

was our pegfilgrastim molecule Fulphila, which was just approved recently and is being commercialized as we speak today.

So with that, Mylan appreciates the FDA's continued efforts to foster biosimilar competition with the objective of building a sustainable biosimilars market. Now, more importantly, we applaud the FDA for recognizing that U.S. patients needs always, always come first. Mylan has previously submitted comment to the docket on several points related to questions posed by the FDA.

In the interest of time and for purposes of this public hearing, I'll focus on select topics impacting the viability of the U.S. biosimilars market. Further detail will be provided in written submission to the docket.

Now, the FDA has immediate opportunities within its existing authority to foster biosimilar competition without compromising biologics innovation. Some commercial and contracting approaches taken by originator manufacturers have created market barriers to biosimilar utilization. These barriers may and in

some cases do have a direct impact on patients and patient access to these important biosimilar treatment options.

As an example, formulary restrictions on biosimilar medicines, as you all know, have the potential to block access to FDA approved biosimilar medicines.

Now, we've identified several recommendations for rectifying the situation, which are outlined in our response to the HSS blueprint. While we recognize that most market barriers are not within FDA's mandate to fix, all of us, all of us, including the FDA, share a responsibility to foster a sustainable biosimilar market for the benefit of American patients.

If the current tactics continue, competition may become highly limited and has the potential in some cases to completely halt any future investment in biosimilars development. The consequence of limited competitions that biosimilars will never realize their full potential.

FDA should be cognizant of the impact its actions have on commercial competition, as well as the

impact to patients. FDA plays a unique role as a trusted -- and I'm going to say that again, a trusted voice to increase confidence and trust in biosimilar medicines.

The FDA biosimilars education campaign is an excellent beginning, amplifying -- amplifying these educational activities is an immediate step that FDA could take to improve acceptance of biosimilars and increased competition.

Bold statements on the FDA website or via social media to underscore key facts could have and will have a huge impact. For example, an interchangeable biologic is not a better biosimilar. Reinforcing this message has the effect of building confidence in biosimilars, as well as removing doubt about the safety, the quality and efficacy of these products.

FDA could also take a stronger stance in tackling misinformation about biosimilars. As an example, some clinical guidelines today exclude biosimilars due to a perceived lack of sufficient data to justify use and extrapolated indications.

As another example, some formularies require patients to fail first on a reference product prior to being able to utilize a biosimilar.

We're always asked about data. As we know, there's a robust data set from the European unit as well as around the world, 700 million patient days of clinical experience. I perhaps wonder if I told you there's 701 million days, would that convince you?

Finally, such falsehoods are not only contrary to science but they truly create unsubstantiated doubt and are potentially harmful for both healthcare providers and patients.

From a market perspective the use of suffixes for biosimilars and not for reference biologics, it's just confusing, can be misinterpreted as it is with some of the back office staff, and may apply meaningful differences between the biosimilar and the reference product. If meaningless suffixes are to continue, they should immediately be applied to reference biologics, as was outline in the final guidance.

Some originator life cycle management approaches, such as product switches, product

reformulations or device changes are used by manufacturers with the intent that patients will remain on the originator medicine when the competition from biosimilars is eminent. FDA should be aware that this is a market barrier tactic to prevent obviously biosimilar competition.

True product innovation should always be encouraged but should not be used as a competition prior to biosimilar market entry. Life cycle product switches should not be used to gain the exclusivity system through multiple staggered or non-coinciding exclusivities. As we know, umbrella exclusivity is ruled out by the language of the BPCIA and was not appropriate in the context of biologic medicines.

As FDA works to draft and finalize biosimilar guidance, this Agency should recognize the tremendous potential for streamlining development approval for biosimilar medicines by increasing flexibility in use of non-U.S. reference products, as well as to refer to previous submission from the global biosimilars industry.

So in conclusion, with at Mylan not only thank

you but on behalf of the many biosimilar stakeholders, we all thank you for the opportunity to participate in this very important public hearing. We look forward to the impact the FDA can have with these immediate actions, which ultimately will serve most importantly, most importantly, to patients here in the U.S.

Thank you.

DR. SHERMAN: Thank you for your comments. Questions from the panel? Mustafa.

DR. UNLU: Can I echo the question asked to the last presenter about umbrella exclusivity? In your written comments if you haven't already done so, we're more interested in why it's not appropriate in your case or why it is appropriate, if you have that view.

MR. KOKINO: Sure.

DR. UNLU: Especially in light of the patent --

MR. KOKINO: Yeah. I'm going to purposely withhold my answer on that question, provide written comment for that.

DR. UNLU: Thank you.

MR. KOKINO: Yeah, but thanks for the

question.

DR. SHERMAN: Other questions? Thank you.

MR. KOKINO: Thank you.

DR. SHERMAN: So we will now start our open public hearing. Speakers, please remember that the time slot is three minutes and Dr. Hoffman is standing at the microphone that you should use. So our first speaker is Ms. Mary Jo Carden from Academy of Managed Care Pharmacy.

MS. CARDEN: Good afternoon. I'm Mary Jo Carden, Vice President of Government and Pharmacy Affairs at the Academy of Managed Care Pharmacy. AMCP is the leading organization representing pharmacists and other healthcare professionals who provide healthcare services and health plans, pharmacy benefit management firms and emerging care models for 270 million Americans covered by a prescription drug benefit.

AMCP appreciates the Food and Drug Administration's initiatives, including the Biosimilars Action Plan to support the implementation of a robust biosimilars pathway to ensure Americans receive access

to safe, effective and affordable biologics and biosimilars. AMCP believes that releasing a revised or new interchangeability guidance is critical to promoting a robust biosimilars pathway.

AMCP also encourages FDA to reconsider its naming conventions to allow for a shared non-proprietary name with biologics and biosimilars and use national drug codes to track use and dispensing.

Like FDA AMCP has also made biosimilars education for healthcare providers a key priority and looks forward to potential opportunities to partner. AMCP encourages FDA to focus educational efforts on providing resources to help healthcare providers and consumers understand that biosimilars are safe and effective alternatives to reference products and to provide resources on interchangeability standards.

Work to ensure biosimilar safety and effectiveness is already taking place through AMCP's biologics and biosimilars collective intelligence consortium or BBCIC. This was establish in 2015 to use real world evidence to address the active post-marketing surveillance evidence for biosimilars and

biologics. BBCIC is not directly associated with FDA, but leverages significant scientific investment by the Agency and in the sentinel initiative. BBCIC will help to generate evidence that is not available from clinical studies with restricted populations and restricted duration.

AMCP and FDA's focus on the need for interchangeability standards and education for healthcare providers is also shown here in a study of 57 health systems published in the December, 2017 Journal of Managed Care and Specialty Pharmacy.

The study identifies the key challenges and the use of adopting a biosimilar for infliximab. Payment and reimbursement are identified as primary reason for challenges associated with the adoption of a biosimilar, but the need for interchangeability and education to shift patient and provider preferences are also critical factors that have been identified.

To this end AMCP offers several suggestions. AMCP welcomes the opportunity to partner with FDA using its biosimilars resource center platform as a way to educate healthcare providers about biosimilars and

interchangeable products.

AMCP also encourages the use of FDA's social network platforms and other channels to provide education about biosimilars, particularly interchangeability standards that do not require physician consultation by a pharmacist prior to dispensing. AMCP also supports the release of a new or revised guidance with reasonable standards for interchangeability to encourage the designation when possible. AMCP supports the ability of applicant seeking interchangeability designation to use switching studies for non-U.S. licensed reference products.

AMCP also urges the FDA to consider the following issues in regard to --

DR. SHERMAN: Ms. Carden, can I ask you to wrap up your comments?

MS. CARDEN: Sure.

DR. SHERMAN: Thank you.

MS. CARDEN: Whether new or expanded indications would be used, naming interchangeability from biosimilar to biosimilar, dispensing standards for interchangeability, and whether follow-on products

approved under the 505 pathway, will be considered interchangeable or biosimilar, when incorporated.

Thank you very much and we will submit comments to the record.

DR. SHERMAN: Terrific. Thank you very much. Our next speaker is Professor Peter Pitts from Center for Medicine and Public Interest.

MR. PITTS: Good afternoon. It's been a real biosimilars bar mitzva today. My name is Peter Pitts and I'm President of the Center for Medicine and the Public Interest.

There are many issues surrounding the introduction of biosimilars into the American healthcare eco system, but biosimilars are here. They are safe and effective. They are less costly and they deserve a seat at the therapeutic table.

How can the FDA drive biosimilar innovation and competition? By being aggressive, creative, predictable and practicable. Aggressive, because we are already behind our European counterparts in both regulatory and marketplace experience. If we do not prioritize both, we will achieve neither, and that is

not an acceptable public policy outcome.

We must learn from Europe's mistakes and create better regulatory standards that instill confidence in patients, providers and payers.

Creative, because we needn't just copy the experience of others. We must learn from their successes and mistakes and then improve on the process. Through more 21st Century pharmacovigilance strategies and tactics, validated real world evidence collection and analysis, helpful labeling information, patient and physician education and more regular and intense collaboration with developers, FDA can, must and will become the global standard for innovative biosimilar regulatory science.

Issues related to the particularities of biologics, sources, process, quality requirements and evolving safety profiles, require sophisticated new thinking.

The Agency must work towards validated predictive models of potential hotspot products, base ingredients and suppliers. Consequently biosimilar pharmacovigilance will have to evolve at the same time

as new medicines are launched into this space.

Predictable, because it's regulatory predictability that drives a developer's desire to invest and compete, and it must be rhetorical prophecy, but practiced policy. Predictability is power in pursuit of the public health and nowhere is that more acutely felt than the evolving regulation of biosimilars.

Without regulatory predictability investment in a still evolving commercial marketplace will remain quiescent. A predictable FDA process facilitates speedier marketplace competition.

When it comes to healthcare, clarity is better than confusion, especially when it comes to drug safety, the cine qua non of medicine's regulation, and that means clarity in biosimilar nomenclature.

Practicable, because that's where the rubber meets the road. We don't need more biosimilar theory. We need more biosimilars. Biosimilars need earlier, regular and swifter access to good advice. The Agency must be both regulator and partner in advancing the development and review of biosimilars. Minus that,

nothing happens. This is not an academic exercise.

As Scott Gottlieb surmises, there is no silver bullet here that will make the biosimilar market go gangbusters. It's going to be a slow build, but build we must.

If the process is the product, we're interchangeability. We're label extrapolation. We're reference products in a world with multiple biosimilars in the same class. These are key regulatory issues that will directly and powerfully impact marketplace behavior in investment and contracting formulary development physician confidence, patient access and cost. And they must be addressed by FDA aggressively, creatively, predictably and in a practical manner now.

When it comes to biosimilars, the USA isn't behind Europe. We're learning from their mistakes and doing it better. It's not about lowering standards. It's about creating better standards. The stakes are too high, both in policy and patient outcomes, to cut corners or cave in to outside pressure. Steve Jobs said innovation distinguishes between a leader and a follower. FDA is a leader and must remain so. The

world is watching and patients are waiting.

Thank you.

DR. SHERMAN: Thank you. Our next speaker is Dr. Angus Worthing from the American College of Rheumatology. Oh, I goofed. Sorry. Our next speaker is Ms. Stacey Worthy from the Aimed Alliance. Sorry.

MS. WORTHY: No problem. Thank you. Good afternoon. I'm Stacey Worthy, counsel to Aimed Alliance. We're a nonprofit that works to improve access to quality healthcare. Thank you for this opportunity.

We commend the FDA on its efforts to preserve safety while also speeding up the approval process for new biologic products. The Agency should be proud of its work in creating competition in the drug marketplace and helping patients to access effective and affordable treatments. To ensure confidence amongst stakeholders we encourage the FDA to preserve safety over speed.

Although there is urgency to bring about cost savings, we must prioritize scientific rigor, given the complexity of large molecule drugs. In particular the

FDA should not lower the standards for interchangeability. The U.S. is the only country with a formal interchangeability designation, making us a leader among other nations. In that role safety must be top priority.

Additionally, as others have already said, the FDA should consider how cross interchangeability may impact patients. In the near future patients could be switched from an initial reference product to an interchangeable biosimilars and again to a second interchangeable biosimilars. While the two biosimilar products may be deemed interchangeable with the reference product, they may not be interchangeable with each other. These switches could result in an immune response.

We need data or at minimum educational awareness about the implications of these cross switching between biosimilars that are not interchangeable with each other to ensure that there is no harm.

Building on the FDA's biosimilar education and outreach campaign, the FDA should also take steps to

improve awareness of interchangeability designation by creating educational materials for various audiences, including insurers, health systems, pharmacies and practitioners. The Agency should provide practitioners with data on the safety of switching a patient from a biologic to biosimilar so they can make educated decisions.

However, it is important to discourage insurers and health systems from forcing practitioners to switch stable patients from one product to another for non-medical reasons.

Additionally, some health systems, pharmacy and therapeutic committees or P&T committees have been deeming products interchangeable for the purposes of setting up their formularies. Given that only the FDA has the authority to make a formal interchangeability designation, this -- it can be confusing and misleading for a P&T committee to use the same verbiage.

Moreover, as a result of some pharmacies have stocking reference biologics, and health systems are mandating that practitioners witch their stable patients from their current medications to different

products regardless of whether their practitioner deems such a switch medically appropriate. This type of non-medical switching should be discouraged.

Finally, as an evolution in the marketplace will require -- an evolution in the marketplace requires reform among payers. Insurers are currently restricting access to life saving biologics and biosimilars alike. We were encouraged to hear Commissioner Gottlieb's recent comments, in which he noted that rebates should be applied directly to lower out-of-pocket costs for patients who need biologics and biosimilars, rather than allowing pharmacy benefit managers and insurers to pocket rebates, as additional profits or spreading the benefits of rebates across all plan members. As he noted, high co-pays are not going to discourage overutilization among individuals with cancer, who have limited treatment options.

Therefore, rebate reform can have a meaningful impact on the increased use of both biologics and biosimilar medications.

Thank you, and we'll submit comments.

DR. SHERMAN: Thank you for your comments.

And our next speaker is Dr. Angus Worthing from the American College of Rheumatology.

DR. WORTHING: Thank you. We're going from Worthy to Worthing. Appreciate that. I'm Angus Worthing. I'm a practicing rheumatologist in the D.C. Metro Area and very grateful to represent the 9,500 rheumatologists and rheumatology professionals of the American College of Rheumatology as their volunteer Chair of Government Affairs.

ACR strongly believes that safe and effective treatment should be available to our patients at the lowest possible cost, and in the absence of other large scale levers to control U.S. biologic drug prices, FDA approvals of biosimilars may be the only tool to keep costs within reason.

Unfortunately many of our patients struggle to afford these complex therapies, due to their high costs and the coverage restrictions, like step therapy, cost sharing and tiering that result from their high prices.

I'm going to focus briefly on the interchangeability pathway and refer you to our statement in the record about clarifications to the

prescriber information, PBM transparency, importance of careful extrapolation and pharmacovigilance and non-medical switching.

About interchangeability, we strongly support the FDA's proposal to require manufacturers to use robust switching studies to determine whether alternating between the biosimilar and its reference product impacts the safety and efficacy of the drug. Exposing patients in the experimental arm to each drug twice, a protocol that requires three switches at a minimum, is a reasonable attempt to simulate what our patients are likely to experience with the changing formularies in a multi-payer, multi-state, ever changing market.

The requirement for multiple switch studies to demonstrate the safety of interchangeability is particularly vital in light of the fact that providers will often not know that their patient's prescription has been switched or substituted.

The ACR was very pleased to see the FDA issue draft guidance on biosimilar interchangeability. The guidance brings us one step closer to the shared goal

of lowering prices in the biologics marketplace. We believe that the draft guidance strikes a good balance between insuring safety and efficacy, while also getting biosimilar products to market as efficiently as possible, while also providing prescribers with the confidence about robust data from three switched studies. And we, therefore, encourage the FDA to finalize the guidance with all due haste.

Thank you again for the opportunity to share the views of the American College of Rheumatology.

DR. SHERMAN: Thank you for your comments. You get a prize. Two-and-a-half minutes. Our next speaker is Mr. Thair Phillips from RetireSafe.

MR. PHILLIPS: Good afternoon. My name is Thair Phillips. I'm the President and CEO of RetireSafe, a nationwide, nonprofit advocacy organization for older Americans. I'm here today representing over 100,000 supporters and activists, many of which are patients receiving these new life-extending and life-enhancing medicines being discussed today.

Today we have listened to a wide range of

approaches to not only the question of facilitating price competition and innovation, but also on virtually all approaches to the use of biologics, biosimilars and interchangeables. While there are forces that pull in many different directions, I find comfort in the knowledge that the FDA's longstanding goal for medical care is to ensure that the right drug or device is delivered to the right patient at the right time. RetireSafe's hope is that we will see some day soon a marketplace where doctors and patients will have an unencumbered access to the right reference biologic, biosimilar and interchangeable, unencumbered meaning that the doctors have the information they need to make an informed decision on which of these medicines is right for their patient, that the cost isn't a barrier, and most importantly that they feel the medicines are safe.

There is work to be done in all of these areas. The mere fact that we heard the term "interchangeables" to describe different aspects of today's marketplace underscores the wild west nature of our current environment. Some biosimilars are being

treated like they are interchangeable, before there is even a final definition of what an interchangeable biosimilar is.

Through placement negotiations, formulary manipulation and step therapy requirements insurance companies and PBM's are deciding today which drugs are interchangeable. This type of environment does not build confidence and biosimilars will not be successful if doctors are subjected to this type of manipulation.

Doctors can't feel safe about switching from one biosimilar to another, when there's no information or testing on this type of switch. Doctors can't feel safe when a change in the formulary necessitates a switch away from an effective medicine. We can't expect perspective biosimilar manufacturers to be eager to develop biosimilars and interchangeables when lawsuits and regulations allow reference product manufacturers to withhold needed information.

Drug prices and all of this talk about price competition means nothing if the patient doesn't see a reduction in their out-of-pocket costs.

Here are RetireSafe's recommendations. To

make doctors feel safe in prescribing these medicines we need detailed informative labels and requirements to test a biosimilar-to-biosimilar switch. We need a final workable, effective and safe definition of interchangeable medicines.

And finally, the sick can't continue to foot the bill. There continues to be cost barriers for the use of reference biologics and biosimilars. We need to lower the patients' out-of-pocket costs, even if it means an increase in premiums. There are barriers to getting the right drug to the right patient at the right time. It should always be the doctor and the patient who defines what is right.

RetireSafe will continue to work toward the goal of reducing the barriers in accessing the right drug.

Thank you.

DR. SHERMAN: Thank you for your comments. Our next speaker is Dr. Dennis Cryer from Biologics Prescribers Collaborative.

DR. CRYER: Good afternoon. My name is Dennis Cryer. I'm the lead physician co-convener of the

Biologics Prescribers Collaborative. We're BPC.

My training is in genetics and metabolic diseases. Our seven member organizations represent physicians who regularly prescribe biologics and include the Alliance for Patient Access, the Coalition for State Rheumatology Organizations, the American Association of Clinical Endocrinologists, the American College of Rheumatology, American Gastroenterological Association, the Society of American College of Allergy Asthma and Immunology.

I personally serve on the boards of several nonprofit organizations whose missions are complimentary to the FDA and sadly I have no conflicts of interest.

BPC is enthusiastic about the Biosimilars Action Plan, the BAP, and we reiterate our support of scientifically based patient centered standards. We believe the FDA to be the paradigm of the regulatory bodies around the world and advocate maintaining the highest standards of safety and efficacy, while encouraging innovation and competition.

Among the elements of the BAP, education and

communication are critical. While improving efficiency of the biosimilar and interchangeable pathways is a critical goal of BAP, it is important to provide more information rather than less. Prescribers and to patients, to support clear understanding of these rigorous processes.

And we do believe that many patients these days are becoming sophisticated enough to appreciate some of these details, believe it or not.

The FDA guidances provide clarity around regulatory pathways and we join with others in encouraging the FDA to finalize its interchangeable guidance with all reasonable haste. Supportive data must be rigorous and risk based, and we strongly recommend clinical studies which include a minimum of three switches between the reference product and proposed interchangeable.

And lastly, BPC will continue to advocate for a finalized interchangeability guidance, distinguishable, nonproprietary, names for all biologics, physician and patient involvement in all switching decisions, including non-medical switching,

clear and thorough labeling, case-by-case determination of extrapolation, and to a sister agency, unique J-codes for each biosimilar product.

On behalf of the Alliance of the Biologics Prescribers Collaborative, a project of the Alliance for Patient Access, I thank you.

DR. SHERMAN: Thank you for your comments and you made it right under the wire. Our next speaker is Dr. David Charles, Alliance for Patient Access. Dr. Charles, do you mind, we'll call up another speaker while finding your presentation? And the next speaker before Dr. Charles will be Dr. Fred Atuf (phonetic) from USP.

DR. ATUF: Good afternoon. My name is Fred Atuf. I'm Vice President of Global Biologics at the United States Pharmaceutical. On behalf of USP I would like to thank the Agency for the opportunity to comment on the competition and innovation in the biologic product marketplace, including facilitating availability of biosimilars and interchangeable product.

USP is a scientific nonprofit organization

dedicated to protect and improving public health. We have a long history of collaborating with FDA and other stakeholders to develop public standards and related programs that support quality of medicines, including biologics and drug ingredient.

Public standards have an important role in helping ensure medicine's quality, including enabling development and market entry. USP has a longstanding program in biologic standards development. For example, we have developed and maintained standards for insulin product and have contributed to development of international standard for this widely-used rug.

This type of standard gives diabetes patient confidence that the insulin they take is of reliable and consistent quality. USP's portfolio consists of several hundred of documentary and physical reference standard that helps biosimilar manufacturers in the development and manufacturing of biologics, including biosimilars.

Based on the engagement and input from stakeholders, including the FDA, we have focused in the past several years on the development of performance

standards. These type of standards are broadly applicable to product families and product classes and are intended to address common quality challenges associated with technologies and methodologies.

In the last year we conducted roundtables with organizations like the Biotechnology Innovation Organization but also the International Federation of Pharmaceutical Manufacturers and Associations, and their membership with a goal to prioritize those performance standard that most typically address challenges that companies face throughout the product development cycle.

We believe that the cycle support key areas identified in the FDA's Biosimilar Action Plan. It will also help maximize the scientific clarity for the product development community, and it will play a role in the development and availability of quality biosimilars.

In conclusion, public standards support the priorities of all stakeholders, including drug developers, drug manufacturers and regulators by identifying quality attribute, creating predictability

and facilitating product innovation.

USP is committed to actively gathering early input from healthcare practitioners, industry and regulators before and during development of standards for biologics. As the marketplace of biologic product continues to expand and evolve, USP stands freely to work closely with FDA and other stakeholder to increase the development and manufacture of these critical drugs.

Thank you again for the opportunity.

DR. SHERMAN: Thank you very much for your comments. Are we good to go? So now Dr. David Charles from Alliance for Patient Access.

DR. CHARLES: Thank you for the opportunity to join you today. My name is David Charles. I'm a neurologist. I serve as Chief Medical Officer at Vanderbilt's Clinical Neuroscience Institute in Nashville, Tennessee. I conduct clinical trials and see patients with movement disorders and related conditions.

I also serve as Chairman of the Alliance for Patient Access. The Alliance for Patient Access is an

organization of over 800 healthcare providers advocating for patient access to approved therapies in clinical care, and today I'm speaking on behalf of the Alliance for Patient Access.

The Alliance for Patient Access consists of several physician working groups, which span a number of disease states and areas. One of those working groups is the National Physicians Biologics Working Group, which brings together physicians in neurology, rheumatology, oncology, dermatology and so forth, to address policy issues relevant to biologics and biosimilars.

The group consistent produces educational materials about relevant policy issues, advocates to state and federal officials, and is instrumental in organizing the Annual National Policy and Advocacy Summit on Biologics and Biosimilars each year in Washington. We've had the pleasure of Dr. Christl and Dr. Kozlowski participating in those meetings in the past. We thank you.

Many of the speakers today have described the all-inspiring power and complexity of biologics and

biosimilars and at annual meetings of AFPA's Physicians Biologics Working Group, I hear similar stories. In fact, when I was training several years ago as a young neurologist, I saw patients with debilitating diseases like multiple sclerosis, struck in the prime of life causing incredible disability and what do we have to offer them for treatment? It was steroids and physical therapy.

And today for people with MS we have a completely different story. Biologics have far surpassed the treatments we had before and now biosimilars can provide still more treatment options and more choices for patients and physicians. But for that to happen, we need biosimilar uptake and to achieve uptake we need physicians to have the fullest confidence in biosimilars.

First, physicians want rigorous testing on biosimilars, particularly interchangeable biosimilars. Allowing pharmacists to swap an interchangeable biosimilar with its reference product without the prescribing physician's involvement suggests utter confidence in the therapy's similarities. Therefore,

it demands thorough evidence.

In particular, clinical trials should explore not only the clinical indication, but explore switching, not just a single switch, but multiple switches, so that data will actually predict real world use.

Second, physicians want to see the data for themselves. They want transparency, complete and readily available information.

Physicians are scientists and educators by training, and many continue a scientist conducting clinical trials like I do. As such, we find confidence in data. Plain and simple, physicians want proof.

We'd like to see the data on how multiple switches affects patients' response to treatment, the toll it takes on their immune system and the impact it has on the therapy's efficacy.

Physicians welcome more therapeutic options for our patient and we'll be on the front lines ensuring uptake. FDA's approach to date has been rightfully careful, building on a base of knowledge that can be utilized going forward, and we respectfully

request that the FDA should continue seeking and sharing the data that shows not just safety and efficacy but also focusing on how these medicines will be used in practice. This approach will ensure confidence in these therapies, leading to more competition and more treatment options for our patients.

Thank you.

DR. SHERMAN: Thank you for your comments. Our next speaker is Mr. James Love from Knowledge Ecology International.

MR. LOVE: Thank you very much. I represent a group in Washington, D.C. that does advocacy work on drug prices, intellectual property and innovation policies.

We recently were asked by someone -- we met with some people on the Hill about biologics competition, and we just thought it was well known that there wasn't as much competition for biologic drugs as there is for small molecules, but the staffer was I guess new and she insisted we show her some evidence of that, so we had to crank out some evidence.

So one thing we looked at was from 2005 -- from 1995 to 2005, we look at all the novel drugs that were approved, and we tried to figure out how many of them by the end of last year, of 2017, face competition. For at least the same API.

For biologics, of course, therapeutic equivalence was basically zero for that group, but at least for the API's, about 17 percent of the biologic drugs face competition for similar API, but the number for the small molecules was like 61 percent.

And then we looked at how long did it take before you observed competition, and it was roughly six years longer on average for the biologics and the small molecules. And then we looked at the number of companies that were competing, and it was something like average of one-and-a-half for the biologics that faced any competition for the same API, and it was close to nine for the small molecules.

So in every dimension, every way you could describe it, the biologics market is less competitive than small molecules market, and the whole incentive system of granting a temporary monopoly to help recover

your R&D cost, works very differently for small molecules than it does for biologic drugs, even though there's no -- there's no real evidence of the cost of research and development, are much different between the small molecule products an the biologic drugs. In some cases the risk, for example, Phase III trials is more favorable for novel products for biologics than it is for small molecules.

I'll just -- the next thing we ask is what would it take to make the biologics market more like the small molecule in terms of competition, and we have a scientist to work with us and she's not here today. She's in Canada.

And I'm always kind of afraid I'm going to mispronounce some of the things that she told me to say, but in essence the question we had is if you didn't have to worry about patents or test exclusivity, what could you do? What could regulators do to make biologics not only more competitive but to make patients -- my wife is right now alive because she's on Concello, which is a Roche biologic drug and she'd be dead without it. And if I was to ask to switch her

from this drug to a biosimilar drug, she's been on chemotherapy since 2010, I would be, like most patients, maybe a little worried about that, because you don't really know and people are always trying to scare you about that stuff. So things that actually make you more confidence -- more confident rather than the biosimilar work the same as the originator's drug, those would be a positive for the patient.

And so she recommended that as a condition of being regulated at some point the company that sells the biologic be required to provide access to certain materials like cellular clones and highbroma (phonetic) stocks. Maybe somebody knows what those things are. Plasmid maps, sequences of antibiotic complementary and determining regions, and physical, chemo, biophysical characterizations, as well as also methods of growth conditions and protocols, attenuation or inactivation protocols.

DR. SHERMAN: Excuse me. Could you wrap up your comments?

DR. CHARLES: I am wrapping up. Thank you for reminding me of the time.

But I'd be happy to sort of follow this up in my written testimony. Thank you very much.

DR. SHERMAN: Thank you. Our next speaker is Mr. (indiscernible). I wasn't even close, was I?

Mr. Let me correct the name. My name is Sang Ju Lee from Sartrian (phonetic). Good afternoon. My name is San Ju Lee. I'm with the SPB with Sartrian. Thank you for this opportunity.

Initially biosimilar products developed as an alternative treatment for the original product. What's the next? As a developer of biosimilar products, I'd like to talk about innovation of biosimilar.

Biosimilar innovation includes two things maybe. One, adding a new indication which doesn't exist in the original product. Second, adding or introducing a new drug delivery system of the product. Specifically, our company is developing subcutaneous version of Remicade biosimilar. Now I encourage the FDA to be more open and flexible in biosimilar innovation.

In consideration of marketing approval for a change of treatment option, it is desirable to have

more flexible requirements, so that patients benefit from compensation treatment options.

Thank you.

DR. SHERMAN: Thank you for your comments. Our last speaker is Sondron Lee.

MR. LEE: it was me. Thank you. There was an error.

DR. SHERMAN: Oh, okay. So that concludes our meeting. Are there any additional questions from the panel for anyone?

On behalf of the panel I'd like to thank all the presenters and everyone in the audience, whether you attended in person and, therefore, braved post-Labor Day traffic, or if you webcast for participating in today's public hearing, which was very interesting and very productive.

We appreciate your attention, your interest and the time and effort you spent on your presentations.

As a reminder, and this is a theme you heard over and over today from the panel, we look forward to receiving your comments in the docket with as much

specificity and as much detail as possible. We did in the FR call up some very specific topics, but we are interested in anything -- any comments you have, any thoughts you have that relate to our biosimilars program, and it can be a topic that's the subject of another docket that's already open or perhaps a future docket, and we will make sure those connections are made.

If we can put up the slide with the -- how the people on the webcast can send the information for submitting to the docket is in the FR notice, and will soon be perhaps on the screen. The docket will be open through September 21st of this year.

A transcript from this hearing should be posted to the hearing website within 30 days, and the presentations from today's -- copies of the presentations from today's presentation will be available upon request. The information is also at the table -- and there's everything you need to know.

Once again, thank you for your time, for your attention, and on that note, I close today's meeting. Oh, one last thing. I'd also like to thank the FDA-ers

who made today happen, Alicen Hoffman, Theresa Wells and Tony. Thanks. Have a good evening and a safe trip home.

(Off the record at 3:43 p.m.)

CERTIFICATE OF NOTARY PUBLIC

I, Michael Farkas, 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.

Michael Farkas

Notary Public in and for the

State of Maryland

CERTIFICATE OF TRANSCRIBER

I, Sandra K. McCurdy, do hereby certify that this transcript was prepared from audio to the best of my ability.

I am neither counsel for, related to, nor employed by any of the parties to this action, nor financially or otherwise interested in the outcome of this action.

September 13, 2018 Sandra K. McCurdy

DATE Sandra K. McCurdy

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