FDA/FTC WORKSHOP ON A COMPETITIVE MARKETPLACE FOR BIOSIMILARS

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FOOD AND DRUG ADMINISTRATION

FDA/FTC WORKSHOP ON A COMPETITIVE MARKETPLACE FOR BIOSIMILARS

Monday, March 9, 2020

9:05 a.m. to 4:18 p.m.

FDA White Oak Campus

White Oak Conference Center

10903 New Hampshire Avenue

Silver Spring, Maryland

C O N T E N T S

C O N T E N T S (continued)

C O N T E N T S (continued)

C O N T E N T S (continued)

P R O C E E D I N G S

(9:02 a.m.)

Welcome - Eva Temkin

MS. TEMKIN: Good morning. I'm told that we're already two minutes behind, so I'm going to jump in and get started.

Welcome to the FDA/FTC Workshop on Competitive Marketplace for Biosimilars. I'm Eva Temkin. I'm the acting director for policy in CDER's Office of Therapeutic Biologics and Biosimilars, and I am thrilled to be here to kick off what I'm sure will be an exciting and informative day.

The purpose of our workshop today is to discuss FDA and FTC's collaborative efforts to support appropriate adoption of biosimilars, discouraging false and misleading communications about biosimilars, and deterring anticompetitive behaviors in the biologic product marketplace.

From my perspective, to improve patient access to life-saving therapies, we need to look at some key factors that we're going to touch on

during our time today.

First, there has to be availability of biosimilars, that is developers make choices to develop and seek approval of biosimilars; second, there has to be awareness of biosimilar products and their promise for patients and from healthcare provider communities; and third, we need adoption. License holders need to bring biosimilars to market and people need to use them.

Navigating these three steps successfully requires a competitive marketplace and fair business practices. Done right, it can ultimately result in access for more patients to important biologic therapies.

Before we begin, I also want to make a few administrative announcements. First, please silence any cell phones or other mobile devices, as they may interfere with the audio in the room today.

Second, we ask that all attendees sign in at the registration tables outside the meeting room. We are a sold-out event, so if you did not

preregister to attend but are in this room, you might want to head to Room 1504. That's our overflow room today. We will be streaming live audio and video to this room.

Third, this Workshop is bringing together several speakers from FDA, FTC, and stakeholders who may use different terminology and bring different perspectives. Please note that views, thoughts, and opinions expressed throughout the day by any individual are not attributable to any other participant.

This is the most glamorous part of my day. The restrooms are located in the lobby past the coffee area to the right and down the hallway. And finally, copies of today's presentations are available upon request.

Contact information is also available at the registration table out in the hall. For media inquiries, our press officer today is Jim McKinney. If any members of the media are here today, please sign in, and if you have questions or are interested in speaking about this workshop, please

contact Jim.

There are no rules of evidence for this workshop today, but there are some general procedural rules that I will read very quickly in the hopes of moving things along. Attendees should not interrupt the presentations at any of the planned panels, which will not be taking questions from the audience. There will be an open public comment period at the end of the day once the panel presentations have concluded.

This workshop is 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 today's proceedings.

This workshop will also be transcribed, and copies of the transcript can be ordered through the docket or accessed on FDA's website approximately 30 days after the workshop. And on that note, I would ask that all of the speakers and panel participants make sure to speak into a microphone

because the transcriptionist needs us to do that so that the transcription can be accurate.

For the open public comment period of our day today, we have approximately 17 speakers registered to speak, and each one of them will be allotted 4 minutes to present.

At this point in time, I believe all of the oral presentation time has been allotted to preregistered speakers. If that changes, though, a preregistered speaker doesn't attend or something opens up, there may be an opportunity for additional oral presentations at the end of the workshop. Please sign up at the registration table outside the meeting room if you're interested in doing that by 10 o'clock.

We also encourage you to submit to the docket. You can see the Federal Register notice for details on how to submit comments to the docket. And I would say from my perspective, we always review written comments. They're very very helpful, so I really encourage folks to do that. Please submit written comments by April 9, 2020.

This workshop is being webcast live, however, the webcast is not interactive, so viewers cannot comment or ask questions.

With that, it is my great pleasure to introduce FDA Commissioner Hahn. Dr. Hahn came to FDA in December of last year after serving as the chief medical executive at the University of Texas MD Anderson Cancer Center.

In just a few short months after coming to FDA, Dr. Hahn has helped bring the FDA and FTC joint statement to life, reinforcing the agency's commitments to taking key steps to reduce gaming of current FDA requirements and coordinating with the Federal Trade Commission to address anticompetitive behavior. Dr. Hahn and Tara Koslov, FTC's chief of staff, will be providing opening remarks for today's workshop. Thank you.

(Applause.)

Opening Remarks - Stephen Hahn

DR. HAHN: Good morning, and thank you, Eva, for that kind introduction. I'm really pleased to see so many of you all joining us today, both

virtually and in person. This is a really important topic, and I'm especially delighted to welcome to White Oak -- it's far away from downtown D.C., so I appreciate your being here -- Tara Koslov, who's the chief of staff of our partner agency, the Federal Trade Commission.

I just want to stop and take a moment here. This is an incredibly important topic. We'll spend a lot of time today talking about it. But I do want to spend a moment to acknowledge those who've lost their lives to the coronavirus outbreak. We very much care about what happens around the world to folks who have been exposed to this and just want to take a moment to acknowledge that.

The other thing I'd like to do is to acknowledge the many people at FDA, CDC, HHS, and around the U.S. government who have worked tirelessly, and I can assure you of that, 24/7, to address this outbreak. They are true American heroes in trying to help us address this across the country and the world.

The focus of today's meeting is an important

one, to discuss the FDA's and FTC's collaborative efforts concerning the biologics marketplace in biosimilars. For those of us who believe in the marketplace, it's really important that the free market work well, and that includes making sure, as my predecessor Dr. Gottlieb had said before, that there are no shenanigans. It's a really important concept, and work together trying to address that issue.

We believe that getting more biosimilars, and hopefully interchangeables, on the market will offer great potential and have a positive effect on the American public, both from an availability point of view but also from a cost point of view.

Last month, as you know, we signed a joint statement on our collaboration, which outlined our shared goals and objectives and discussed how our agencies will work together to support competitive markets for biological products. This truly is an example of the U.S. government in a transagency fashion working together. It also described key steps we intend to take to address false or

misleading communication by biological product manufacturers. This is not meant to be an us versus them situation, but just so that everyone is on the same level working field and moving forward to provide as much transparent information as possible to developers and the American public.

We've also released a draft guidance for industry called Promotional Labeling and Advertising Considerations for Prescription Biological Reference and Biosimilar Products: Questions and Answers. That's a mouthful but really important information contained in that draft guidance. We're expecting to get comments on that, and we'll work with our partners around that, and today we're holding this workshop, the next important step in our collaboration.

What the partnership of our two agencies means is that our combined extensive resources and efforts in this area can have a dual focus on both the scientific and the legal fronts. This means we will do everything possible to support a robust market place for biological products, including the

adoption of both biosimilar and interchangeable products.

On the scientific end, and we are very much a scientific organization at FDA, we are working to support innovation and advance the scientific development of these groundbreaking products. We're also engaged in very close participation, our partnership with FTC, in activities designed to help ensure that healthcare professionals and patients receive truthful and non-misleading information about biological products and to deter anticompetitive behaviors in the marketplace related to them.

I came to this job as a provider of cancer care. I can't tell you how important it is that we communicate with patients and providers about this and give them the most accurate information. That will go a long way to ensuring that these products are available to the American public and providers. What these activities have in common is the goal of helping to reduce costs and enhance patient access to these important and potentially life-saving

products.

The development of biologics offers us one of the best examples we have today of the potential offered by unprecedented advances in medical science. What we're seeing across the world, and particularly in the United States, is unprecedented, and we are very much interested in bringing science innovation to the patient bedside for providers and patients alike.

These products, which may be produced through biotechnology in a living system, are used to diagnose, prevent, treat, and cure diseases and medical conditions. We've seen enormous progress in this field in a relatively short period of time. We're all working to catch up with that amazing acceleration of innovation, and these products are increasingly playing a central role in the treatment of the many serious and life-threatening diseases. In fact, in some situations, these are the only products available to treat patients with life-threatening situations.

So there's an urgent unmet medical need for

us to do as much as we can in this sphere, and that will likely continue to grow, and we certainly hope it does grow. Last year, we approved 10 biosimilars. That makes a total since 2015 of 26 for 9 different related reference products; and in the early months of 2020, we have continued to see strong momentum. Congress recognized this promise 10 years ago, and to support it, passed the Biologics Competition and Innovation Act.

Just as a brief moment here, we know from the generic space, the prescription side, the drug side, that the more generics we have available -- and I'm making a relationship between generics and biosimilars, and I realize the translation isn't a hundred percent correct. But we know when we introduce generics on the drug side that we significantly reduce costs, so let me give you a few facts about this.

If one generic is introduced to a reference product, on average, that reduces the price of that product by about 35-36 percent. If we introduce up to 6 generics in a product space, that can reduce

the price of those products by as much as 95 percent. We're hoping to get the same sort of scale and approach in the biosimilar and certainly in the interchangeable space. The more we can do in this area, the better it's going to be for competition and choice for the American people.

We think, and our estimates are, that over the last decade, competition in the generic space has saved Americans in the healthcare system more than a trillion dollars, and we need to get working to have this occur in the biosimilar space and interchangeable space as well.

Biologics account for a disproportionate amount of the overall spending of prescription drugs. They're 2 percent of the total of prescription drugs but account for, by our estimates, 40 percent of the cost of prescription drugs.

Where we are right now is where we were before in the prescription drug side of the house and, again, the more we do work on the biosimilar interchangeable side, the better it's going to be

for the American public, again, with choice and competition. We've taken Congress' goal to heart and are doing everything, particularly with our great partners at FTC, to increase accessibility and help Americans realize the promise of biosimilars.

We're already making some significant strides, but we have more work to do, and we realize that, and we're always looking for ways to improve. We've improved the efficiency of the biosimilar and interchangeable product development approval process.

Across the agency we're looking at this. How do we make it more efficient? How do we make it easier for developers to provide the information to us? How do we on our end make it easier for our reviewers so that the number of review cycles goes down and the process and the timeline for approval goes down as well?

We are maintaining our gold standard of safety and efficacy, but we definitely want to maximize efficiency and want to provide as much

regulatory clarity for developers as possible. We're also doing our best to try to strengthen effective communications with the American public, providers, and with innovators.

The last point has special relevance for our partnership with FTC, and I want to focus on that for a moment. We know that a free market, as I mentioned before, and enhanced competition supports increased innovation, so it has the virtuous effect of not only helping in terms of decreasing prices as we've seen on the generic side, but also stimulating further innovation. But for it to be a free market and a fair market, it has to absolutely be free.

Unfortunately, since the earliest stages of the development of the biologics market, there have been obstacles to increase competition. That's not okay. We've seen efforts by manufacturers to delay competition for biosimilar products and we've seen the publication of materials that seem designed to create uncertainty about biosimilars and discourage patients and healthcare providers from using them.

These behaviors have the potential to put innovation at risk, erode public confidence in the product, weaken efforts to lower healthcare costs through competition, and ultimately undermine advances in healthcare, as potential treatments and cures are unavailable or go unrealized. At FDA, as at FTC, we are very committed to empowering the American consumer and the American provider, and we must do more in that area.

To counter these activities, we've taken a number of actions from the creation of the biosimilar product development program to a public education campaign that you all know about.

Our collaboration with the FTC is the next step in our efforts to end these types of counter-productive activities; and, Tara, I want to thank you and Commissioner Simons for the terrific work that you've done in partnership with us. It will help and support and ensure an environment in which biosimilars can fulfill their promise and reach the patients who need them because the market is a competitive and fair one.

The FDA, as I mentioned, is a science-based organization and data-driven, and our work is premised on the understanding that decisions must be based on good data and sound science. In this way, we can promote innovation and support the development of new treatments and cures. But this activity must be conducted on a fair playing field that the patients and our public and our providers depend upon.

Our collaboration with FTC, as I've mentioned, is designed to help ensure this, and I very much want to congratulate FTC in all they've done. Today's meeting, as I mentioned, is that next step and, again, really appreciate the partnership with FTC.

So on that note, it's my great pleasure to introduce the chief of staff of FTC, Tara Koslov. Ms. Koslov has served as Chairman Simon's chief of staff since he was sworn in as chairman of FTC on May 1, 2018. She has worked on healthcare competition matters throughout her 23-year career at FTC. That's really impressive staying power.

Thank you for your service to the American people, including on biologics and biosimilars. Just in our brief conversation, I know you feel so passionate about this subject. Prior to her position as chief of staff, Ms. Koslov was acting director of the Office of Policy Planning. She is a graduate of Harvard Law and Brown University.

Ladies and gentlemen, Tara Koslov. Thank you.

(Applause.)

Opening Remarks - Tara Koslov

MS. KOSLOV: Good morning, everyone. I'm delighted to join Commissioner Hahn in welcoming you all here today, and on behalf of FTC, Chairman Simon, he truly regrets not being able to be here with us today, which is why you get me instead. But as Commissioner Hahn mentioned, I have long worked on these issues, and I am indeed passionate about them. So I'm pleased to be here representing my agency.

Let me begin with a few thank yous. This workshop is part of the decades-long collaboration

between the Federal Trade Commission and the FDA to promote competitive markets for pharmaceuticals. Today, our focus is on biologics markets and what can be done to spark competition for these innovative new treatments.

I would like to thank former FDA Commissioner Scott Gottlieb for initiating this joint agency effort and Commissioner Hahn for continuing it. I would also like to thank the FDA for hosting this workshop and the many FDA and FTC staff who made this workshop happen. An incredible amount of work went into planning and executing this event. As someone who has done plenty of events at the FTC, I know exactly what goes into putting together something like this, and I'm very grateful for everyone's efforts.

Biologics, as we all know, our innovative treatments for serious and life-threatening diseases like cancer, diabetes, and Crohn's disease. Often biologics are the only effective treatments for these diseases, but biologics can be very expensive, some costing tens of thousands and

others costing millions of dollars. Total U.S. spending on biologics is growing rapidly and reached $125.5 billion in 2018.

I'm going to provide the FTC's perspective as a competition and consumer protection enforcement agency. As many in this room already know, the FTC has a broad mission to protect consumers and promote competition by preventing anticompetitive, deceptive, and unfair business practices.

Because of the critical role competition plays in reducing prices and fostering innovation, the FTC has long been interested in promoting competition in pharmaceutical markets.

One way the FTC does this is by conducting industry studies. More than 40 years ago, for example, the FTC published a report on state laws that prevented pharmacists from substituting generics for branded drugs.

The FTC concluded that these laws imposed substantial unwarranted costs on consumers by unduly restricting price competition between

generic and branded drugs. These findings helped pave the way for now familiar state laws that allow automatic substitution of a generic for the brand.

Similarly, a 2002 commission study on generic drug entry recommended the brand name companies and generic applicants, settling patent litigation under the provisions of the Hatch-Waxman Act, should be required to submit those settlements to the FTC.

This recommendation was incorporated into the Medicare Modernization Act of 2003 and is now the primary means by which the FTC learns about potentially anticompetitive patent settlements between brand and generic drug manufacturers. Following the 2018 amendments to the Medicare Modernization Act, the FTC now also obtains and reviews patent settlement agreements involving biologics and biosimilars.

Another way the FTC promotes competition in pharmaceutical markets is by vigorously combating anticompetitive conduct. Notably, the commission has a long record of successful enforcement actions

against brand and generic drug manufacturers seeking to gain the Hatch-Waxman process by entering into anticompetitive reverse payment agreements.

The agency's victories include a landmark decision by the Supreme Court in FTC v. Actavis, holding that such agreements can create antitrust liability. We've also seen favorable interpretations of activists in other federal courts and sweeping settlements that prevent major manufacturers from entering into anticompetitive reverse payment agreements.

Perhaps as a result of these successes, the number of potentially anticompetitive reverse payment agreements has dropped precipitously.

The FTC's experience with pharmaceuticals also extends to the biologics industry. In fact, the FTC brought its first enforcement action involving a biologic almost 30 years ago. More recently, the FTC provided technical assistance as Congress developed the abbreviated pathway for approval of biosimilars.

In 2008 when Congress was weighing options for an abbreviated pathway, the House Committee on Energy and Commerce requested, and the FTC provided, lessons learned from Hatch-Waxman to help structure the new pathway, and in 2009, the FTC testified before Congress about a follow-on biologic drug competition to inform the debate on the legislation that became the abbreviated pathway.

As an aside, the commissioner who provided that testimony at the time was actually the commissioner I was working for at the time as her attorney advisor, which shows you how far back my involvement goes in these issues. So it's kind of nice to come full circle.

Competition between reference biologics and biosimilars is just as important as competition between brand and generic small molecule drugs. Biosimilars, which are as safe and effective as their reference biologics, hold the promise of reducing price, and therefore increasing access to these treatments. This is because when given a

choice between two highly similar products, well-informed consumers typically choose the less expensive option.

This competition in turn drives prices down, but competition only works when consumers have reliable and truthful information. In some instances, statements from reference biologic manufacturers and the groups they fund may mislead patients and physicians into believing the biosimilar is not as safe or as effective as the reference biologic. Such deception might violate both consumer protection laws and antitrust laws.

On the consumer protection front, while the FTC generally supports comparative advertising, that advertising must be truthful and not misleading. Advertising that creates an impression of clinically meaningful differences between a reference biologic and its biosimilar is likely false or misleading, and therefore would constitute an unfair or deceptive practice.

Similarly from an antitrust perspective, maintaining or growing share by deceiving patients

and physicians about competitors offerings is not competition on the merits. It also erects artificial barriers to entry and creates costs for biosimilar manufacturers who have to counter the deception. Such deception, therefore, likely would constitute an unfair method of competition.

The FTC is committed to taking appropriate enforcement action against false or misleading communications involving biologics and biosimilars, but the FTC's enforcement priorities in this industry extend beyond deceptive conduct. The FTC will also seek to deter behavior that impedes access to samples needed to develop generics and biosimilars.

For example, just this past January, the FTC brought its first case alleging a restrictive distribution scheme that anticompetitively blocked competition for a small molecule drug. The FTC will also continue to review patent settlement agreements involving biologics and biosimilars for, among other things, anticompetitive reverse payment agreements.

In closing, I want to reiterate the importance of the more than 65-year history of collaboration between the FTC and the FDA. I believe this collaboration has benefited American consumers in untold ways, but most concretely by making safe and effective treatments more widely available and at a lower price.

On behalf of Chairman Simon and the FTC, I thank the FDA for its critical support of the FTC's investigations and industry studies, and we look forward to continuing this legacy of collaboration. Thank you all for your time this morning. I'm sure you will all have a very productive and engaging day. Thanks.

(Applause.)

MS. ANDRUS: Good morning. My name is Meredyth Andrus. I'm an attorney in the healthcare division of the Bureau of Competition at the Federal Trade Commission. This first panel we put together are some experts in the field to discuss the development and licensure of biologics and biosimilars and the post-approval uptake process.

I'm going to let all of the panelists introduce themselves. The way we will conduct this panel is there will be two brief presentations by Christine and by Eva, and then we will go through a series of questions and answers that we have prepared. So without further ado, let's jump in and let's do some introductions first.

Surya?

DR. SINGH: Hi. Thank you for having me. I'm Surya Singh. I'm an independent consultant, an internist by training, and former chief medical officer of the Specialty Pharmacy at CVS/Aetna. I've been interested in these issues for a long time, so thanks again.

MS. BURICH: Hi. Molly Burich, director of public policy at Boehringer Ingelheim.

MS. SIMMON: Hi. Christine Simmon, executive director of the Biosimilars Council, which is a division of the Association of Accessible Medicines, which represents generics and biosimilar manufacturers.

MS. TEMKIN: Hi. Again, Eva Temkin. I am

the policy director for the Office of Therapeutic Biologics and Biosimilars.

MS. ANDRUS: Why don't we start with Eva, who will kick it off for us with a short presentation.

Presentation - Eva Temkin

MS. TEMKIN: Sure, with the goal of making all of you sick of me before 10 a.m.

I have a short presentation that I'm going to walk through. I started with this slide because I thought it was an interesting perspective. We often hear, as we just did, parallels drawn between the promise of biosimilars and that of generic drugs, and many of the challenges, I think, may be parallel to including allegations of anticompetitive behavior and what to do about them, which is why we're all here today.

To kick it off, though, I want to talk a little bit about terminology and regulatory framework just so that we can all be in the same place. What this slide lays out is essentially we have two pathways for bringing biological products

to market,, 351(a) of the Public Health Service Act, which is for stand-alone or reference biologics, which are approved based on a demonstration that the proposed product is safe, pure, and potent, also known as safe and effective in some camps. Then we have the 351(k) pathway, which is the abbreviated pathway to licensure for biosimilar and interchangeable products.

Now, these pathways, again, parallel what happens in the small molecule world, but they're different by design. Heterogeneity across all biological products is expected. That's why we have the standard that we have for biosimilarity.

What is that standard? Well, I've put up the definition, and I know there are a lot of words on this slide, but I really want to focus on and highlight actually what's at the bottom.

When we're talking about biosimilars, we're talking about products that have been demonstrated to be highly similar to the reference products and to have no clinically meaningful differences from those reference products. This is not a

re-establishment of safety and effectiveness; it's a demonstration of the relationship between the proposed product and the reference product.

Once approved, we have a biosimilar product, and the labeling will include relevant data and information from the reference product labeling; although notably, biosimilar product labeling may differ from reference product labeling for a variety of reasons, and we can talk about that a little bit more if it is useful for the discussion.

As an example, I think it's helpful to note that a biosimilar applicant can seek licensure for fewer than all of the indications for which a reference product is approved, so that's an example of where the labeling may differ.

The approved biosimilar is expected to be safe and effective just like the reference product in patients who are treatment experienced, that is in treatment with a reference product, or treatment naive, that is they haven't yet been treated with any product or with the reference product at all.

What does this demonstration mean? I wanted

to touch briefly on the data requirements. For demonstrating biosimilarity, we have a fair bit of guidance out in the world on this, and I'm happy to talk about it at great length, but I will endeavor to do so in one slide and one minute, essentially.

Essentially, we have a stepwise approach to generating data to support a demonstration of both similarity, and what the picture does is attempt to demonstrate that the analytical similarity data, the comparative analytical data that we're looking at in a biosimilar application, is really the foundation of the analysis and the demonstration of biosimilarity.

At each step, we take stock and we evaluate what residual uncertainty might be remaining, and we move on to the next step of data generation. So ultimately, the nature and scope of clinical studies will depend on the extent of residual uncertainty that remains after analytical assessment and to the extent, relevant animal studies.

Generally, we consider all of these pieces

of data together in the totality of evidence approach to evaluating the biosimilarity, but we generate the data typically stepwise in this way.

Then we have interchangeability. 351(k) has both biosimilarity and interchangeability in it. An interchangeable product is defined actually in Section 351(i) of the Public Health Service Act as a product that can be substituted for the reference product without the intervention of the healthcare provider, and I think we'll talk a lot, both in this panel and over the course of the day, about what that means and the importance of interchangeability.

I wanted to make sure that we included a little bit about the additional data requirements that we typically look for -- well, that we hope to typically look for. We don't have licensed interchangeables at this point.

We do have final guidance on demonstrating interchangeability, which is where this can all be found, but essentially it's still a totality of the evidence approach.

We're still talking about stepwise data generation, but we do require for an interchangeable, the statute requires that the proposed product be demonstrated, that it will be expected to have the same clinical result as the reference product in any given patient, and that there won't be an increased risk either in safety or in reduced effectiveness from switching back and forth between the reference product and the proposed interchangeable.

So that's a lot of words about regulatory standards. I wanted to close by circling back to how enthusiastic we are about biosimilars and interchangeables and how excited we are about the potential for these products to really enhance patient access.

We at the FDA have and continue to play a critical role in facilitating access to biosimilars and hopefully interchangeables some time in the soon future. We have 76 development programs referencing 38 reference products, and we're feeling pretty good about the promise of

biosimilars as we go into this exciting day.

Presentation - Christine Simmon

MS. SIMMON: Great. Thank you, Eva, and good morning to everyone. I actually want to start with my second slide because it's a Monday, so that fits.

I think, as was mentioned this morning, there are now 26 biosimilars approved by the FDA, which is very exciting. I think we should all take a moment to bask in that. Twenty-six. Many of us have sat in this room, many, many, many, many times, at ADCOM meetings and public workshops around biosimilars, and here we are with 26 approved.

This slide indicates the 15 that are on the market. Think about the 26 that are approved. There's the five-year anniversary of the FDA's approval of Sandoz's Zarxio just this week or last week maybe. The most recent biosimilar to reach the market a couple of weeks ago is the third, Herceptin, which I think, as Commissioner Hahn mentioned this morning, with greater competition

and multiple products in the marketplace, you start to see increased access and savings for patients, which is of course all of our mission here.

So that's very exciting. Yet, if 15 of the 26 approved are marketed, that obviously means that there are 11 --

(Brief pause.)

MS. SIMMON: Well, what it will show, when we see it, are the 11 that are not yet approved -- excuse me, not yet marketed.

I think as we talk about biosimilars here in 2020, we have every reason to be optimistic. But there's a difference between being an optimist and being a cockeyed optimist. I think that we do have to be mindful of the challenges that we still face -- where we can have a slide, and I promise you a different slide --

(Laughter.)

MS. SIMMON: -- that has 11 that are not on the market. So let's try to go backwards.

(Technical difficulty.)

MS. TEMKIN: This is not FDA trying to avoid

talking about the biosimilars that have not been marketed; I promise.

MS. SIMMON: I'm going to put the really optimistic slide up, and that's the one that made it. This is the middle slide of three, and the prior slide talks about the challenges that we're going to talk about somewhat today.

There are some challenges, obviously, around biosimilars, and we want to focus on those so that we can reach the point of cockeyed optimism. You think about these in a couple of different categories, the challenges around development and then the challenges to a viable and competitive biosimilars market.

Ha! There they are, the ones not yet marketed, but we've so moved on from that, but thank you.

(Laughter.).

MS. SIMMON: The challenges around biosimilar development, you can think of those around the clinical studies, particularly the bridging and the confirmatory studies in phase 3.

All these are very costly studies and very necessary to achieve the FDA designation of "no clinically meaningful differences."

But as you look at the cost to develop biosimilars, and ways to work on the bridging, and think about what's really necessary in terms of clinical studies -- which I do think the FDA is looking at hard and has been helpful and somewhat flexible in their guidance, particularly in the insulin guidance which came out, which was very helpful in its flexibility -- these are things we want to continue to examine.

Obviously patent abuses and patent thickets, these are critically important to combat in order to get biosimilars to the market and through the development process. When you look at the market itself, exclusionary contracting practices has been a lot in the news of late. This is, again, something that's stymieing the ability of a biosimilar to get on the formulary and get to the market.

Similarly, the rebate trap, I think we're

all familiar with that. We're familiar with the lawsuits that have been filed around that. I know today we'll be talking about misinformation. I think misinformation is a really broad category.

You can have explicit misinformation, which the agency, FDA, is addressing, and FTC, in their guidance document around communication, but also implicit misinformation, which we at the Biosimilars Council would argue includes current policies around naming and even the very existence of the interchangeability designation, which of course is part of the statute but is also unique to the United States.

Finally, reimbursement and formulary replacement issues we may not get to today but, again, are very important. Really, more under the purview of the Centers for Medicare and Medicaid Services, they did, in their most recent draft call letter, seek to potentially address this through the potential for a preferred and non-preferred tiering system in the specialty category, which would be useful for biosimilars.

So again, optimism, somewhere between cautious and cockeyed. I think that we have a lot of good things to discuss, so I look forward to the questions. Thank you.

Panel Discussion - Meredyth Andrus

MS. ANDRUS: Thank you, Eva and Christine.

The first question we have involves the development of biosimilars. Every single year, for the past four or five years, there have been increasing numbers of approved biosimilars, but there still are questions and uncertainty.

Are there any areas where the FDA could provide additional guidance that would be helpful to manufacturers, to consumers, and to healthcare providers?

MS. TEMKIN: I can jump in for a second. Some of you have probably heard me talk about a white board that I have in my office, which has a list of policy development projects and guidance development projects that we hope to undertake, and that that list is constantly shifting in priority. But what we do know -- and I point to the

biosimilars action plan that the agency put out in the summer of 2018, I guess.

The whole point here is to provide additional clarity and certainty and to help with efficiency in biosimilar development to support biosimilar development. That biosimilar action plan includes FTC collaboration and a lot of this work that we're doing, but it also includes areas of additional guidance, and reviewing our regulations, and modernizing those, and a lot of big ticket projects that we have been undertaking and continue to undertake.

All of that by way of background, it's super useful from my perspective to hear what folks need, what industry needs, and what people in the world outside of the agency are thinking as priorities for additional clarity, so we certainly would appreciate hearing those thoughts. I'm sure we'll hear some of them during the open comment period as well.

MS. ANDRUS: The United States is the only major jurisdiction worldwide with an

interchangeable designation for biosimilars. As demonstrated with the recent draft insulin immunogenicity guidance, FDA has significant flexibility in interpreting the statute as well as the authority to issue product class-specific guidance.

Two questions: Does the designation still hold value here in the United States, and does FDA have a role to play in determining that?

MS. BURICH: I'll start on that. I think the answer to does the designation of interchangeability hold value in the U.S., the answer is yes, although it depends on the product and it depends on whether the product is, in fact, physician administered, a medical benefit product, or a pharmacy benefit product.

The reason why that's meaningful is, as Eva noted earlier, the primary draw of interchangeability is that automatic substitution that can occur at the pharmacy level. In other words, if you don't have that pharmacy interaction, whether retail or specialty, interchangeability

doesn't have a whole lot of significance if there isn't that pharmacist interaction.

As Christine's slides noted, the number of approved products, all 15 of those products, are medical-benefit, physician-administered products. I think that's an important piece of context around why interchangeability continues to be talked about, but we haven't seen it yet. It's really, in part, because of the type of products that interchangeability is relevant to. And while we have several approved self-administered biosimilars, we have none that are launched and won't be launched for the next couple of years.

So we still have some time until we see an interchangeable potentially come to market and until we see the products where interchangeability has value in terms of that pharmacist interaction. We still have a little ways to go until we get there.

MS. SIMMON: I would just add, again, that it is important and helpful to have product-specific guidance on interchangeability, as

we did see in the case of insulin. Also, we look forward to FDA making more of a determination around what the name of an interchangeable product will be. It's really not clear. We know that transition insulins won't have a suffix, so it could be that there might be special considerations for interchangeables, and we'll want to hear more about that.

On the point Molly made, interchangeability is more important, in some ways, at the retail pharmacy setting and when it becomes part of the Part D benefit and you see it more frequently. We have heard from pharmacists that they might not be comfortable doing the switching if the name is going to be something that's going to be different and confusing for them and their patients.

Of course there are state laws. We've made a lot of progress in amending the state laws to account for interchangeable biosimilars, but there may be some state laws that still have to be addressed.

DR. SINGH: One quick comment about the

products that have launched already in terms of the complexity of the competition, I think in the case of infliximab, where you have actually both medical and pharmacy adjudicated and the presence of both benefits being used, it introduces a whole other area, again, of a marketplace complexity.

The deals that get arranged and the influence of rebate bundling, competition, and the application of formulary that can be run cross-benefit is very splintered to the marketplace right now and different by health plan and PBM.

So you have that presence as well as the medical benefit side, and that makes it even more complicated, which I'll return to when we come to the latter questions.

MS. ANDRUS: There are, as we saw, 26 approved biosimilars in the United States, but only 15 are actively marketed. What might explain why the other 11 are not actively marketed?

DR. SINGH: I can start, and I'm sure others have comments about this, too, because it's sort of a central theme.

Thinking back to the slides that Christine showed, and she articulated this well, I think I'll just elaborate a little bit. The first one, before I get to some of the purely marketplace commercial issues, is the idea of the patent thickets. I think there's a paper in JAMA last year -- and this is publicly available information, so I'll quote a couple of statistics.

Adalimumab as an example has over a hundred patents. Eighty-nine percent of them were filed after the original launch of that medication. So you just think about that and think about the barrier to having a biosimilar for that particular medication, or any others into the marketplace, it's certainly a lot more complicated to wade through that patent thicket, if you will, to use that terminology that's taken over the market.

The second and third are really interrelated about the other 11 and why they haven't launched. They're both commercial and contracting issues. One is that the same manufacturers, or sometimes marketplace arrangements between manufacturers, are

involved in both the innovator, if you will, the originator biologic, and the biosimilar.

So the contracting, especially the big consolidated procurers of drugs on the specialty pharmacy side of the market and the way that the contracting happens, there's a relationship between the contracting for those new biosimilars and the originator biologic that are very hard to disentangle.

That bleeds into the third issue of what was called before -- I think part of what was underneath the rebate trap, and you may want to elaborate on that, is that the rebates in that particular category may be driven by a bunch of different factors.

It's different on the medical benefit side, again, and the pharmacy benefit side. You'll hear all of us, I think, agree that the issues in contracting and procurement are pretty unique on the medical benefit side where the market is much more splintered.

If you have a few major entities doing

contracting on behalf of a lot of covered lives on the pharmacy benefit side, the bundling of rebates, if you will, across categories, where there are interdependencies, is much more common than when you have individual practices or hospitals and health systems doing the contracting on the medical benefit side. So that's the other major issue.

But getting back to the question of why have some of these other 11 not launched, I think what I've observed and then heard in a variety of different forms in the market is that some of the manufacturers are taking a bit of a wait-and-see approach, especially in what's going to happen with the rebate trap or changes structurally, and the way that rebates are both contracted and then ultimately invoiced and administered in the market. It's a dynamic issue.

There was obviously a lot of talk about removing the anti-kickback protection for rebates last year and Medicare, and I think a lot of the manufacturers are just watching the changes that

may happen structurally very closely before they make a decision.

MS. SIMMON: Surya, you made a lot of great points, and I think that's exactly right. A lot of these issues are clearly around the rebate traps, the exclusionary contracting, and the cost of litigation. I would add on to that a couple of things.

With respect to litigation, we want to commend the FDA for its recent changes to the Purple Book, making it more easily searchable electronically. That's a huge benefit for biosimilar manufacturers and others.

Of course what would help even more, and we know this is outside the agency's purview, is to require patents to be listed for biologics and reference products in the Purple Book. We support legislation. There's a bill that's been introduced by Senator Susan Collins around this called the Biologic Patent Transparency Act -- it rolls right off the tongue -- and to ensure that this happens to foster the potential for development.

Let's say you're a biosimilar manufacturer and you get to see patents listed in the Purple Book. Once you've cleaned up your coffee from spitting it out when you saw the number of patents listed, you start to contemplate litigating them. It's about $3 million to get through this litigation, which is a large expense for biosimilar manufacturers.

Think about that Humira, for example, was first approved in 2002, and there are 5 biosimilars approved for it, but none are on the market. We know that there will be a bunch coming onto the market but only due to the ability to enter into patent settlement agreements with AbbVie.

Because of patent settlement agreements, which in this case are very pro-competitive, these biosimilars will get to the market 11 years earlier than might otherwise be possible. This is alluded to in the introductory remarks. The FTC of course has been very active and has done a lot to ensure that patent settlement agreements are pro-competitive.

So hopefully we can put to rest the misnomer of pay-for-delay and think of them as they really exist, and how much it will help the patients who might not otherwise receive Humira until 2034 without these settlement agreements.

We continue to work to make sure that biosimilar manufacturers have the ability to enter into these settlements and also to use inter partes review, which is an administrative process to challenge patents that are constantly under threat. There are those who seek to exclude pharmaceutical products from the ability to pursue inter partes review and settle these patent issues or address them administratively, which can be more efficient and less expensive than going through litigation.

These are some of the issues I just wanted to bring to light as to answer the broad-based question of why they're not all on the market, in addition of course to the rebate issues as Surya pointed out.

MS. ANDRUS: Thanks.

Are there any significant differences in

uptake rates between biosimilars that are approved to treat ongoing or chronic conditions and biosimilars approved to treat acute conditions, and what might account for that if there are?

DR. SINGH: Yes, I can start here also. I think the distinction between the acuity or chronicity of the underlying condition is helpful, but it draws back into focus the very specific conditions and the benefit under which they're adjudicated commonly that were on the list that Christine presented. I think that distinction has more impact on what adoption has looked like so far than the acuity or the chronicity of the underlying condition.

Just very specifically, now that we have bevacizumab, trastuzumab, and rituximab biosimilars on the market, as soon as we have enough data to be able to really examine what the uptake curves and the adoption curves have looked like for those medications, we'll be able to validate what I'm saying.

I think in the example of the white and red

cell growth factor biosimilars, the adoption curves versus infliximab, where I was saying it's been more complicated because of this dual benefit approach, that there's a lot of that particular category for -- just to broaden it a little bit -- both GI and RA, issues or conditions, rheumatologic and gastroenterologic conditions, that the drug treats.

The management of it, from both the utilization management or formulary management standpoint, has been more complicated because of that dual benefit approach; whereas on acute or for a finite period of time, administered medications purely under medical, again back to the health system and provider procurement of the medication, we see a better degree of steeper uptake curve.

So I think that's what we're going to see with bevacizumab, trastuzumab, and rituximab once the data is available, but that's kind of how I frame it.

MS. SIMMON: I think that's right. You can sort of put some names to it. You can see that

systems like Kaiser and smaller health systems that have integrated delivery networks are going to have greater uptick for all the products. Large academic medical centers like Mayo and Johns Hopkins are not having such rapid uptick of biosimilars.

So it does speak to the financial component that's at play in these systems, which speaks to the perniciousness of getting to all the factors that are influencing biosimilar utilization and uptake.

DR. SINGH: I just wanted to make one other following comment because you've raised a point, and I'm not sure if there's another place to say this. So I just want to make sure that I put it out there.

I think the idea of misinformation or misleading information influencing prescribers decisions about biosimilars, I think we've sailed past that. There's a lot of survey data to support this but anecdotally also. A lot of leaders of large multidisciplinary practices, Kaiser included

but large oncology practices, rheumatology practices, et cetera, there's no reluctance anymore to speak of to use biosimilars. Really, the market is being driven by economics, and I think that's what's going to dictate the adoption curves that we see.

MS. ANDRUS: So if there's no lingering reluctance on the part of the physicians and there's no real difference between acuity and chronicity, are there any unique characteristics in any of the therapeutic categories where biosimilars have been approved and launched that have slowed uptake?

MS. BURICH: I think the points that have been raised are really important. I think that in the same way is it acute versus chronic, is it immunology versus oncology, I think what we see is the mix of products, the benefits they're covered under, and it's sort of all of these factors that are coming together that are making -- while we're seeing significant strides in the number of approved products and the number of launched

products, we still know that uptake in a lot of areas is lower than we want it to be, both from a overall outlook of the sustainable nature of the biosimilar market, but also just to generate savings at a time when drug pricing is in such focus within the U.S.

So I'm sort of in a similar boat as the other panelists, which is that I think it's maybe less about the specifics of the products and more about where the existing launched products sit within our system and what some of those dynamics are. I think that is what is proving to be an important piece that we haven't quite connected all the dots to, to get the market moving consistently across all the products.

MS. ANDRUS: Do providers have varying incentives to use biosimilars or to use the reference product? Generally speaking, what role do insurers play in moving share to a biosimilar, and what is the impact of most biosimilars and biologics that are dispensed not in a pharmacy setting but rather in hospitals, and clinics, and

doctors offices, through a medical benefit plan?

DR. SINGH: I can start on this also. The first question in there, I think that provider incentives do vary a lot, so let me just take a step back and give a little bit of a macro picture using some of the specific classes and agents where we have biosimilars in the market already, particularly infliximab.

Again, I'll start with the point that when it's purely, or at least let's say 90 percent, adjudicated under the medical benefits, it's a very different picture than when there's a lot of pharmacy benefit involvement.

At the inception of white-cell growth factor, the introduction of biosimilars for both filgrastim and pegfilgrastim now, much more of it on a percent basis, if you look at the most recent publicly available reports from IQVIA and others, I think they illustrate the point that there's been more shift towards some white-cell growth factor going through the pharmacy benefit and being adjudicated as a pharmacy drug, then medical over

time over the last five years.

As that's happened, and then we watch what's happened with infliximab, you start to get to the point that the provider incentives -- there's a lot in the word "incentives" there. There's the economic incentive. There's also the ease of administering the same agent and inventorying the same agent in your practice for all patients that you see.

The complication has been the action of the other stakeholder group that you mentioned in the second question, is insurers. Insurers have increasingly used their leverage, basically, to be able to say we're only going to allow pharmacy adjudication of some drugs, and we're either going to, quote/unquote, "white bag" or we are going to supply through our affiliated specialty pharmacy or our network specialty pharmacy's drug to a practice.

That further complicates this issue of the provider incentive because now the provider, if you put yourself in their shoes, is stuck saying I have

this inventory of drug that I contracted the best rate possible. I'd like to give it to all patients, but I can't use it for everyone. I'm required to accept drug from a specialty pharmacy and administer to patients and bill just for my services rather than billing for the drug.

So the provider incentives vary a lot, and the complications on their business and how they do their drug inventory and all that can't be basically overstated. I mean, it's a huge issue for many of these practices.

The last thing I'll say before I give others a chance to comment about the insurer role, there's both the supply chain aspect and then this idea that they're not going to allow providers to contract and bill them for whatever version of drug, the incumbent or the biosimilar, the original biologic or the biosimilar.

There's that issue, and they will, quote/unquote, again, "deliver or white bag" drug to the practice, and that's more a common practice now than it was five years ago for sure. I can't

give you a percentage because it's definitely different region by region.

The other issue for insurers is this whole idea of fail first and being able to use utilization management and prior authorization, which is much more streamlined than it was, but much more omnipresent I guess on the medical benefit than it used to be.

PA is used on the medical benefit a multiple of where it was five years ago. It's always been used extensively, as I think everyone is probably aware, on specialty pharmacy drugs on the pharmacy benefit, but it's much more common on the medical benefit now as well. So insurers are really using that as a way to drive their preferred product strategy.

MS. TEMKIN: Can I ask a little bit of a follow-up question? I'm going off script, so forgive me.

Just to tie it back to some of the discussion about interchangeability and where that fits in, how does the avenue of interchangeability

versus biosimilarity impact some of the incentive structures, if it does?

MS. BURICH: I think it's a really important question. I think this is why I think your question is quite apropos on why this medical benefit versus pharmacy benefit is such a significant difference, and therefore impacts the overall flow of incentives and everything else.

I think when you think about an interchangeability designation, your physician does not have the same financial skin in the game as they do on the medical benefit side because, again, interchangeability is very likely tied to products that have that pharmacy interaction, so that inherently changes the incentive structure because physicians aren't inventorying and managing the cost of those drugs.

DR. SINGH: I'm going to paraphrase what you said. I think that was really good. I think substitutability, substitution, as a result of having interchangeable designation for a practice, when they have all the issues that I was just

talking about with inventory and so on, they've already chosen what they're going to procure and gotten best price on what they're going to procure and stick in their inventory.

Forget the white bagging that gets sent to them on a patient-specific basis to get administered. They've already chosen, and they're going to prescribe that specific agent. So interchangeability basically does nothing in that case.

Under the medical benefit, when you've chosen what you're going to inventory, and you're the big practice, and you have 40 sites to manage, and everybody got shipped out the same version of pegfilgrastim now, and it's a biosimilar, that's what they're going to prescribe. It's in their EMR, it's in the protocols, et cetera.

Flip it over to the pharmacy benefit side, and now interchangeable really matters because it's specialty pharmacy. If I'm the specialty pharmacy, it's only going to ship out what is my preferred product, and I can only do that if the pharmacist

in my specialty pharmacy has the right to substitute. They get the right to substitute, without having to go back to the provider to, to the prescriber, if they have the interchangeable designation.

So on the pharmacy benefit with drugs, it really matters. You'll see, I think, a completely different uptake curve, adoption curve, on the pharmacy benefit because of interchangeable designation. It'll make virtually no difference on the medical benefit side.

MS. SIMMON: Just before I move on, I think we'd be remiss if we didn't talk about some of the legislative proposals out there around provider incentives. There is a bill to increase the reimbursement for providers in Part B from ASP plus 6, the average sales price plus 6 percent of the reference biologic ASP; to increase that by 2 percent to ASP plus 8. We know the ASP plus 6, some of the folks are I think wonky in the audience and know that sequestration impacts that, so it's not a true plus 6.

This is interesting and useful, but I think ultimately a limited opportunity to try to increase provider incentives. What we support -- many of us here at the table support, that might have a longer term benefit -- is the opportunity to do a shared savings program.

This practice, which is known as gainsharing in Europe and has had success there, would allow the provider, and in some cases could be extended to the patient, to share in the savings that a biosimilar provides to the Medicare program. So taxpayers, providers, and patients could benefit from the shared savings, which would also increase utilization and uptake of biosimilars.

These are some opportunities, and shared savings is something that can be done administratively right now by the administration via CMS and could also be a legislative proposal and has been introduced as an amendment to current legislation and introduced today. I think we're expecting a bill to be dropped today on that.

So these are some, again, opportunities

outside the FDA-FTC purview or our ability, but that could have a significant impact.

MS. ANDRUS: What educational efforts to support biosimilars have worked well? What educational efforts are needed to counteract misinformation being published about biosimilars?

MS. BURICH: I'll start. The materials that the commissioner referenced earlier have been tremendously helpful and important for all stakeholders, physicians, and patients.

I think the materials that have been developed by the agency are very palatable. They take complex concepts from A to Z, from biologics all the way to biosimilars and interchangeables, and really try to break it down in a way, depending on where you sit in the chain of using a product, that you can consume that information in a way that's reasonable.

While I hate to add to the list of the FDA -- and I'm looking at Sarah and Eva -- I think that we do need more education from the FDA. I think the education that's been developed thus far

was tremendously helpful.

It also brings a validity and an impartiality coming from the FDA, and I think we need to see that specifically around some of the topics we've already talked about, the interchangeables, what they are, what they aren't, where they fit in terms of the product specifics as we've talked about on this panel, and also where physician-led switching can and should play an important role for products that don't and will not have an interchangeable designation for all the reasons that we've talked about today.

I think that we've seen a tremendous amount of resources that the FDA has put out, and we would love to see a few more that are focused on a few emerging areas because they are so important to have that voice and those tools from a trusted and reliable source like the FDA.

MS. ANDRUS: So we're down to our last couple of minutes, but I wanted to throw out one question about what we can learn, lessons learned both from the generic industry, our experience

there, and what, if anything, we can learn about the European experience with biosimilars.

MS. SIMMON: Real quickly, I'll touch on the parallels to the generic experience. I think we do see some parallels, but there are significant differences. When generics were introduced in 1984, there was slow uptake.

I just saw something with one of my documents from 2006, back before I needed to wear glasses to read them. I was talking at a conference saying generics were 56 percent of the drugs dispensed, so now generics are 90 percent of the drugs dispensed.

Will we see that with biosimilars? That's not completely likely, but the uptake did take some time. There was misinformation. There were the same efforts to mire generics in patent litigation, and that goes on today.

So it's sort of the same playbook. Change can be hard. And while we all applaud and appreciate innovation, what comes with that is that some companies go to great lengths to protect their

ability to charge monopoly prices and prevent competition. So we will continue to, I think, make progress in the biosimilars area, and I think we have already made progress so far, but we'll continue that.

I think the substitution interchangeability issue remains one of the thorniest because generics were always designed to be substitutable and interchangeable. So that's a difference that we'll have to continue to work to overcome.

MS. BURICH: I would just say from a European experience, I think what's probably most important is that while the European pathway across the countries of Europe has existed longer than the United States pathway, the countries across the EU really took a very active role, in a lot of different ways, to drive a robust and sustainable biosimilar market.

You have countries who are implementing shared savings or gainsharing programs, doing robust educational dialogue between physicians and patients, and setting up incentives across the

supply chain. And again, while the systems that exist over in Europe look very different than the systems we have here, there are some important lessons around market preparedness that we can and should be implementing now to get this market moving in a very positive direction to really generate those savings and improve access.

MS. TEMKIN: I would just add from my slightly different lens on all of this -- and I was not here during the early days of the generics. Don't worry; I was doing something else.

I think the people that are working in the agency on biosimilars and on these issues have had a takeaway of the importance of educational outreach and the importance of engaging market questions and incentives so that we can understand and do the best that we can to try to build a similarly robust structure for our different products.

DR. SINGH: I guess my one quick comment -- taking a step back to the macro issue of trying to use biosimilar introduction and all this

competition to be able to create some headroom, basically, to pay for all of the new innovative treatments within your premium dollar with your insurance plan -- I have a lot of hope.

I guess parallel to the generics industry, even though we've harped on and had this refrain about the difference between the benefits, and even on the medical side, more competition is better, it's going to help us drive prices down. It gives you a better ability. Even though it's splintered in different health systems, you can procure differently to drive prices down. So I have a lot of enthusiasm that we're going to achieve the long-term goals and create that headroom that I was just talking about.

MS. ANDRUS: Thank you very much. We thank our panel, and our next panel will begin at 10:30.

(Applause.)

(Whereupon, at 10:16 a.m., a recess was taken.)

MR. SCHILLER: Well, good morning. We're going to begin the panel now on FDA and FTC

Approaches to Help Ensure Truthful and Non-Misleading Advertising and Promotional Communications. I'm Lowell Schiller, and I'm the principal associate commissioner for policy here at FDA.

As we've been discussing this morning, biosimilars can offer significant benefits in terms of competition and patient access. But for those benefits to be fully realized, it's critical that patients, healthcare providers, and others in the healthcare system have an accurate understanding of what biosimilars are and aren't and how they fit into the overall armamentarium of therapeutic options.

That's why as FDA has been implementing our biosimilars program, we've made education and engagement a critical part of our efforts. We also recognize that sometimes incorrect or misleading information may be disseminated about drug products, including biosimilars, and that misinformation can have negative consequences for the public adoption of biosimilars, for the public

health, or both.

For example, if a biosimilar manufacturer falsely states that its product is identical to the reference product when in fact it's not, that can mislead patients, providers, and others. On the flip side, we've seen troubling examples of biological reference product manufacturers disseminating information that could frighten patients and healthcare providers away from using biosimilars.

For example, we've seen communications that could sow seeds of doubt by suggesting to patients and healthcare providers that biosimilars are less safe or less effective than their reference products, or that there may be clinically meaningful differences between a biosimilar and its reference product when in fact a biosimilar cannot be licensed or marketed unless it's first been established that there are no clinically meaningful differences from the reference product.

Some of these communications may avoid making overtly false statements, but even material

without an overtly false statement can be misleading. For example, if it selectively deploys a series of statements, which may be true in isolation and perhaps omits other important information, it's possible for the overall message to be misleading and potentially harmful to the public health.

We've seen this trick before. After the Hatch-Waxman amendments passed in 1984 and American patients were starting to learn about and accept generic drugs, some manufacturers of branded drugs disseminated materials to scare patients from using generics, for example, by creating the false impression that these drugs were less safe, or weren't therapeutically equivalent, or were inadequate in other ways. Some of the communications we're seeing today about biosimilars use the same old play from the same old playbook.

In looking at what's happened on the generic side, the good news is that patients and healthcare providers have come to learn the value of generic drugs, and the adoption rate has been overwhelming,

as we've heard. I believe we're also on a path to a more vibrant biosimilars market, and part of how we get there is by encouraging truthful and non-misleading communications and by addressing misinformation in the marketplace.

We can do that in several ways. One is through our own education efforts. Another is by making our expectation clear that manufacturers cut the shenanigans. We have a system of balancing innovation and competition that has worked very well for many years. The system incentivizes innovation through patents and market exclusivity, but with the expectation that after a limited period of time, there will be a real opportunity for follow-on competition to take hold.

Brand manufacturers obviously have financial incentives to try to stave off follow-on entry, but when they do so through deception or regulatory gainsmanship, it undermines our system for balancing innovation and competition, and ultimately we risk undermining the promise of biosimilars.

In some cases, other forms of government intervention may be appropriate. If a communication about a biosimilar crosses the line and presents information that's false or misleading, it may be appropriate for the government to act. Both FDA and FTC have certain tools and authorities to encourage truthful and non-misleading communications about drug products, including prescription biological reference products and biosimilar products.

Our panelists today will be providing an overview. Now, speaking today we have Dominic Cirincione, who's a regulatory counsel in FDA's Office of Prescription Drug Promotion or OPDP. He regularly provides advice and regulatory counseling on policy and compliance matters to both OPDP reviewers and OPDP management.

Our other speaker is Richard Cleland, who's assistant director of the Division of Advertising Practices within FTC's Bureau of Consumer Protection. He joined the Division of Advertising Practices in 1991. His primary area of expertise

is in the advertising and marketing of health-related products and services, obviously relevant today.

So without further ado, Dom, do you want to take it?

Presentation - Dominic Cirincione

MR. CIRINCIONE: Yes, thank you.

Well, good morning, everyone. As Lowell said, my name is Dominic Cirincione. I've been since 2017 a regulatory counsel with the Office of Prescription Drug Promotion, and today I'm here to present how FDA, and more specifically OPDP, helps ensure truthful and non-misleading advertising and promotional communications about prescription drug products.

OPDP'S overarching mission is to protect the public health by helping to ensure prescription drug product information is truthful and non-misleading and includes a fair balance of both benefit information and risk information. Prescription drug information includes promotional communications as in prescription drug advertising

or promotional labeling made by or on behalf of a drug manufacturer, packer, or distributor.

Generally, FDA and OPDP accomplishes this through a comprehensive program, which includes surveillance, compliance, education, and communication with the public. Our compliance tools include issuing warning or untitled letters to manufacturers in regard to their disseminated promotional materials that violate the Food, Drug, and Cosmetic Act, and implementing regulations concerning the promotion of prescription drug products, particularly where the violation poses a risk to public health.

FDA's authority over promotional communications about a prescription drug made on behalf of a drug's manufacturer, packer, or distributor comes from the Federal Food, Drug, and Cosmetic Act, or FD&C or FDCA.

More specifically, two primary or key provisions on which FDA frequently relies are Section 502(a) of the Food, Drug, and Cosmetic Act, which relates to false or misleading labeling,

including promotional labeling, and Section 502(n) of the FDCA, which relates to prescription drug advertising.

FDA has also promulgated a number of regulations related to both drug labeling and prescription drug advertising in Parts 201 and 202 of Title 21 of the Code of Federal Regulations or CFR. FDA and OPDP rely upon these statutes and regulations throughout the course of our work.

OPDP helps to ensure truthful and non-misleading promotional communications about prescription drug products through a variety of tools. As noted on our previous slide, that includes a robust surveillance and communication program with the public, and part of that communication plan with the public includes OPDP's response to industry's voluntary request for comment on specific draft promotional materials.

This process allows OPDP to provide feedback on draft promotional communications if the manufacturer chooses to request it. This process also allows for OPDP to engage with the

manufacturer on specific Communications prior to their use in the public domain.

FDA and OPDP also provide guidance for industry in areas related to promotional communications. The guidance such as the most recent guidance, the Q&A on biosimilar reference product communications, provides the public with FDA's current thinking on particular subject matters, and many of these guidance documents are informed, in part, by OPDP's social science research program.

OPDP's research program is designed to investigate applied and theoretical issues of relevance to direct to consumer, or DTC, and professional promotional prescription drug materials.

OPDP's research supports the FDA's goal of science-based policy while maintaining our commitment to protect public health. And as always, we invite the public to visit OPDP's website to learn more about our social science research program to determine more about the

studies that are being conducted and to review the new research and progress.

OPDP also employs a robust surveillance and compliance program to monitor compliance with applicable FDA-administered laws and regulations. For example, OPDP regularly attends conferences and other events to observe industry promotion, as well as reviewing the many promotional materials submitted to the FDA by firms in accordance with the postmarketing reporting requirements.

OPDP also reviews and investigates complaints from healthcare professionals, consumers, and competitors regarding violative promotional materials in the public domain. And while I'm on the topic of surveillance, I did want to remind the audience and the public that OPDP's BadAd program may also be used to report potentially false or misleading prescription drug promotion to FDA and to OPDP.

You may send an email to badad@fda.gov or by calling the toll-free number, 1-855-RXB-ADAD. Reports can be kept anonymous, however, we would

encourage reporters to leave their contact information in case we need to follow up and receive more information.

If as a result of our surveillance activities we see an apparent violation of the Food, Drug, and Cosmetic Act or implementing regulations regarding promotional labeling or advertising for a prescription drug, particularly ones that pose a risk to public health, most commonly we will send a warning or an untitled letter to provide notice of the observation of the apparent violation and then seek compliance.

The vast majority of our concerns are typically addressed in this way, but if these efforts to obtain compliance are not successful, FDA can work with the Department of Justice to pursue enforcement actions to address violations of the Food, Drug, and Cosmetic act. These can include, for example, seizures and injunctions.

To help you better understand FDA's role in helping to ensure compliance with the Food, Drug, and Cosmetic Act and implementing regs concerning

the promotion of prescription drug products, we thought it would be helpful to provide you with some of the more common issues FDA, and more specifically OPDP, observes across all prescription drug advertising and promotional labeling that could render a presentation false or misleading.

While the issues I'm about to discuss do not constitute an exhaustive list, FDA will most commonly send a warning or an untitled letter to provide notice Of our observation of these kinds of apparent issues and seek compliance.

Before I continue, I do want to remind the audience that the agency's warning letters and untitled letters are publicly available on the FDA website, and each letter is also typically accompanied by the violative piece, and the application of FDA's authorities in this space is necessarily fact specific. So the details of a particular piece, including both its content and the matter of the presentation, are important.

The first common issue OPDP often sees in prescription drug advertising and promotional

leveling is a mission of risk information. Promotional materials that include claims regarding a drug's efficacy must also include information regarding the important risks associated with the drug.

For example, imagine a sales aid for a drug that has a black box warning. The sales aid has multiple pages of information regarding the efficacy of the drug, but the black box warning isn't presented anywhere in the sales aid.

The lack of this important risk information about the sales aid that has numerous claims regarding the efficacy of the drug would be misleading. It's an omission of risk. It's important to also note that the regulation regarding omission of risk applies to all prescription drugs, not just those of black box warnings.

The second common issue related to the first is the minimization of risk information in prescription drug promotional materials. Risk information must be presented with a prominence and

readability reasonably comparable to the presentation of the efficacy information. Many factors can impact prominence and readability; for example, the size, the style, and color of the font and layout of the piece and use of white space.

Imagine, for example, that your own ad presents efficacy claims in large bold font with colorful graphics, but the risk information, however, is buried at the bottom of the page in very tiny font with no headings or no signals in any way to alert the reader to the presence of that important information. This format in which the risk information is not presented with comparable prominence to the efficacy claims minimizes the risks of the drug.

The third issue we often see in promotional materials is an overstatement of the effectiveness of the drug. Promotional materials would be considered false or misleading if, for example, they; one, overstate or exaggerate the effectiveness of the drug; two, make claims regarding the efficacy of the drug that aren't

appropriately supported or; three misrepresent data from clinical studies.

For instance, if during a sales call, a sales representative is promoting a prescription drug product and the sales representative presents a flyer which contains the claim "it works in as little as 3 days," however, according to the package insert, the primary endpoint in the clinical trials used to support the approval of the drug was "relief after 10 days," and there is no available data or evidence to support a shorter duration of treatment. Therefore, the claim misleadingly suggests the drug works faster than what has been demonstrated.

A fourth common issue often seen in prescription drug promotional materials is misleading drug comparisons. Claims or presentations in prescription drug promotional materials that suggest that a drug is safer or more effective than another drug would be considered false or misleading if they are not appropriately supported.

For example, imagine at a conference there was a promotional booth for a prescription drug product. A bar chart on a convention panel at the booth compares study results from the prescription drug's package insert and study results from its main competitor's package insert and includes a claim stating that it showed improvement in significantly more patients than its competitor.

This comparison would be misleading because comparing the response rates for two different drugs in two different studies does not support a conclusion that one drug is safer or more effective than another because, for example, these studies may have been conducted in different patient populations or using different clinical study designs and methodologies.

Just to round out my presentation here, we provided a graphical representation of observed violations noted in OPDP's warning and untitled letters for the last five years, from 2015 to present, and although false or misleading claims about the risks of drug products, or complete

omissions or minimization of risk information, are the largest share of our observed violations and letters since 2015, FDA does still take very seriously false or misleading benefit claims about drug products, including comparative claims that lack adequate substantiation.

In conclusion, I hope this presentation highlights some of FDA and OPDP's work to help ensure truthful and non-misleading advertising and promotional communications from manufacturers, packers, and distributors of prescription drug products. On this slide, please do find our contact information, and thank you very very much for your time.

I'm going to pass it over to Mr. Rich Cleland, assistant director for advertising practices in FTC's Bureau of Consumer Protection.

Presentation - Richard Cleland

MR. CLELAND: Good morning. I hope you hate the morning after daylight savings time as much as I do.

(Laughter.)

MR. CLELAND: If I fall asleep, give me an elbow or something. I saw a lot of people doing this, this morning.

This is not my usual audience. I more talk to dietary supplement companies and OTC drug companies, but I don't deal a lot in the prescription space.

So this morning, I thought I would provide you with a quick tutorial on what enforcement might look like with regard to promotional material that is communication that falls outside of the FDA's jurisdiction. This includes promotional communications that don't refer to a manufacturer's or distributor's drug by name, as well as promotional communications made through what amounts to surrogates for the drug company.

As a threshold matter, the FTC's jurisdiction only extends to commercial speech, and I know I've seen some stuff out there that I really question whether it would meet that threshold. We look at a number of factors to determine whether or not something is commercial speech, the content of

the speech and whether it contained a message promoting the demand for a product or service.

It could also be denigrating a competitor's product as well, whether the speech refers to specific products or services, whether the speech included information about the attributes of a product or service such as type, price, or quality, including information about the health benefits associated with the product; the means used to publish the speech; traditionally is it paid advertising, is it recognized, and would it be recognized by consumers as advertising?

Then finally, the speaker's economic interest in motivation in disseminating the speech. In this regard, context matters. For example, a peer-reviewed scientific article or a press release may or may not be considered commercial speech depending upon how its disseminated and how it's used.

Now, looking specifically at advertising, assuming we get over the commercial speech barrier, the FTC enforces two sections of the FTC Act that

are relevant here, Section 5 and Section 12. Section 5 prohibits unfair methods of competition and unfair deceptive acts or practices in commerce. Section 12 prohibits the false advertisement of a food, drug, and service.

False advertisement is defined under Section 12 as an advertisement that is misleading in any material respect, including the failure to display material information. The FTC has provided some gloss over these general principles. We don't have all the statutes as the FDA has, but we think these two statutes give us some pretty good tools.

A company is responsible for both express and implied claims. In express claims, as you heard some reference to this morning, the statement says what the message is. They run the gambit between express claims, virtual express claims, to statements that few consumers would even consider to convey a particular message.

With regard to determining add meaning, the FTC's position is that extrinsic evidence such as copy testing an expert testimony is not necessary

to establish implied message where the implied claim is reasonably apparent on the face of the advertisement.

Advertisements are interpreted based on the net impression of the advertisement from the viewpoint of a reasonable person in the target audience. For example, the net impression of an advertisement may be different depending on whether the advertisement is targeted at a person suffering from diabetes or a physician treating diabetic patients.

Reasonable consumers you have to understand don't read everything in an advertisement. They read the headlines. They may read some of the text. It is rare that a footnote in an advertisement will ever alter the net impression of an advertisement.

A reasonable interpretation does not have to be an interpretation that's accepted by a majority of the viewers of that ad. If a significant number of consumers would take a message away from an ad, the advertiser is liable for any misrepresentations

or deceptive content in that ad.

I think this is an important point, particularly in this area of biosimilars. When an ad conveys more than one meaning and only one only one of which is misleading, the advertiser is liable for the misleading interpretation, even though a non-misleading interpretation of that advertisement is possible.

In this regard, consider the general statement that a biosimilar product is not interchangeable with this reference product. A very knowledgeable consumer might understand that to mean that to receive the biosimilar instead of the reference product, the consumer may need a prescription from the healthcare prescriber written specifically for that biosimilar product. That would be a correct interpretation of that phrase.

However, a consumer, like I think most consumers out there, relying on the common meaning of the word "interchangeable" might interpret that to mean that an approved biosimilar could not be prescribed in lieu of the reference product, and

that would be misleading.

Claims can essentially run afoul of the FTC Act in three ways. It can be a false claim, it can be an unsubstantiated claim, and it also can be deceptive because it fails to disclose a material fact.

Looking at some specific claims now that I've observed, for example, there are clinically meaningful differences between a reference product and a biosimilar or that the products are not similar. Biosimilars may be highly similar to their reference products, but there's still a chance that a patient may react differently; the biosimilar product is less safe or effective than the reference product or that the reference product is safer or more effective than the biosimilar.

These statements could all be potentially challenged as false, as unsubstantiated, and for the failure to disclose material information. The particular remedies that are available to the FTC, we also have on occasion used warning letters where we thought education was an appropriate first step,

but we also have enforcement tools that don't require us to go through the Department of Justice, which gives us a great deal of flexibility. We can bring our actions. These are either administratively or we can use our Section 13(b) authority and file them directly in district court. Thank you.

Panel Discussion - Lowell Schiller

MR. SCHILLER: Well, thank you both. I think we have time maybe for one question, so let me start with this. We've just heard about two different frameworks, I think, hopefully complementary frameworks, for helping to ensure truthful and non-misleading communications. I'll ask both of you.

How do you see the recently announced collaboration between FDA and FTC helping to ensure the protection of public health and fair competition in the marketplace with respect to prescription biosimilar products?

Dom, do you want to start?

MR. CIRINCIONE: Sure. I think the

collaboration will showcase how FDA and FTC both support and protect public health and competition in the marketplace for prescription biologic products. Our organizations I think have serious concerns about false or misleading statements about prescription drug products and biologic products and the negative impacts on public health and competition.

I think with these shared goals in mind and using our respective authorities, FDA and FTC will help to ensure that healthcare professionals and patients receive truthful and non-misleading information about biosimilar products. It leveled the playing field to support biosimilar uptake and I think facilitated more competitive marketplace for everyone involved.

MR. CLELAND: Let me take a 42-second shot at this. We're going to talk more about competition later on in the program today, but just focusing for a second on the consumer protection side, together I think we can cover the whole waterfront. I think the FTC is here to try to deal

with manufacturers or others that are trying to avoid the FDA jurisdiction by using promotions that aren't subject to your authority, so I think together we can cover the full waterfront.

MR. SCHILLER: On that note, let me thank you both for very helpful presentations, and I'll try to keep us as on time as we can be. Thank you.

(Applause.)

MS. GRAY: Good morning. My name is Caty [ph] Gray, and I'm the supervisor for the advertising and promotion policy staff in the Office of Prescription Drug Promotion or OPDP, as you heard from both Lowell and Dom. I share Rich's dislike of the Monday after daylight savings time, so thank you to you all for being here and joining in this important conversation.

I'm joined by Betsy Pepinsky and Dom Cirincione to discuss FDA's draft guidance for industry titled Promotional Labeling and Advertising Considerations for Prescription Biologic Reference and Biosimilar Products Questions and Answers.

As Lowell mentioned, Dom is a regulatory counsel in OPDP. Betsy is also an attorney, and she works as a health science policy analyst in our group, primarily focused on guidance and policy development regarding prescription drug promotion. I'm delighted that both of these experts are here to speak on this important topic, and I'm going to turn it over to Betsy to get us started.

Presentation - Elizabeth Pepinsky

MS. PEPINSKY: Thanks for that introduction, and good morning. As Caty said, Dominic and I are here to discuss the draft guidance that published just in February of this year on Promotional Labeling and Advertising Considerations for Prescription Biological Reference and Biosimilar Products Questions and Answers.

FDA issued the draft guidance to answer questions that firms may have when developing FDA-regulated promotional materials for their reference products and biosimilar products and to help ensure that these materials are truthful and non-misleading. This draft guidance represents one

piece of the broader effort to address false or misleading communications about biological reference and biosimilar products and the negative impacts of such communications on public health and competition.

The draft guidance was issued by CDER's Office of Prescription Drug Promotion in consultation with CDER's Office of Therapeutic Biologics and Biosimilars and in cooperation with the Center for Biologics Evaluation and Research.

Again, OPDP's overarching mission is to protect the public health by helping to ensure that prescription drug information is truthful and non-misleading and includes a fair balance of benefit and risk information. Generally, FDA and OPDP accomplish this comprehensive program, which includes surveillance, compliance, education, and communication to the public.

Starting with a bit of background on why FDA issued this draft guidance, as the number of biosimilars increases, we have started to see promotional materials for some of these products

and get questions from firms on promotional issues related to biosimilars and reference products. We are especially concerned about promotional claims and presentations that make false or misleading comparisons between a reference product and a biosimilar in a way that misrepresents the safety or effectiveness of either of these products.

The goal for this draft guidance is to discuss considerations to help ensure that FDA-regulated advertising and promotional labeling for reference products and biosimilars are truthful and non-misleading.

The guidance covers promotional issues involving both reference products and biosimilars, but some questions are focused only on biosimilar product promotion, and the guidance does not discuss considerations unique to promotional materials for interchangeable biosimilars.

In terms of the general requirements for the content of FDA-regulated promotional materials for reference products and biosimilar products, FDA regulates promotional labeling and advertisements

by or on behalf of manufacturers, packers, and distributors for prescription drugs, including those that are biological reference and biosimilar products.

Under the FD&C Act in implementing regulations, these promotional materials must be truthful and non-misleading, convey information about a drug's efficacy and its risks in a balanced manner, and reveal material facts about the drug. All these requirements apply to promotional materials for reference products and biosimilar products licensed under Section 351 of the Public Health Service Act, the same as they would apply to any other FDA-regulated promotional materials for prescription drugs.

When concerning promotional presentations, whether a promotional presentation is truthful and non-misleading involves a fact-specific determination that takes into account such factors as how the information is presented, the type and the quality of the data relied on to support the presentation, and the contextual and disclosure

considerations.

The draft guidance is intended to help firms understand how to support and present information in promotional materials for their biosimilars and their reference products in a truthful and non-misleading way.

How should firms identify reference products and biosimilar products in promotional materials? A biological product may be identified by its proprietary name, proper name, or core name in promotional materials, depending on the context in which the product is being described.

When developing promotional materials for their products, firms should carefully evaluate the information presented in their materials to ensure that in each instance a product is addressed, the materials correctly and specifically identify the product to which the information applies.

Clearly and correctly identifying the relevant biological product or products in promotional materials can help prevent presentations that are inaccurate because they

attribute data or information to the wrong product. It can also help the audience identify which product or products are the subject of a particular promotional presentation.

For instance, if a biosimilar's FDA approved labeling uses the core name of the reference product followed by the word "products" to convey that a risk applies to both the biosimilar and the reference product, it would be appropriate for similar presentations about this risk and promotional materials for the biosimilar to use this nomenclature.

As another example, if promotional materials include information from a study that used a non-U.S. licensed comparator biologic or otherwise mentioned such products, the non-U.S. licensed comparator should be accurately identified as such in the materials.

Questions 3 and 4 of the draft guidance are focused on promotional considerations for biosimilars and they address questions regarding the inclusion of study data and information in

promotional materials for these products.

In its guidance entitled Labeling for Biosimilar Products, FDA recommends that a biosimilar's FDA-approved labeling incorporate relevant data and information from the reference product's FDA-approved labeling, and this includes incorporating clinical data that supported FDA's finding of safety and effectiveness for the reference product in the biosimilars labeling.

If a firm wants to provide information from studies that supported the licensure of the reference product in promotional materials for its biosimilar when this information is included in both the reference product labeling and the biosimilar labeling, the firm should refer to the biosimilars labeling for this information.

For example, in the case where a biosimilar is licensed for fewer than all conditions of use for which the reference product is licensed, the biosimilar's labeling generally will include information from studies on the reference product that is relevant to those conditions of use for

which the biosimilar is licensed. The firm developing promotional materials for its biosimilars should look to the biosimilar's labeling for this information.

FDA has also recommended that the FDA-approved labeling for a biosimilar generally not include data and information from the studies conducted to support a demonstration of biosimilarity between the reference product and the biosimilar.

We have heard that firms are interested in communicating data and information from these studies to healthcare providers and other interested parties, however, and have questions on whether and how this kind of information can be presented in promotional materials for their biosimilar.

If a biosimilar's FDA-approved labeling does not include information from studies conducted to support a demonstration of biosimilarity between the reference product and the biosimilar, promotional presentations of such information

should be consistent with the biosimilar's FDA-approved labeling and be truthful and non-misleading as described in FDA's guidance on medical product communications that are consistent with the FDA required labeling, which is referred to as the CFL guidance in the draft guidance.

This guidance describes FDA's thinking when examining a the consistency of a product communication with the product's FDA-approved labeling. It discusses how FDA determines whether a communication is consistent with the product's FDA-approved labeling and provides general recommendations for conveying this type of information in promotional materials in a truthful and non-misleading way.

When information from the studies that supported a demonstration of biosimilarity is not included in the biosimilar's FDA-approved labeling, firms should apply the principles outlined in the CFL guidance if they include information from these studies in promotional materials for their biosimilars.

As generally discussed in the FDA-FTC joint statement, ensuring that advertising and promotional communications subject to FDA regulation are truthful and non-misleading can help to protect and promote public health by enabling patients and healthcare providers to make decisions based on the accurate information.

FDA is concerned that false or misleading comparisons between reference products and biosimilars in FDA-regulated promotional materials can undermine public confidence in these products and negatively affect public health.

What should firms consider when comparing reference and biosimilar products in their promotional materials? FDA's licensure of a biosimilar means that the agency has determined that a biosimilar is highly similar to the reference product notwithstanding minor differences in clinically and active components and that there are no clinically meaningful differences in terms of safety, purity, or potency.

FDA recommends that firms carefully evaluate

presentations that compare reference products and biosimilars and avoid presentations that represent or suggest that a biosimilar is not highly similar to the reference product or that a clinically meaningful difference in terms of safety, purity, or potency exists between the products.

Although assessment of each promotional presentation involves a fact-specific determination, such presentations, including those suggesting that the reference product is safer or more effective than the biosimilar or that a biosimilar is safer or more effective than its reference product, are likely to be false or misleading.

For example, a presentation suggesting that a biosimilar is superior to its reference product, based on a difference that is not clinically meaningful between the rates of occurrence of a particular adverse reaction observed in a study that supported the demonstration of biosimilarity between the two products, would be misleading.

It's also possible that individual

statements of accurate information could contribute to a misleading presentation when provided in the comparative context.

For example, in the case of a biosimilar that is licensed for fewer indications than the reference product, presentations that create the net impression that the biosimilar is, in general, less safe or less effective than the reference product, simply because the biosimilar is licensed for fewer indications than the reference product, would be misleading.

Also, presentations suggesting that a biosimilar is less safe or less effective than the reference product in a particular indication, because the biosimilar's licensure for that indication was based, in part, on extrapolation, would be misleading.

Promotional presentations about a biosimilar's licensure, a biosimilar to a reference product should accurately describe the biosimilar product. For example, promotional materials for a biosimilar that FDA has not licensed as

interchangeable should avoid creating the impression that the biosimilar has been licensed as interchangeable with the reference product because this would not be accurate. Promotional materials for a reference product should avoid creating the impression that a biosimilar is less safe or less effective than the reference product because the biosimilar has not been licensed as interchangeable with the reference product.

A biosimilar is not required to be identical to the reference product in order to be licensed, rather licensure as a biosimilar means that the biosimilar has been found to be highly similar to the reference product notwithstanding minor differences in clinically and active components and that there are no clinically meaningful differences between the biosimilar and the reference product in terms of safety, purity, or potency.

Therefore, representations or suggestions that a finding of biosimilarity means that FDA determined that the reference product and the biosimilar are identical to one another generally

would not be accurate, but promotional materials for a reference product should avoid presentation suggesting that the biosimilar is not as safe or effective as the reference product because it is not or may not be identical to the reference product.

I'll now turn it over to Dom to discuss the examples talked about in the draft guidance.

Presentation - Dominic Cirincione

MR. CIRINCIONE: Great. Thank you, Betsy. Thank you very much.

(Pause.)

MR. CIRINCIONE: Well, I'll just keep going.

Question 7 in the draft guidance provides three longer examples to help illustrate some of the general considerations discussed within it. For the purposes of these examples, we used a fictional biosimilar called NEXSYMEO and a fictional reference product called JUNEXANT. NEXSYMEO and JUNEXANT are both replicamab products.

The first example describes a scenario in which a firm provides the route of administration

dosage form and strength of the biosimilar NEXSYMEO in promotional materials for NEXSYMEO, and it includes a claim that NEXSYMEO has the same route of administration, dosage form, and strength of the reference product.

FDA would not expect to object to this kind of a presentation because it is supported by NEXSYMEO's licensure as a biosimilar to JUNEXANT, which is based, in part, on information showing that NEXSYMEO has the same route of administration, dosage form, and strength as JUNEXANT.

In the same materials, the firm includes a claim that NEXSYMEO can be considered for patients who are new to replicamab product therapy for the treatment of a licensed indication and for patients currently being treated with JUNEXANT for the same indication.

The claim is supported by information submitted as part of NEXSYMEO's application for licensure as a biosimilar to JUNEXANT, including data from a comparative clinical study that included patients who underwent a single transition

from JUNEXANT to NEXSYMEO and patients who were new to replicamab product therapy, which supported a demonstration of no clinically meaningful differences between NEXSYMEO and JUNEXANT. FDA, again, would also not expect to object to this kind of presentation.

The second example describes another scenario in which FDA would not expect to object to the presentation described. In this example, as part of NEXSYMEO's application for licensure as a biosimilar to JUNEXANT, FDA evaluated a comparative clinical study that included patients treated with a non-U.S. licensed comparator product to support a demonstration of no clinically meaningful differences between NEXSYMEO and JUNEXANT.

NEXSYMEO's firm wants to present data that is not included in NEXSYMEO's FDA-approved labeling about outcomes observed in that study. So the firm develops a presentation that is consistent with the recommendations in the CFL guidance, which Betsy mentioned earlier, including recommendations on appropriate scientific and statistical support.

The firm clearly and prominently provides contextual information about the study design, the methodology, the role the study played in the biosimilarity evaluation, relevant data on NEXSYMEO's FDA-approved labeling, and any material limitations in that data. The firm also accurately describes the comparator used in the study as a non-U.S. licensed product. FDA, again, would not expect to object to this kind of presentation.

Example 3 illustrates a presentation that FDA would consider misleading, however, in this scenario, promotional materials for JUNEXANT state that in a clinical study, patients on JUNEXANT experience a numerically higher overall response rate than patients on NEXSYMEO JUNEXANT.

The basis for the statement is a comparative clinical study that supported a demonstration of no clinically meaningful differences in terms of safety, purity, and potency between JUNEXANT and NEXSYMEO.

Although this statement accurately conveys the reference product's higher numeric overall

response rates observed in the study, the materials do not disclose that this difference in response rates was not statistically significant, and they do not describe the study design or include any other appropriate context.

By focusing on the numerical differences in response rates, which was not statistically significant, the presentation misleadingly implies JUNEXANT is superior to NEXSYMEO. It also misleadingly implies that there is a clinically meaningful difference between the products when the data presented in the promotional materials do not support that conclusion.

How can firms request FDA review of draft promotional materials? Well, FDA encourages firms voluntarily to seek feedback on promotional materials for reference products or biosimilar products before their dissemination to follow the current process for submitting draft promotional materials to FDA for comment.

We remind firms that they are also subject to the postmarketing requirements for submitting

promotional materials to FDA like all other prescription drugs under Form 2253. Firms can visit OPDP's website for more information on the submission of promotional materials to FDA and for general information on our regulation of prescription drug and biological product, advertising, and promotional labeling.

We remind firms that in addition to the considerations specifically outlined in this guidance, they should ensure that their FDA-regulated promotional materials otherwise satisfy all the applicable requirements from the Food, Drug, and Cosmetic Act and FDA's implementing regulations related to promotion for prescription drug products.

Firms should also ensure that they comply with the provisions obligating them to update the FDA-approved labeling for their products to ensure that the labeling is not false or misleading or for any other reason.

This is a draft guidance, as you all are aware, and as such, we are looking forward to

receiving and then reviewing the comments submitted to the docket. As noted in the Federal Register notice that announced the availability of the guidance, in addition to the draft guidance itself for comment, we also are seeking input on specific promotional considerations for interchangeable products as well.

Thank you very very much. I'll turn it back over to Caty.

Panel Discussion - Catherine Gray

MS. GRAY: Thank you, Dom and Betsy. I wanted to follow up with just a few questions for you.

Dom, the draft guidance states that it does not cover considerations you need for promotional materials for interchangeable products. Does that mean that the Q&A's in this guidance don't apply to interchangeable products at all?

MR. CIRINCIONE: The guidance does not address considerations unique to promotional materials for interchangeables because FDA is still contemplating what, if any, considerations are

unique to such promotional materials.

We are looking forward to the stakeholder input regarding what, if any, interchangeable specific promotional considerations exist and what other considerations can help FDA-regulated promotional materials convey truthful and non-misleading information about interchangeables for a variety or various audiences.

MS. GRAY: Thank you. I can echo Dom's comments that we're looking forward to feedback from our stakeholders on this topic as well.

MS. GRAY: Betsy, the examples throughout the draft guidance suggest that an evaluation of whether comparisons between reference products and biosimilars are truthful and non-misleading can be quite nuanced. Do you have any more advice on how firms should approach these presentations and promotional materials for the reference and biosimilar products?

MS. PEPINSKY: Yes. FDA appreciates the complexities around these types of presentations, and as noted in the draft guidance, they do require

consideration of the specific facts. In general, however, firms should keep in mind that whether presentation is truthful and non-misleading depends, among other things, not only on the specific claims in isolation, but also the net impression to which those claims contribute.

So we encourage firms to carefully consider individual claims in a promotional piece, as well as the presentation as a whole, considering the overall impression it makes about the safety and effectiveness of the product.

I would just note that we make the same recommendation not only for firms evaluating proposed comparisons between reference products and biosimilars, but also for firms developing any presentation in FDA-regulated promotional materials for prescription drugs and biologics.

MS. GRAY: Thank you very much for your attention to our panel. At this point, we're going to wrap up for the morning session. I encourage you to enjoy your lunch, and we will see you back here at 12:15. Thank you very much for your

attention.

(Applause.)

(Whereupon, at 11:21 a.m., a lunch recess was taken.)

A F T E R N O O N S E S S I O N

(12:15 p.m.)

MS. FALB: Thank you for your attention. This panel is What's at Stake? The Benefits of Competition. I want to let you know for this structure, we've organized this panel into three sections. There will be a presentation by one of our panelists at the beginning of each section and then some prepared questions and answers. The sections we will cover our biosimilar markets overview; the impact of biosimilar entry; and barriers to biosimilar entry.

Before we get started, I would like to ask the panelists to introduce themselves. I will go first, and then we can continue to my left. My name is Alison Falb, and I am a regulatory counsel in CDER's Office of Therapeutic Biologics and Biosimilars.

DR. HERNANDEZ: My name is Inma Hernandez, and I am faculty at the University of Pittsburgh.

MR. BRILL: Hi, everybody. I'm Alex Brill, and I'm a resident fellow at the American

Enterprise Institute.

MR. SCHMIDT: Good afternoon. I'm David Schmidt. I'm an assistant director in the Bureau of Economics at the Federal Trade Commission.

MR. SCHICK: Hello. I'm Andreas Schick. I'm the director of economics at the FDA's Office of Program and Strategic Analysis.

MR. AITKEN: Good afternoon. I'm Murray Aitken. I'm executive director at the IQVIA Institute.

MS. FALB: We're going to be starting with a presentation of slides by Murray Aitken, so I think we can pass you the clicker and hope for the best.

(Laughter.)

Presentation - Murray Aitken

MR. AITKEN: I'm going to spend a few minutes just to frame out the overall biologics market so that we can also understand biosimilars in the context of the overall market and talk a little bit about the market dynamics that we see playing out based on IQVIA data and measurement of the market, both on a dollar and a volume basis.

Just a comment about the data that I'll be drawing from; this is data that we gather at IQVIA from a variety of sources, including wholesalers who track the flow of medicines, all types of medicines, through the distribution system. We also gather data from manufacturers who are direct shipping their products.

We also gather data from retail pharmacies for that part of the market. We also have access to insurance claims data. So we tend to take a 360 degree-ish view of what's happening and consolidate all of that to develop an overall perspective of the market.

When we measure the size of a market in dollar terms, we generally use what we call invoice price, which is what we capture from wholesalers. So you can think of it as list price, but it's before the application of rebates and discounts, which we know can be significant. However, we do estimate the magnitude of the rebates and discounts and other forms of price concessions that go on in the marketplace.

So you'll see some of the charts where we are using net prices, and when we say net, we're looking at that from the perspective of manufacturers, so the net amount that is received by a manufacturer.

Let me summarize the points, and I've got slides to support these. As we've already heard today, biologics are a growing share of the overall market, and certainly relative to small molecules, we've got different dynamics playing out both on what happens when a drug loses exclusivity front, as well as the mix of new drugs coming out of the pipeline through FDA approval and into the marketplace.

When we look at the pipeline, particularly the late-stage clinical development pipeline products that are in phase 2 clinical testing or later, it suggests that we're going to continue to see the growth dynamic of biologics not only in traditional biologic oriented therapy areas but in other disease areas as well.

Biologics reach the market through multiple

channels and pay types, and this is where things get complicated quickly as, again, you've heard reference to this morning. I don't think we're going to have enough time to go through all the pieces of the market and all of the characteristics and payment dynamics, but understanding at least a relative size and importance of different parts of the market we think is important in order to understand not only what's happening in biologics, but specifically in biosimilars as well.

We'll take a look at the dynamics that we see play out in the small molecule part of the market and then the large molecule or biologics part of the market, and we look at this in a couple of ways.

One is what share of the dollar value of the market is subject to generic competition or biosimilar competition for large molecules, and then for that part of the market, what's the relative volume dispensed or used as the generic or biosimilar relative to the total use of those molecules. Those are the two metrics that we use

to try to assess how the market is evolving.

Starting with the big picture, and this is on an estimated net price basis, we've got a total medicine market in nominal dollars of $344 billion in 2018. We're still polishing the 2019 numbers. That total is up 21 percent since 2014. But you can see in dark blue, the small molecule share has fallen from 70 percent to 58 percent over this 5-year period, so all the growth is essentially coming from the biologics part of the market at the top, which has gone from about $85 billion dollars in 2014 to $144 billion in 2018.

Again, that's a reflection of the shift in science, the movement, the gradual movement towards biologics in R&D, as well as the impact of the entry of new competition when patents expire or other forms of exclusivity expire.

If we just convert things to a real net per capita basis -- we've made those adjustments to the earlier numbers, adjusting for inflation and adjusting for population growth -- the pattern is similar, but I think it's also useful just to look

at the number at the top, $1044 per person -- this is in 2019 dollars, I believe -- that was spent on all medicines of which $435 was for biologics, up from $291 in 2014, and then the spending on small molecules has fallen by about 12 percent.

So you've got a 50 percent growth in the top of the chart and a 12 percent growth in the bottom of the chart. That's why we're all here.

Just looking into the pipeline, the trend of new drugs towards biologics will continue to grow. Sometimes, frankly, it gets overstated. Right now, about 40 percent of new drugs are biologic; 60 percent are small molecules. Not all innovative targeted cancer treatments are biologics. There's a good number of small molecules in there as well.

I do notice sometimes there's a little bit of confusion as to what's biologic and what's small molecule when it comes to innovative medicines, but we show here a number of the therapy areas, again, including ones that in the past have not been particularly biologic oriented, and just show the share of the late-stage pipeline in these disease

areas that is represented by biologics or biotech products.

In terms of how these biologics reach the market, and now I'm switching to an invoice price level because, frankly, we don't have net prices at the payer type or channel level, so we can only estimate net prices at the overall market level. On an invoice price basis, retail and mail represents about 60 percent of the total biotech market and 40 percent in non-retail.

On the right-hand side, we've got some of the smaller segments of the market. So starting at 12 o'clock and moving clockwise, we've got the retail and mail commercial payer market, which is 26 percent of the total; then we've got retail and mail Medicare Part D market, an additional 17 percent; retail and mail Medicare Advantage, 5 percent; and then retail and mail managed Medicaid at 8 percent; followed by retail and mail fee-for-service Medicaid at 2 percent; and then we've got 1 percent retail and mail cash.

Then continuing on, we've got the non-retail

part of the market, non-retail commercial hospitals about 3 percent; commercial office site about 13 percent; and then non-retail Medicare fee-for-service, 2 percent; followed by non-retail Medicare Advantage, 11 percent; and non-retail Medicaid and other, 12 percent.

As you see on the chart, these are directional estimates. Frankly, I don't think anyone has a good way of teasing out these different parts of the markets, but I think it is important and relevant to understand the different segments of the market to the extent that there are different incentives. There are different reimbursement levels that play out in each of these segments. I'm sure we'll talk about this as we get to the discussion.

Just looking at the top 10 biologics that are on the market as of September 2019, this is invoice price sales. I just thought it was useful to look at the cumulative invoice sales of these drugs since they were launched and through September of 2019. This is for the branded version

of the drugs if there's a biosimilar in the market.

As you can see, all the top 10 have cumulative sales of more than $40 billion. I also just indicated the number of years since their launch, which also speaks to these are pretty old drugs by now.

I think we don't have quite enough discussion about the extent to which there is a next-generation treatment available in the case of these molecules in particular and the extent to which the dynamic of investing in and promoting a next-generation of biologic, to the extent we're going to see likely see more of that going forward than we have in the in the past, where manufacturers have not necessarily been particularly motivated while they don't face competition from biosimilars.

Just to wrap up in terms of what we see happening, again, at the overall market level in terms of the dynamics of generics and biosimilars, this is our view of the small molecule market. The bars are measuring the percentage of the small

molecule market that's accessible to one or more generics by molecules, so we build this up molecule by molecule. This is in quarterly view, and from 2014 to the fourth quarter of 2019 we're at 40 percent.

Basically, 40 percent of the value of the small molecule market is subject to a generic, and then the green bar at the top, when a generic is available, it's dispensed in volume terms 96.5 percent of the other time. This is what we're used to in terms of the small molecule market.

Here's the same view but now for biologics, starting at q1 of 2013. So again, the bars show what percentage of the value of the market is subject to a biosimilar. You can see the additional biosimilars entering the market. These are not approvals; this is entering the market. You can see that now 17.5 percent of the value of the biologics market is now from molecules that have one or more competitors as biosimilars.

The green line is tracking, again, the volume share that the biosimilar has of the

molecule for which there is a biosimilar available, and that of course goes up and down with the entry of new biosimilars, so it resets the denominator. But we're now at 20.2 percent of the volume of biologics dispensed. When there's a biosimilar available, it goes out as a biosimilar.

This is what we watch the most, I would say, in terms of the impact and the uptake, at least from a market dynamic perspective, a separate discussion on pricing a course. But if we just look forward a little bit, the dark blue bar here and the green line are the same as on this chart, just rescaled because we've introduced now the biologic molecules for which a biosimilar has been approved but not yet marketed, so that's the light blue.

That includes adalimumab, etanercept, and teriparatide, where there are biosimilars approved. If you include those in the calculation, then we're at 50 percent of the value of the biologics market subject to biosimilars. Now, that won't actually happen until 2023 or some time later, but it's a

sign of where we're going in terms of the overall market place for biosimilars.

So with that, I will pause. Thank you.

MS. FALB: Thank you.

As we continue our conversation about the biosimilars market, what aspects of that market are most important to keep in mind, or would anyone on the panel like to highlight?

MR. SCHMIDT: Sure. I'll take a first crack at that. I'm going to adopt an unfamiliar position for me, which is to caution against too much pessimism. I think we see statistics like what Murray put up, which are incredibly informative and useful, but we shouldn't interpret it as evidence that the biosimilars are a failure or are in some way lagging way behind what these small molecule generics have accomplished.

It's very early days for the biosimilars right now, and it's also very early days for economists and others to be analyzing these markets. So we're still working on gathering good data, and I know many of the people on this panel

are contributing to that and it's great to see.

But to get to the heart of the question, I think what would be really useful would be able to look at good comparison groups like how are biosimilars doing relative to other drugs that are paid for by the same types of payers in the same dispensing settings and do we see a huge difference there.

Is it something inherent about the payer type or the dispensing setting that's causing the innovator products to hold on to market share more than they do for the stereotypic small molecule drug dispensed at your local pharmacy?

I think, as of yet, we don't know the answer to that, and I think some of these researchers are pushing in that direction, and it's great to see. But I think, obviously, it has been highlighted, payer type is important, dispensing location is important, and keeping that in perspective when we're looking at some of this information I think is incredibly important.

MR. BRILL: Just a quick addition or comment

on Dave's comment. First, I fully agree that we can say we're in transition. We're not in equilibrium at the moment. We are in the beginning of a process and the market is continuing to evolve.

The question that we're all wondering, I think, is what will that equilibrium look like and what can we be doing to make sure that it is as robust a marketplace as possible? But these snapshots are just that, snapshots in a moment as we move towards a more robust market that's evolving.

But I would also say that with regard to trying to find comparators, there's, in my mind, two ways to think about that. One, if I understand correctly, Dave's comment is to try to find similar scenarios in the small molecule world and look for differences. I think that there are lessons to be learned from those types of comparisons, but also within the biologic/biosimilar marketplace by payer type.

One of the things we know in the small

molecule generic space is that we have really high utilization rates of generics pretty much all the time. Shortly thereafter of a launch, we don't see wide disparities by payer type and generics. Another way to look at this in this market is to say are there differences by payer type, or location, or dispensing mechanism. I think it's reasonable to think that there shouldn't be.

So not necessarily are we're going to achieve the realization rates that we see in the small molecule space; I think the competition dynamics are different there. But there's no reason in my mind -- and I'd be concerned if we saw very different behaviors in the Medicaid market than we see in the Medicare commercial market.

MS. FALB: Following up on that point, are there important differences? It sounds like you don't think that there should be, but perhaps there are between biologics and expensive small molecule drugs that might impact their respective markets.

You can take it or someone else can take it.

DR. HERNANDEZ: Well, I think -- and I'm

going to try to tie it with what I'm going to say in the next few slides -- it comes back to financial incentives. We know that we usually reimburse for generics based on a maximum allowable cost, so then pharmacies can dispense whichever generic they want because everything is going to be at the same level.

For that reason also, discounts don't play an important role in the small molecule generics. We have basically brand names with high-list prices and rebates higher or lower, and then we have generics where there's transparency, and the list price is more representative of what we're paying.

I'm going to talk a little bit about how that's very different for biosimilars, and I think, especially for the drugs that go through the pharmaceutical benefit, that's an important differentiation with small molecules, how we're paying for them and how we're going to continue to pay for them. If biosimilars are not interchangeable, we cannot pay all of them in a similar way as we're paying for generics, and

that's a differentiation that is important to make, I think.

MS. FALB: I think we can use that as a segue to your presentation.

Presentation - Inma Hernandez

DR. HERNANDEZ: I'll get started in the meanwhile and say that I'm going to present a couple of studies that we've done in my research group around biosimilars. The first one of them, we're going to describe what happened to prices of originator biologics when they're faced by similar competition.

On the second of them, we're going to talk about financial incentives in Medicaid in the uptake of the biosimilar for Lantus, that I know is not a true biosimilar because it was not approved through a biosimilar pathway, but for financial incentives, works in a similar way.

So let's start with the first one. I'm so happy the slides are working. Here we looked at all originator biologics that faced biosimilar competition by December 2018. Again, when I say

biosimilar competition, I also include within molecules substitutes that were not approved through the biosimilar pathway. We had the four that are listed on the slides.

Here, we wanted to look at what happened to net prices, list prices, and discounts before and after the launch of the biosimilars. I know that Murray already introduced the contents of list price, but I'm just going to go through them again because it's important to know what's in the net price.

List prices represent what wholesalers are paying to pharmaceutical manufacturers, but we know this doesn't represent the whole picture. If we have a drug covered through the pharmaceutical benefit, the wholesaler will sell the drug to the pharmacy that will dispense the drug to a patient. We often have patient insurance plans, and the health insurer will reimburse the pharmacy through a pharmaceutical benefits manager.

Often pharmaceutical benefits managers and health insurers negotiate formulary placement with

the pharmaceutical manufacturers for discounts or rebates. These discounts are proprietary information because they are confidential, so they are not available to us for research or for any other purpose.

However, we found out a few months ago that there is an investment firm called SSR Health that tries to calculate discounts using company reported sales to stakeholders. Since these data come from company reported sales, they are only available for drugs manufactured by publicly traded companies, so we will not have BI or Purdue Pharma for instance.

The denominator to estimate net comes from Symphony Health, and it tries to estimate all the units sold in the U.S. in a given quarter. Because of this calculation, net represents the average amount that pharma gets per unit of product, and this is net of all discounts, not only rebates to payers but also coupon cards, 340(b), discounts to federal service, anything that you can make. Using this net price, the discount is estimated as the difference, and they are able to separately

estimate discounts in Medicaid and in other payers.

I'm not going to present another paper where we've validated the data, but we got last week in JAMA a big paper using all of these, and we showed in very comprehensive sensitivity analyses how this data is pretty robust to the research. So if you are wondering about the validity, I'll refer you to that.

Now I'll show you the results of this one. This is for filgrastim. You can see that list and net prices increase in parallel until 2013 or so. Net prices for the originator biologic started to decrease in 2015 around the time that Zarxio reached the market, and this was driven by discounts in payers other than Medicaid.

Obviously, the Medicaid discount was not going to increase if the list price is not increasing any further. You can also see how the net price continues to decrease over time with the entry of more competition.

For pegfilgrastim, we only have one data point after biosimilar entry, so the data is not

very robust. But you can see a very similar story where list and net prices increased in parallel, and then once we have competition, list prices stagnate and net prices seem to decrease.

This is infliximab, very similar. We see list and net prices increasing in parallel until 2013. You can see that net prices have started to decrease around 2013, which is a few years before biosimilar entry. I would like to acknowledge that there are many other factors in the market other than biosimilars.

In this case Simponi Aria, which is a direct competitor, was approved in 2013, so it's hard for me also sometimes to say that all of these decreases that we are seeing are just a product of biosimilar competition. Anyway, you can see that a few years later when biosimilars did come to the market, prices continued to decrease.

Finally, these are the results for Lantus. You can also see the net prices have started to decrease before Basaglar was approved, but there were other molecules in the long-acting insulin

market. I'm not sure of the direct competitors of Lantus, really, but there's also been a lot of social pressure against prices of insulin, so I think there's also a lot of factors that play in account here. All of these results were published last year if someone wants to look at them in more detail.

I think this shows, in general, as a summary, the list price of originator biologics is stagnated but did not decrease after biosimilar entry, however, net prices did decrease. This was driven by increasing discounts in payers other than Medicaid.

I was asked to talk where the net prices start to decrease before or after biosimilar entry. In the case of infliximab and Lantus, we see that they start to decrease before but, again, there are factors at play in the market, so I don't want to fully attribute these two biosimilars.

I was also asked to talk about the more biosimilars that come into the market, the higher the discounts we see. I think we don't have enough

data to answer that question yet. For instance, for filgrastim, we see three competitors and net prices have decreased substantially, but the others, I have data to compare only half, one data point after the entry.

So I think once we have more data, we'll be able, really, to compare what's the difference in net price between biologics that have seen three biosimilars versus those that have seen one. But again, I don't think this is a fair comparison right now because I don't have enough to say that.

With that, we'll change pace to the second paper, which is very similar. It looks at the uptake of Basaglar in Medicaid. Since the passage of the ACA, states collect rebates for drugs that are reimbursed under Medicaid managed-care organizations.

What does this mean? We have the same scale that we had before, and this patient is covered under Medicaid. In this case, it's under a Medicaid managed-care organization that has a contract with a state Medicaid agency. Before the

ACA, the rebates for the drugs used by this patient could go to the MCO, which are the ones paying for drugs.

After the ACA, the rebates for these drugs go directly to the state. So basically the MCO is paying the list price, but the rebates are going to the state. This creates differential incentives in the sense that states are incentivized to use drugs that maybe have higher list price, but after discounts have a lower net. However, MCOs are incentivized to use drugs with a lower list price because they don't see the rebate money, because it comes back to the state.

In some cases, to promote the use of branded products among MCOs, Medicaid and state agencies are implementing preferred drug lists, which are a compilation of drugs that they have to favor over others.

Here, we look at the utilization of Basaglar in 2018 before four types of states: states that have fee-for-service Medicaid only; states that had managed-care organizations but with carved-out drug

benefits, meaning the drug benefits were still paid on a fee-for-service basis; states that had MCOs, and the MCOs did not have to follow preferred drug lists for insulin glargine; and finally, states with MCOs where there were preferred drug lists for insulin.

We looked at all the states with preferred drug lists, and we saw that all of them that included insulin glargine in the preferred drug lists, they all preferred Lantus over Basaglar, 100 percent. The data to use these comparisons was Medicaid drug list utilization data, which as you may know is publicly available. The outcome was the proportion of insulin units paid for insulin glargine that was accounted by Basaglar.

Here you can see the results. You can basically see that the market share of Basaglar is close to zero in all the states, except for the ones that have Medicaid managed-care organizations that are not subject to preferred drug lists. In the paper, we go a little bit further and we show the correlation between the penetration of

managed-care organizations and the uptake of Basaglar, and you can see that it's pretty significant.

In summary, we only see a substantial uptake of Basaglar in the states that have Medicaid managed-care organizations that are not subject to preferred drug lists. I think this is timely because more states are implementing preferred drug lists these months and these years, and they are also including more drugs in the preferred lists. Originally, many PDLs started just with the drugs for hep C, but increasingly, they are implementing more drugs that are subject to the preferred drug lists.

As a summary of my presentation, I don't think the biosimilars are showing they're exerting some competition in the market. It does seem like all the competition happens in the discount space, so it's very important to not only look at what happens in the list price but trying to use these estimates, the same as Murray talked. The best system we have is net prices because it's really

where we see the competition. That's all I have.

MS. FALB: Thank you.

When thinking about the impact of biosimilar entry on the market, what impacts do we see or do we anticipate that are positive, how do we further those, which do we see or anticipate that are negative, and what could be done to either minimize or prevent them?

DR. HERNANDEZ: I always make this comment when talking about list and net prices, and I'm also going to make it here. I think it's good that net prices are decreasing. I think that's always a good sign now. It means that premiums are not going to increase at least.

I'd still like to point out that there are a lot of patients exposed to list prices. We know that co-payments are usually based on list price, and we know that patients on high-deductible plans or without insurance, they're also exposed to list price.

So as much as we like to look at the net price data because it's probably a good sign now of

what payers are supposed to, I think we need to remember that the patients that probably have the most access barriers are the ones that are exposed to list. So I think we still need to keep that in mind that there's value in list price.

MR. SCHMIDT: I agree with that, but I would also add that I think it would be useful to look directly at what the patients are paying to the extent that we have claims data sets that might identify exactly what the incidence is on patients and not just realize list price as a proxy for that.

DR. HERNANDEZ: I forgot to say that. Yes. We haven't looked at out-of-pocket payments yet, but I would like very much to do so. But I'm looking for a grant to do that, so if anybody's interested in funding this type of work, [indiscernible].

MR. BRILL: I'll just add that when we think about the winners, we want to think, just as Inma's presentation shows, that the effects across the whole market on all the reference product prices

are relevant when we think about the savings. I think this illustrates one of the real differences in the market for biologics and biosimilars relative to the market in the small molecule space for brand and generic products.

We're seeing, at least initially, a very different dynamic, where as we know in the small molecule space, the reference products, the brand products, are generally holding their price constant when generics enter and giving up large market shares, and we're seeing a very different behavior among reference products in the biologic space.

I think that that's interesting. I think that that was unanticipated by many of the folks who were trying to think about what the cost savings in this market might be. But at the same time, it may present challenges ultimately for the desired maturity of this market because is it the ability of the biosimilars to compete or is their ability relative to the reference product, their pricing relative to the reference product?

So there needs to be some opportunity for them to earn back their large fixed-cost investments, so there's a little bit of a tradeoff in that dynamic.

MR. SCHMIDT: The thing I was really struck by is it suggests to me that the competition here is more similar to the classic brand-on-brand competition that we see in small molecules, where they don't generally compete on list price and do compete on rebates and other sorts of discounts, co-payment programs and such. I think that's an interesting dynamic in this market.

MR. AITKEN: I think what we see is not so much the distinction between the small molecule and the large molecule, but it's more the distinction of the payer type and the channel. This notion that we've had for a while that biologics are different, I think we need to get beyond that and say more different payment types.

Fee-for-service Medicaid is different than MCO managed-care Medicaid; that Part B and Part D is different; that commercial is different than

Medicare and so on, and to look through that lens at what's going on as opposed to is it a large molecule or a small molecule, now that we have the cohort of large molecules approved and able to access the market that we didn't have three years ago or five years ago.

MS. FALB: What impact do you anticipate that the entry of interchangeables will have on the market?

DR. HERNANDEZ: I think we discussed it this morning. I think it will be important for the ones covered under mostly the pharmaceutical side because payers will be less concerned about rebate traps. If they are interchangeable, you're going to be able to virtually shift all of the patients. So I think that will be a big improvement in that sense.

Still, getting back to the point that we're making, it's very important to think about how we are paying for drugs and how we're going to pay for interchangeable biologics and interchangeable biosimilars.

MR. BRILL: I think that's right. I think it's to be determined how the pricing works for an interchangeable obviously because we don't have them. As was discussed in the morning session and as Inma just noted, it's only relevant, I think, in the pharmacy space. But I do think there is the potential for simplicity and reduced friction in the market for an interchangeable biosimilar that could facilitate higher uptake rates.

MS. FALB: Thank you. Alex, if you could present?

Presentation - Alex Brill

MR. BRILL: Thank you very much, and thank you, everyone, for being here this afternoon. I was asked to speak about some of the barriers that we see in the marketplace today for biosimilars, and this is based on some work that I've done in the last few years trying to identify, categorize, and put in buckets these types of barriers. One of the big themes there is there's not one, there's many, and it's the cumulative effect of these barriers that I think may be impeding the market to

some extent.

I want to talk about this from a broad perspective when we think about barriers. I think the first thought when we say "barriers" is we think barriers are bad; they're things that are blocking.

I want to step back a bit and say we need to think about the barriers in the broadest terms possible. There are some good barriers, as I'll get into, and there are certainly many bad barriers. And I think we're here to talk about the bad barriers not the good barriers. But I think it's important to recognize that barriers can be a useful tool, can provide a service, and can provide value, and then I'll talk about some of the consequences and policy implications.

As I mentioned, when we say "barriers" I think we think of that as being a negative. I want to speak of two types of barriers. Besides just being good or bad, we can think of barriers as being barriers to entry and we can think of some barriers as barriers to utilization. The

utilization barriers I think our uniformly going to be bad. Once we have entry, we shouldn't be trying to inhibit the utilization of a product that is biosimilar and is less costly.

When we think about entry, just to be honest, I think it's a little bit more complicated and there are some appropriate barriers to protect both the innovator, to some extent, and to protect the consumer. That's not to say that all barriers to entry are good but it's mixed.

So what kind of barriers might be reasonable? Well, it's actually not controversial. I think that patents are barriers and patents are a valid and important part of this ecosystem here. BPCIA created an additional barrier, an exclusivity period.

I cut my teeth in this industry arguing over this exclusivity period with a Duke University professor named Henry Grabowski and the economics of exclusivity, and I lost that battle. I would have thought that seven years would have been a sufficient period of time, but I also think that

it's true that zero isn't the optimal period and that there's a balance to be struck.

I think this is important, in part, in the policy context because oftentimes the disagreement in policy circles between those who are interested in creating barriers and those who are interested in reducing barriers sometimes gets murky and there can be some crosstalk. I think if we split this debate, recognizing that there can be valid types of barriers, we can disarm some of the debate, and we can focus on those barriers that are negative and adverse to competition.

Finally, I think there's another set of non-controversial barriers, which is, in essence, the approval process is a barrier. Of course it is. It's costly, it's time-consuming, it's uncertain, and it's for the safety and efficacy of the product. It's in the interest of the patient. We all recognize the importance of having high standards. Even though those standards pose a barrier, they are barriers that are yielding good, good for both the patient of course, but good for

the market ultimately.

Then of course there are the bad barriers, the barriers that we need to identify and root out. Many of them were discussed this morning. Christine Simmon described them in the first session. They really fall across a whole host of categories. Some of them are policy related and some of them are more market-based. Some of them are things that regulators could do better or differently. They could try to reduce their burdens that they're imposing on the markets.

Some may be things that agencies could recognize as bad behavior in the market and they can work to mitigate. A few of them are up here, things like the contracting practices engaged in by the payers that may favor in a near-term arrangement a brand product, and thereby inhibiting or discouraging the development or the maturing of their biosimilar marketplace, and the rebate trap that we've discussed earlier.

While I think that patents are an obvious and good barrier in many senses, we should also

recognize that that's a tool that can and I think has been abused, whether that's the thicket or other strategies around patenting that are merely about extending monopoly beyond a reasonably fair period.

Then there are what I'd call knowledge- or information-related barriers, and this may be getting better. I think we're making progress on this front, but I think we still have a lot of education that needs to be done. I think the FDA is doing a great job of late in trying to fill those gaps, but we should recognize that those gaps still exist and they are not comparable. We haven't closed that gap the way we have I think in the small molecule space with generic drugs.

When we think about what the consequences of these barriers might be, the bad barriers, undue barriers to biosimilar entry will have many consequences, and I should say entry and utilization have many consequences. We're extending the monopoly rent period. That's what happens when we don't have competition.

As was just discussed a moment ago in the last presentation here, this can have implications for the patient costs. It depends of course on the benefit design, but the limits on competition are going to mean both higher premiums and presumably higher out-of-patient costs as well.

Also it's important not to think about this in a binary sense of is there a competitor or not, but the number of competitors is important, and we saw that in Inma's presentation. The more competition we can have for a given reference product, the more discounting, both with respect to the price of the biosimilar we should anticipate, as well as the price of the reference product. Together, those two prices are affecting the average price for a given product and the cost to the healthcare system in total.

Finally, there's I think a different type of barrier that's also worth recognizing. What we can do about it I think is tricky, and that's the reality of uncertainty in the marketplace. I think we've faced over the last decade a lot of

uncertainty, and we continue to face uncertainty in this biosimilar market. It's getting better. I think the work in the last year or so from the FDA has helped provide more information. I think that the number of products that have successfully gone through the approval process creates some degree of increased certainty and there's learning on both sides in that regard.

There are uncertainties that remain, and many of these are natural. They're natural in a free and open market, but it is uncertain to the biosimilar how the reference product is going to behave. As I was mentioning a few minutes ago, I don't think it was well anticipated that the reference product prices were going to evolve in the way that we've seen, and that has implications for pricing strategies for biosimilars. That's an uncertainty that over time will resolve itself as we have more experience.

There are a set of uncertainties, again, that can't necessarily be eliminated, but I think we should strive to mitigate, which include the

legislative and regulatory uncertainties, the degree to which, on either end, either at the capitol or in the agencies, new policies are being proposed, getting done, and not getting done. These uncertainties impose costs and in fact can encourage biosimilar manufacturers to wait. I think that there's important economic literature around uncertainty and the dynamic by which it causes market participants to wait.

So if we ask ourselves why isn't more things happening quicker, it's often because it may often be the case that participants in the market are saying if we wait, we'll know more about this market in the future. So we can combat that by trying to educate participants in the marketplace and have quick and clear and certain regulatory guidance.

All of this is to say -- in broad terms again; these aren't action items -- that it's important that we strive for an environment where the biosimilar manufacturers can anticipate the barriers that they're going to face. Barriers can

be okay, as I think I made clear, but they should be predictable. So something like an exclusivity period is a very definitive and clear barrier with a specific duration. Things like patent thickets are very unclear. So there's an incredible lack of predictability if there's a sort of self-help strategy that a reference product manufacturer can pursue.

To the extent possible, policymakers should try to minimize the costs related to approvals. Again, there's a push and pull here. Of course these barriers can be very valuable because they ensure, I should say, that the products are safe and are in fact similar, but that process we should strive -- and I think we will achieve over time streamlining in that process that will reduce those costs; then finally, the education piece, I think, the information gaps that exist in the marketplace.

It's not on this slide, but I think it's also important for policymakers to recognize that in an environment where there are impediments, barriers, that there can be a justified case, at

least on a temporary basis, for incentivizing the market to get over a hurdle. Because there are these natural incentives for biosimilars perhaps to wait, and for other market participants to wait, there may be natural logic for prescribers to wait before they start to prescribe biosimilars, to wait for more information.

To help resolve some of these frictions in the marketplace, I think it's worth considering -- and this was also discussed this morning -- incentive structures to try to help boost the system to get over an initial hurdle, to help address the information gaps, and to help demonstrate the opportunities and efficiency gains from the utilization of biosimilars.

These types of structures, whether it be the Shared Savings Program or the ASP plus 8 program that's been mentioned earlier, can help draw in participants to the market, both on the manufacturer side, as well as the payer and prescriber side.

So I'll just wrap up. I'll say that many of

these barriers have dissipated over time, particularly in the last couple of years as we've seen more guidance. We're doing better, but I think at the same time, there's still opportunities for policymakers to be engaged. They shouldn't be satisfied with the degree of competition we see in this market place today and should be pursuing policies to help further extend competition in the biosimilar marketplace.

Panel Discussion - Alison Falb

MS. FALB: Thank you.

For the panel, which barriers do you think have the greatest impact on the go or no-go decision for a biosimilar manufacturer?

MR. SCHICK: I always think that there are two really important barriers that are particularly problematic in this space. The first one is manufacturing these products consistently with good quality and then to scale up that production. It's just not as trivial in this market as compared to the small molecule market. Of course our small molecules are difficult to manufacture. The

biosimilars are just very difficult. It's hard to get the Coca-Cola recipe, as some people refer to it, right each and every time.

Another thing I think that is always important to emphasize -- and Murray kind of alluded to this in his talk -- is that this is a very lucrative market. This is the up-and-coming market for getting a high amount of sales.

There's a very extensive playbook that's well established for incumbents for how you deal with people not coming into your space and taking away your sales. Unfortunately, the playbook really benefits the incumbents very well. A lot of manufacturers, they're on both sides of this aisle. It's great when they're the incumbent and it's not so great when they're not the incumbent, and how to deal with that is very difficult.

One reason -- in addition to everything Alex mentioned -- why we might be seeing so many barriers is that people are fighting very hard to keep their very lucrative cash cows to themselves as long as possible.

MR. SCHMIDT: One thing I would add to amplify Alex's point about education is that I think one development that was very important in getting small molecule generics such great acceptance, obviously, was all the state substitution laws. I think FDA can play an important role in educating people and state capitals about what the appropriate role is for interchangeable and biosimilar products.

This is complicated stuff. Speaking as an economist, it's very complicated stuff. To the extent that we have scientists here that can help state legislators understand appropriate rules for substitution, I think that could be incredibly helpful.

MR. AITKEN: I would add one comment. We haven't really talked about markets outside of the U.S., but as we recognize, we live in a global world, and there is a relevance to the European markets as it relates to decisions made by manufacturers as to whether they will invest in the production capacity and regulatory submissions for

additional biosimilars to come to market.

I think when we observe what's going on in Europe, there's been a significant decline in the prices there for biosimilars: heated competition, use of winner takes all

price-based tenders and so on, all of which reduces the attractiveness of that part of the market; and it's not an insignificant share of the global market for biologics and the potential for biosimilars.

So there is an interconnectedness I think as we think about what's it going to take for us to have sustainable levels of competition in this market. We need more than just one or two players in biosimilars. We want to see 3 or 6 or 9 different types of competitors to make this market really effective. To that extent, I think just watching what's going on in other parts of the world, in particular Europe, is also very relevant.

MR. BRILL: Just to add on to Murray's point, what we've seen so far is competition in the blockbuster market of biologics, and when we think

about what other barriers exist, this is a high-fixed cost business. It's hundreds of millions of dollars to get in, not millions of dollars. And over time, I think there's a technology piece that we need to see evolved so that we can see competition in the smaller and the lower size market space as well.

MS. FALB: Thank you all very much.

(Applause.)

MS. IKENBERRY: Hi. My name is Sarah Ikenberry, and I'm the senior communications advisor in CDER's Office of Therapeutic Biologics and Biosimilars. I'm pleased to be able to discuss a very important topic related to biosimilar uptake and acceptance, and unfortunately it's not medical extended reality.

(Laughter.)

MS. IKENBERRY: It is improving stakeholder engagement, education, and understanding.

While we're working on the slides, I'll go ahead and let you know that the objective of the session will be to discuss some real-world

considerations surrounding biosimilars and how healthcare providers' and patients' knowledge, awareness, and perceptions regarding biosimilar and interchangeable products can impact uptake and acceptance.

I'm co-moderating this panel with Elizabeth Jex, an attorney advisor specializing in biopharmaceutical health policy in the Federal Trade Commission's Office of Policy Planning. Just to kind of give a brief sketch of how we'll work this panel, I'm going to briefly introduce everyone, and then I think give a quick presentation about some of FDA's education and outreach initiatives, and then I'm going to turn it over to the panelists.

What's unique about this panel is that we have one of our panelists beamed in from Canada, and she will be presenting remotely, so I believe that she will be on the screen. Her name is Cheryl Koehn. She's from the Arthritis Community Experts in Canada.

Do you know if Cheryl can hear us on the

line? Is her mic unmuted?

MS. KOEHN: I can hear.

MS. IKENBERRY: Oh, great. Wonderful.

MS. KOEHN: I can see myself. I'm not sure you can see me there in the room, but I don't think that matters, as long as you can hear me.

MS. IKENBERRY: Okay. Well, I think we'll work to get your face on the screen as soon as we can.

Cheryl is from Arthritis Community Experts in Canada, and she is a patient that lives with rheumatoid arthritis, and in over the last 30 years has become a national patient community leader, a patient research partner, and published author.

Let's see here. At the end of the table, we have Michele Andwele. She's the editorial director for health content at the Arthritis Foundation, where she oversees the content strategy and development of patient education materials.

We have Sameer Awsare, associate director for the Permanente Medical Group in charge of pharmacy, adult and family medicine, mental health,

and many other areas; I did not write them all down; and Hillel Cohen, the executive director of scientific affairs at Sandoz, where he helps explain the principles of biosimilars and related policies to the healthcare community, patient advocacy groups, and other stakeholders. He is also the co-chair of the Education Committee for the Biosimilars Forum.

Just briefly, I'm going to give an overview of our education and outreach efforts here at the FDA that we've done. As noted by many on these panels throughout the morning and the day, education has been mentioned quite a lot.

Here at the FDA, we take this very seriously, and we've been working for a long time to help improve understanding of biosimilars among patients, healthcare providers, and payers. We've been doing this in a couple different ways, by engaging with various stakeholders and developing materials for the stakeholders to use.

The thing is that this requires multistakeholder engagement. What that means is

that FDA can't do it alone. We can develop the materials, but what we need is for these healthcare provider organizations and patient stakeholders to take them and disseminate them to the people. People can take our materials and use them, however they would like, to get the information to their constituents.

This is just a snapshot of some of our healthcare provider materials. We have an infographic, various fact sheets, some ads, and other web content. I'm not going to go into details.

Most recently, we released some educational materials for patients. It's a website and an infographic that uses patient-friendly language, so we really try to boil it down to the most important concepts that are the most important to patients. We tested this, reworked it, and tested it again and reworked it. We're happy with this basic foundational piece, but we are also working on a lot more things.

This is just to build a foundation of basic

understanding that highlights the similarities of biosimilars and reference biologics, and it highlights the benefits of increased access, so the goodness of biosimilars for patients, and access, and hopefully lowering costs. It demonstrates our efforts to always ensure the safety and efficacy of biosimilars or just patients to talk to their doctor and visit our site for more information.

As I alluded to, we are developing additional materials for patients and healthcare providers, and we're going to begin testing for additional patient materials soon. Hopefully, we'll be able to provide some real quality pieces of video and some other information for patients soon, in addition to developing additional materials for healthcare providers.

As always, you can go to our website's biosimilars page, our Purple Book, and drugs@FDA for information.

I'm going to end that, and turn it over now to Cheryl Koehn, from Arthritis Consumer Experts, to provide her presentation. Thank you very much

for joining us, Cheryl.

Presentation - Cheryl Koehn

MS. KOEHN: Thank you very much, and I apologize I'm not there in person. Given the events of the day, it's probably a good thing that I'm not. But I want to thank the FDA and the FTC for organizing this important meeting, and I look forward to hearing and learning from my fellow panelists.

Can you hear me ok, Sarah?

MS. IKENBERRY: Yep, we can hear you great.

MS. KOEHN: Okay, great.

Following on Sarah's comment, I was parachuted in from Canada to give you that perspective. We're this little country just north of your border --

(Laughter.)

MS. KOEHN: -- and most of our population is sprinkled along the US-Canada border, so we're very aware of the events that have been going on in the United States with respect to biosimilars and have been engaged in the conversation, as have you, for

as long.

This first slide really speaks to where we come from as a patient organization. I've been a person living with rheumatoid arthritis for the past 31 years and have spent that past 31 years volunteering and working in my community as a health educator and deliverer of evidence-based information.

We were the first to be invited into the conversation around biosimilars, or on biosimilars, nine years ago by Health Canada, by BIOTECanada, and then subsequently by our provincial government. The reason being, we are the largest arthritis patient organization in the country with 50,000 members coast to coast, and Arthritis Research Canada is our scientific partner. So everything we do is based on the evidence.

You've seen my disclosures. I believe they're on the website in my speakers bio. I am employed by ACE full-time, but I'm here today as a volunteer.

Truth to power is really an important piece.

Really, I think what's most important for this audience to hear from us is, from the beginning, we really clearly articulated what our patient organization rules and responsibilities are. I think that's a really important part of this conversation when we speak about information and education.

Knowing the truth and speaking the truth is what we are all about. Operating independently and disclosing all sources of funding in this conversation, and in every conversation, about therapies in particular given the dollars at stake, is an absolute must. To consult incredible independent clinicians and researchers, and most importantly, our membership, is what is the bedrock of the development of our materials.

So it doesn't come from the outside. It doesn't come from being bombarded by advertising on television. We feel that to be an honest knowledge broker for your community, policymakers, and payers, you have to actually be so morally solid and have that north star firmly positioned in the

sky that you're willing to give up your own financial health, if that's what's at stake, to be credible.

To be reasonable and look beyond the needs of your own organization, if it's the right thing to do, is paramount, especially in this conversation that is so shrouded by myth and by many other things like litigation and so on and so forth. I'm sure you've talked about those things already this morning.

First, I think the most important thing that we do as an organization is to follow the evidence and then deliver the evidence. Our job as knowledge translators is really to take the evidence in a truthful way and reflect on its impact, and then put that into language that is accessible to our community. ACE does that by developing free research-based information and education programs that are relevant to not just us but the patient at large.

Sarah touched on, very briefly, the materials that the FDA-FTC have developed, and

they're fabulous. I think for the first time ever, Canada was ahead of the United States. We launched our information hub about biosimilars back in 2016, and it remains one of those beacons for information sources here in Canada and beyond.

I think one of the most important things that you may talk about on this panel is the nocebo effect. You have seen in this conversation, patients have seen, and the public has seen on the ground a whole lot of white noise. That white noise is like concerns about safety and efficacy, them not being identical, them not being interchangeable. Those things are actually very strategic when it comes to consumer-level information delivered by, in many instances, originators, originator manufacturers.

I think it's really important for everyone to understand that the nocebo effect is real, and the number one way of creating the nocebo effect is actually to speak negatively; to have negative body language in clinic about them; to see ads that use subtle words, or I should say not so subtle words,

such as, "I love my product. I love my brand X." I think these are really important and strategic words that are being chosen to create nocebo effect.

The way in which you manage a nocebo effect is really important, and it takes this solid information, this evidence-based lay language type information, to manage the nocebo effect as you begin to transition patients from their reference product, or their originator brand, to their biosimilar brand.

You heard the previous speaker talk about how this is not an inexpensive proposition making biosimilars or originators. Biosimilars in our view are still brands. They deliver the same thing, but when you use words, like "copy" and "cheaper" and "generic," those things are, in many cases and many instances, intended to create nocebo, and this is just morally wrong when the evidence shows that they're every bit as effective at sustaining efficacy and safety.

So it's super important, when it comes

downstream from our regulators, for educators, patient organizations, and larger health charities such as the Arthritis Foundation, to use really solid, unbiased, and positive if it applies, information about biosimilars, which mitigates anxiety regarding a switch or a transition from patient to patient or in whole-disease communities.

I think lastly, I'll just add this. In Canada, we are, again, finding ourselves in a unique position. We're ahead of the United States in terms of what we call up here transitioning or switching policies.

To date, we have three Canadian provinces that have implemented transition policy, the most recent being the province of Alberta. We have 11 provinces and territories, and the province of Ontario, which is our largest province here in the country, is now contemplating implementing transition policy. So everyone that is stable and doing well on their originator or their reference product will be moved to the biosimilar that has been authorized for use here in the country.

I can say this in closing, that the transition has gone very well. British Columbia's entering almost its first year, and probably 1 to 2 percent of all those transitions make special access or exemption requests, and about 1 percent of those were approved. So it's not as though people who have very specific needs are not being considered, they certainly are, and they're being considered by specialists.

So all in all, here in the country, we're doing exceedingly well at maintaining gold-standard quality of care, as you see there on my last bullet point. I see my slides were jumping around a bit. I hope that wasn't too confusing for folks.

But the bottom line is that we can buy an awful lot of health care for close to $2 billion Canadian in our publicly-funded healthcare system without compromising quality of care. For me as an individual patient, it's not enough that I can find my way or fight my way, because of my literacy level, to the best treatments available. It's up to me and all of our community to make sure that

everyone living with a form of autoimmune arthritis can find their way to effective therapy. So I'll just end there, and thank you for listening.

MS. IKENBERRY: Thank you, Cheryl.

Now, let's see who slides come up next.

(Laughter.)

MS. KOEHN: It's like a caffeine finger. I'm sorry. The slides just kept bouncing around.

MS. IKENBERRY: No, it was fine. They were stuck on the first one for a little while, but we figured out how to move them. But for everyone watching here in the room and at home, you can access all of the slides on the meeting website, so Cheryl's slides will be there as well.

It looks like Sameer is next.

Presentation - Sameer Awsare

DR. AWSARE: Alright. I'm Sameer Awsare. I'm an internal medicine physician, and I still see patients. For those of you who are not familiar with Kaiser Permanente, a quick slide, that we take care of 12 million patients and spend about $12 billion dollars on pharmacy expenses. You can

see we're in eight states and the District of Columbia with a whole lot of clinicians taking care of these folks.

What I wanted to show you is the methodology that we use not only for biologics but also for all of our generics. Unlike the external world, where the health plan actually figures out what the formulary is, and then the physician has to do, "Mother, may I?" we actually do it just the opposite way, where we have the pharmacists and the physicians looking at the research and getting the right specialist involved.

So if it's an oncology drug and it's a lymphoma, then the lymphoma specialists all look at it and weigh in on it before it comes to the pharmacy and therapeutics committee, and then we make a decision. And then we go to contracting and say go find a good deal.

So rather than doing it the other way as the rest of the competition does, this is what we can do; and when we can do that, we can actually promise to move 90 percent of the market share to

whichever product that we're going to then end up choosing. So that really is a big differentiator for us, but it also gets us that engagement.

So we don't really have any preauthorization, we don't have step therapy, and our compliance from our physicians is usually in the 99 percent rate without anybody slapping them or telling them to call someone for permission.

I'm just using this slide for Inflectra, and as you see, look at the evidence; yes, the European evidence, too. Our doctors are like, "What? Are the studies from Europe?" Do we have studies from America? Okay, we found an American study. "How about some studies from Kaiser Permanente?" I'm like, "Oh well, alright, we can do that, too."

So for Inflectra, we initially had to start new patients on the biosimilar. Once we had the experience with about 700 patients, we looked at people who had been on the originator product, and we found no meaningful difference, and people are sold. So it took a little bit of a while.

It also helps when we have specialists in

that particular area who can then endorse it. We have some world specialists in inflammatory bowel disease who have written articles, et cetera. And if we have other GI doctors who are saying, "Well, I'm not sure about this biosimilar," actually talking to a colleague who has expertise really helps that.

We have the right tools in the electronic medical records, and when you're ordering things, the right kind of thing pops up. We actually follow all of these patients to see how they're doing, and we have clinical pharmacists helping our physicians and helping our patients do that, and then we also see what happens post-starting these medications.

For this particular one, we actually did do switching, and unlike the provinces in Canada where it was a statewide decision, we actually have conversations with our patients, and we were definitely able to do a lot of switching. The nocebo effect was mentioned, and actually any of these biologics, whether it's the originator

product or the reference product, don't always work for this particular disease, so our physicians were a little bit concerned that perhaps even the originator product didn't work and we saw that perhaps the switch rate was about 9 percent. So it's a little higher than Canada, but in line with what you see in Europe.

We also found -- and we haven't published this as yet -- when we had clinical pharmacists helping, the switch rate was perhaps 5 percent. So again, patients were quite good at staying on the biosimilar once they had had the right education and the physicians had had the right education.

We just published the data. I think we were on a panel two years ago, and you said, "When will Kaiser Permanente actually publish any of this?" So about two weeks ago, we published in BioDrugs, and it's the largest U.S. study on the Inflectra-Remicade switch.

We actually found no meaningful difference and no inferiority at all, so patients did just as well on both. It's only available electronically

right now. It will be published in the journal very shortly. I think you have to pay $3,000 or something crazy to get this right now, but electronically you can see it.

We have similar experiences with the other two biosimilars that have come out for Avastin and Herceptin. What I would want to point out is when the first biosimilar came, it took a little bit of effort. We had to actually educate our physicians, educate our patients, get the specialists to talk to the right specialists, and it took 3 or 4 months to get that market share.

With the last two biosimilars, this uptake to almost 100 percent happened in a 2-week period. So once physicians felt very comfortable with the first one, the next ones have been a lot easier.

So I'll stop there and wait until the Q&A to give you other details. Let's see whose name shows up next.

MS. IKENBERRY: Thanks, Sameer.

(Laughter.)

MS. IKENBERRY: I think Michele might be

next.

Presentation - Michele Andwele

MS. ANDWELE: That's why I wore green, but I am next.

Hi, everyone. For those who are not familiar with the foundation, we're the largest nonprofit patient advocacy organization for both adults and children with musculoskeletal and rheumatic diseases.

We started collecting patient insights around biosimilars when the first biosimilar was approved, the biosimilar for Remicade in 2016. As you can see from the slide, we found naturally a lot of other misleading or confusing information that was available for patients. We did another round when the fifth biosimilar was available, but we recognized that the key concerns remained, and as you can see from this slide, they fall into three categories.

Efficacy, obviously, "Will I flare if I switch? Will it work as well for me; because I am stable? Are they safe?" which is a normal

medication concern, biosimilar or not. Then the cost coverage matrix gets a little bit more complicated because there are so many variables that determine will I pay less, everything from insurance coverage to are they underinsured, and are they part of a patient assistance program. So navigating that matrix requires a lot more conversation and a lot more variables.

We also found what we call a push-pull dynamic for a lot of our patients with regard to healthcare decisions in general, but medication specifically. The push part of that dynamic is the extent to which the patient is kind of personally motivated to make decisions, but the pull dynamic is a lot stronger because they are trusting primarily their ATP to guide them in the right direction. That's the individual they see that has the most information.

So to the extent to which their physician is not even bringing it up helps them to determine is it a conversation that they should have, and even if they are personally motivated or interested,

that barometer from their physician plays a critical role. To a lesser but also important effect are larger influencers. Are there patient organizations and patient advocates who are looking out for their best interest? That's where foundations like the Arthritis Foundation play an important role.

The three key takeaways for what patients are thinking, first, I like to call it interest without urgency. It's kind of floating out there, but they don't really have this tipping point for them to feel that this is something that they need to really focus on; then, as I mentioned before, the provider influence is key.

From the HCP patient advocacy perspective, we have been doing -- and I'll mention it in the slide in a minute. As a patient advocate, we have been trying to identify ways to strengthen collaboration with other provider and HCP patient advocate organizations so that we're speaking the same language. What we have identified from some of these earlier conversations is a challenge

around language, and that's where education plays a critical role.

Within both provider organizations and patient advocates, there is inconsistency with how we're all talking about biologics and biosimilars and the terms that we're using. We recognize the importance of a consensus among all the patient advocates and provider groups of where language should be.

Some of the provider concerns are independent of biosimilars. There are time constraints in every conversation. Where does a detailed conversation about biosimilars fit into 15 minutes, 20 minutes, 27 minutes, with patients who are dealing with a lot of issues in addition to their medication?

I mentioned insurance coverage earlier. Naturally, if it's not going to be covered or there isn't a patient assistance program, why would a provider even bring it up when they understand their patients unique needs? The last is the issue around liability exposure potential with the

interchangeability -- I'll try to say that fast -- designation and what that means.

There's a shared belief of a promise of biosimilars; we're all clear. We look to the FDA as our continued expert partner, and we recognize their varying levels of knowledge that we really need to address and the role of peer-to-peer information, both from the patient perspective and provider perspective, as Sameer mentioned earlier.

We're going to try to learn from our partners in Europe and Canada, from some of their lessons learned. And this is just a takeaway from a physician who transferred all his patients to biosimilars and the extent to which the trust factor played a critical role in him being able to make that move.

How are we responding? The foundation, independently we have been focused on a strategy of what we call communicating parity, so we have started to create communication materials to reinforce a singularity in the conversation on biosimilars and biologics. We're going to be doing

some additional work with the consortium to see how this needs to evolve and change. We've had discussions about do we keep them separate or do we do them together? We made the decision to test some of our patient education materials around this parity conversation, online and in print, and we also leverage various media as you see here.

I mentioned earlier some of the work we're doing around stakeholder and HCP engagement. We have been leading an initiative that we're calling the Biosimilars Consortium. It has currently 21 provider and patient organizations that we have put together. We've had a series of meetings, the most recent in October of 2019, I believe, and FDA was there.

We are working through our 2020 priorities as a collaborative consortium. Here are the three main areas that we are going to be focused on in 2020. Rather than just researching independently, we want to identify ways in which all our organizations can both share data within our own realm and others. We want to really look

aggressively at language. We recognize the role that bias plays in the biosimilars conversation, so we want to address that.

Once we are able to look at some of those triggers, then we are hoping to collaborate very closely on best practices across all our communication so that we are speaking with one voice, and we think that plays a very important role with regard to consistency in communication and education both for providers and for patients.

MS. IKENBERRY: Thank you, Michele.

Now, we have Hillel Cohen, who is going to speak a little bit. I believe there's a slide.

Presentation - Hillel Cohen

DR. COHEN: Hillel Cohen from Sandoz, but I'm speaking today as the co-chair of the Education Committee of the Biosimilars Forum, a trade association group developing and promoting biosimilar use in the U.S. I see my goal here primarily to identify the problems companies have seen over the past several years and to make recommendations to address them.

We've seen several different types of disparagement and misinformation over the years, since 2015 when Zarxio was first approved in the U.S. as the first biosimilar. These include -- and people have spoken about them, and my apologies that there will obviously be duplication of what I'm saying with what others have said -- misleading information. We've also seen incomplete information that's factually correct as presented but that omits important facts. FTC has talked about that earlier today.

We've also seen negative framing of factual statements to create a negative perception. You can say a patient will have the same clinical outcome, the same safety and effectiveness, or can say there's no clinical meaningful differences. It's the way in which we express it, and I think, Michele, you expressed that a lot just a few moments ago. On occasion, but not often, there actually have been statements that have been factually incorrect.

General targets, we've seen. We've seen

people talking about efficacy. We've seen some comment and messages on safety, on quality, and on regulatory. We haven't spoken about that yet. Let me give you a couple of specific examples of the messages that we've encountered. This is four member companies, not necessarily one company in particular.

On efficacy, we've seen messages that the efficacy of a biosimilar is not yet fully proven. We've talked about the purpose of those trials are not efficacy trials, but still people say it hasn't been proven yet, or we've seen that the efficacy of a biosimilar may not be as good as that of the reference product. We've seen comments about extrapolation. Some type of physicians, or patients, will say extrapolation is not appropriate. It wasn't studied in my indication.

Safety. We've seen statements that the safety of a biosimilar's not yet fully proven. Again, it wasn't the purpose of these studies, but those are comments that have been made to us. Some people have said it's a potential that a biosimilar

may be more immunogenic than that of the reference product.

Switching. We've heard the experience that we talked about in Canada. There still are comments out there that we don't have enough data to let us conclude that switching from a reference product to a biosimilar is safe, the implication being that switching may be unsafe. I realize physicians always have the ability -- we haven't talked about this yet -- to prescribe whatever product they feel is most appropriate. You don't need interchangeability for that. Interchangeability is a pharmacy-level decision. Physicians now have that ability to make the substitution if they make that choice.

We've also seen comments about the quality of a biosimilar. Well, the quality of a biosimilar may not be as good as that of the reference product. Probably more often we've seen people say it's only similar or only highly similar, not identical; never mind the fact that its many differences are not clinically relevant. That's a

mouthful that's difficult to understand.

We've talked about interchangeability. There have been statements out there that interchangeability is a higher standard. Again, I don't want to say everyone is saying that. It's a couple of messages and a couple of statements that have been out there, the implication being that biosimilars are of lower quality than an interchangeable biologic. In fact, it's not the situation. It's just a different standard requiring different additional clinical data. In fact, they're absolutely identical; [indiscernible], so they have to be identical.

The regulatory pathway has also created a little bit of a problem in the sense that the BPCIA talks about an abbreviated pathway. The abbreviated pathway talks about the clinical development. Some people would say the regulatory pathway, it's only abbreviated if it's not as rigorous as a pathway for reference products. Actually, it's very rigorous.

What recommendations can we make? These are

just general messages that we've encountered. Clearly, all parties should be required to share truthful and complete information. There's an information flow that we've talked about, a little more exact: FDA to healthcare professional societies; these societies to their physicians and also to the patient advocacy groups with which they work; and then for the physicians and the patient advocacy groups to patients.

The forum believes that patient discussions with the healthcare providers are really extremely important and will go a very long way towards gaining acceptance.

Positive framing. Cheryl Koehn talked about that to a degree, and we can talk about it later in detail. You want to highlight the quality and the benefits of a biosimilar, to talk about it in a positive sense.

It's also important to have easy to understand messages. The FDA has been developing these messages and making sure that you've been testing them to make sure they're easily

understandable by the patients. That's really critical. It's also important to make sure they can be readily accessible. Most patients, and maybe many doctors, go to Dr. Google as an important source of information.

(Laughter.)

DR. COHEN: Messages should be based on the FDA documents. Not all of the FDA documents are purposely designed to be easy to understand. Some of them are directed to the industry, some to healthcare professionals also, and only some towards patients. But anyway, all the messages designed by the myriad of organizations developing these should be based on the FDA documents and tailored to their audience.

It's also important to realize that there actually is a lot of information out there already available in print on the Web, and the material out there, people should review them, those who put them out to review them, and if necessary, revise them. Of course the forum is willing to work with FDA and other stakeholders to create this easily

understandable information with biosimilars and interchangeable biologics.

Just a few more things. More education is needed for the average patient and the doctor engaged in everyday patient care. I appreciate that for the large purchasing organizations, they may be fully on board with biosimilars. They've read the details, they have now knowledgeable people, and they're on board.

Kaiser Permanente, you've done the analysis; you're on board. In fact, the patient advocacy groups, many of them have delved into them in great detail, especially those which have skin in the game. The Arthritis Foundation and the National Psoriasis Foundation have studied these things in detail, but the average patient is not knowledgeable.

From bottom up, we need education. Patients need to be educated. The physicians need to be educated. Rheumatologists we found are more knowledgeable; gastroenterologists, maybe less so, so specialties may have to be focused on. Also,

obviously, we urge the FDA and the FTC to exercise their authorities when possible and under the jurisdictions to prevent disparagement and misinformation.

Now, there's an initiative that I believe is in the early planning stages that the forum strongly endorses, which is incorporating biosimilar education to the curricula of medical schools, nursing schools, and pharmacy schools. There are a small smattering of schools that are already doing that, but it really needs to be incorporated broadly in the U.S.

Finally, we would recommend that advocacy groups and lobby organizations -- sometimes they're closely linked -- should disclose their corporate alignments, their funding, and the conflicts of interest. Now, let me be clear. There's nothing wrong with someone speaking their positions. That's absolutely fine. Everyone is entitled to their positions on all sides. It's just that we think it's important to have full disclosure in place. With that, thank you very much for your

time.

Panel Discussion

Sarah Ikenberry and Elizabeth Jex

MS. IKENBERRY: Thank you, everyone, for presenting. Now, I'm going to turn it over to Liz, who's going to do some Q&A here with the panelists.

MS. JEX: Thank you, again, FDA for hosting this event and for conducting the joint statement with the FTC on this important topic. We've touched on a lot of the questions that I circulated to you all.

I think the key question I have is the FDA has recently updated its web pages, for both healthcare providers and patients, to explain that FDA-approved biosimilars are just as safe and effective as the original biologic reference product, and provide the same treatment benefits, and could have the same potential side effects as the reference biologic.

How can we best communicate this information to healthcare providers, to the medical professional societies, to patient advocacy groups,

and to patients? What recommendations, in addition to those that you've mentioned today, can we make to either the webpage or to future joint efforts, or research as you've discussed today on these topics? So I just lay that out for any and all.

MS. KOEHN: It's Cheryl here, Liz. Perhaps what I'll do is just let you know that what we did here in Canada was that it's easy to say everybody needs to be educated, but we live in a time, obviously, when people get education on a catch-if-can basis. So we created a series of videos that live on our website. Our provincial governments are referring people to those. We have online materials that can be printed.

I think our little 5-minute video series are super, super helpful, and I would encourage the FTC and the FDA to produce some really bite-size little videos that people can access when it's topical for them. We have to remember, this is not for the general population; this is for the population of people who will be switched or transitioned if in fact that's what happens there. That's what we

did, and they have proved to be one of the most accessed areas on our website.

I'll just say that even in the course of this panel, if we're all saying language is important, I would really encourage you to change the materials and change our language. I've heard now multiple times, just in the span of 45 minutes, the word "biosimilars" and then "biologic." Biosimilars are biologic. So it's really important to let the public and the patient public understand that we are talking about biosimilar/biologic, otherwise, people think they're two different things, and clearly they're not.

MS. ANDWELE: Another thing that I think is important to do is develop an influencer strategy. So much of our decision-making is influenced by peers, whether it is patient peers or provider peers. One of the things at the foundation we have invested a lot of time in is building an online community and establishing a strong support group network across the country because we understand that patients like to see themselves and talk to

people who get it and who understand.

A lot of people have a positive opportunity to impact and influence other people, so we think that identifying where those influences are and being able to leverage that I think will have a great impact in terms of acceptance.

DR. AWSARE: I think the panelists have highlighted the same sort of strategy we used. We also created educational materials for our physicians and for our patients, and then getting the right specialist. But for the FDA, I think working with some of the national societies, the American College of Gastroenterology or Rheumatology, like you are. When Inflectra first came out, some of the GI societies were not in favor of the biosimilar.

So having the right education to the right people, people are looking to these folks to give them direction, and if they don't see that coming, they're not interested in switching. I mean, the patient's stable. Why am I going to do that? You're going to call me, you're going to make more

visits to my office, and you're doing well on your current biologic. Why am I going to even switch if my professional society is not endorsing that?

DR. COHEN: We actually asked that of the four member companies, what key messages we would wish the FDA to have. Obviously, it's different than disparagement, so I'm talking in the positive sense.

The positive messages we want, same safety profile and effectiveness if possible. I think that would go a very long way. That's probably number one. Evidence requirements of biosimilars are very high. We would like people to be aware that there's lots of experience with biosimilars. It's at least 700 million patient-days, and I think it's actually quite a bit more right now.

There's a lot of experience. The EMA is on the record with their document that came out in November of 2019, saying they don't see any difference in safety with the originators. Another key message is that the scientific methods used to characterize the manufacturer and evaluate them are

rigorous, and they show that the biosimilars work just as well as the reference products. So to get back to will it work for me, the answer would be yes.

Finally, the fifth point that we had as a group is that the regulatory pathway is based on sound scientific policy. Doctors and patients are used to looking at clinical trials. You don't have it with biosimilars. It's a different paradigm. But these methods are very sound, and they use methods that really ensure the safety, efficacy, and the quality of a biosimilar.

I think a coordinated effort from the FDA to the professional societies, working with the patient groups -- and I know that this is an effort that you've been initiating; the forum has been part of that as well. As I said before, it's a cascade that has to come down.

MS. ANDWELE: One thing I'd like to add is some work around message segmentation because you're going to have patients who are treatment-naive, who a biosimilar may be their first

medication versus someone who is stable on a biologic. To the same extent, you'll have physicians who have been working with biologics for a very long time and those who are newer with biologics. I think looking at segmentation, both on the patient and provider perspective, may have an impact on the communication strategy.

MS. JEX: I see we're out of time. I want to thank my panelists for your excellent insights into the patient and doctor experience with biosimilars and ask everyone to give them a hand. Thank you very much.

(Applause.)

MS. IKENBERRY: Thank you, all. I think we could have sat up here for at least another half an hour and discuss this. But as always, we're interested in everything and what everyone has to say about this, and take that into consideration as we develop additional materials and information.

MS. TEMKIN: We're going to have a break now, and we'll be back at 2:15.

(Whereupon, at 2:04 p.m., a recess was

taken.)

MR. WEINSTEIN: Everyone, welcome back. My name is Randy Weinstein. I'm an attorney at the Federal Trade Commission. Earlier today, we've talked about disparagement in the context of FDA and FTC enforcement, but what about private rights of action? Does disparagement resonate in the context of antitrust enforcement, either by the government or private litigants? These are the questions we're going to talk about right now.

Joining me today are Michael Carrier. Michael carrier is a distinguished professor at Rutgers Law School. He is an expert in intellectual property and antitrust law. Rebecca Tushnet is the inaugural Frank Stanton professor of First Amendment law at Harvard Law School. Her work focuses on copyright, trademark, and advertising law. I also learned, in fact, that she's an expert on the law of engagement rings.

Professor Carrier, by chance, are you an expert in any matrimonial hardware?

(Laughter.)

DR. CARRIER: No, I'm not.

MR. WEINSTEIN: Okay.

Of course you all know Rich Cleland, my colleague, from the Federal Trade Commission who spoke earlier today.

Both Professors Carrier and Tushnet are experts in their respective fields, which happened to be the topics of this panel. More information about their prestigious backgrounds can be found on our web page.

Let's begin. We talked a little bit earlier today with some examples of disparagement that we're seeing in this industry, but is there a way to kind of organize these thoughts into some buckets, for example, or a way to kind of think more broadly about them?

Presentation – Michael Carrier

DR. CARRIER: Yes. We certainly have heard a whole bunch of examples. Let me categorize them into four categories. The first category is the most extreme. We haven't heard it, but it was explained in a Washington Post article in January

2019. It will be discussed by a couple people who will show up in the public comment period, things like -- and this is from the Alliance for Safe Biologic Medicines -- "We need to proceed cautiously with moving to biosimilars," quote, "'so we don't end up with another thalidomide.' That's when we had children with birth defects," or, quote, "'all the other things that happen when safety is not considered.'"

Then we had another quote from someone affiliated with the organization who said that, "Switching," quote, 'disrupts the continuity of care. You could end up in an emergency room or being hospitalized. You can exacerbate or flare your disease or even bring it out of remission.'"

So this is not appropriate given that, by definition, biosimilars are highly similar to and have no clinically meaningful differences from. That's the first category that really makes a joke of what the standard is, and then we get a little more subtle.

The second category is where we hear that

the biosimilar is not identical to or acts differently from the original reference product. A lot of this stuff shows up in the Pfizer citizen petition, so if you look at that filed with the FDA, we see that Amgen says that no two biologic medicines are identical; they behave differently in the body. You look at an Amgen tweet, "Biologics or biosimilars. It's not just apples to apples. It may be highly similar, but the patient may react differently." The Genentech website says that the FDA requires highly similar but not identical.

So the benefit to the FDA's proposed guidance is that it takes on these misrepresentations precisely. If you look at question 6, the biosimilar is not required to be identical, that's really important, and I'm glad to see that.

The third category deals with interchangeability, and as we've heard this morning, there are some intimations that just because a biosimilar's not interchangeable, maybe it doesn't meet that highest standard of safety and

efficacy. For example, Janssen said, "Even though the biosimilar is very similar to Remicade, it doesn't mean it's interchangeable," and really emphasized that throughout its materials. And there in question 6 in the FDA's guidance, we see that just because it's not interchangeable doesn't mean it's not safe and effective.

Then finally, and perhaps most subtly, is where the company says that the drug acts similarly. Janssen for example says you may be asked to switch to a biosimilar that works in a similar way to Remicade. This is a little more subtle than the others, but still the assumption is that it doesn't act the same way. And we see the FDA in question 5 on its guidance, the FDA also saying you don't look at the number of indications for which the product is licensed; that doesn't tell you how safe it is.

So with all of this, we see different levels of categorization, but in all of them there is some sense in which there is not equivalency with the biosimilar and that it presents real issues. As we

go through this panel, it's worth thinking about what the net impression is. If there is one interpretation that really shows that it's not as safe or effective, what can we do with it? So that would be how I would categorize these statements.

MR. WEINSTEIN: Thank you, Professor Carrier.

Professor Tushnet, we talked in an earlier panel today about the FDA and FTC enforcement paradigm. What about private rights of action in the context of disparagement?

Presentation – Rebecca Tushnet

DR. TUSHNET: Great. I'm just going to give a quick overview of the Lanham Act false advertising cause of action. Private competitor plaintiffs can often also bring state law claims, but they probably shouldn't detain us for very long.

The key element of the Lanham Act claim are the falsity or misleadingness of a statement, the materiality of the statement to a reasonable consumer's purchase decision, and the likelihood of

harm to the plaintiff. In the kind of case that we're talking about here, the likelihood of harm to the plaintiff is probably fairly clear.

A couple things that are mostly unique to the Lanham Act cause of action compared to an FTC or state consumer protection claim, the key thing is the sharp doctrinal difference between false and misleading claims. False and misleading claims are actionable, but in a Lanham Act case, the burden on the challenger is much greater if a claim is misleading than if it is literally false.

That puts a premium on distinguishing falsity from misleadingness. How does a plaintiff establish that a claim is false? Courts ask what is the explicit meaning of the claim? Once you know the explicit meaning, you can then determine whether that factual claim is false. However, of relevance here is that courts are sometimes willing to make general inferences from disparagement about what the claim is. It is also important to distinguish lay audiences and expert audiences. Different people may differ or different groups may

differ in their understanding of the term.

My favorite example of this is a case where the defendant said that the competitor's product was subject to catastrophic failure. It was a medical device, and the engineering dictionary says catastrophic failure is failure that happens without any warning; the device is performing, performing, performing, and then it stops. But the plaintiff established that, to doctors, catastrophic failure meant a failure that harms a patient, which is a very different thing, and the court found literal falsity because of the meaning of the term to doctors. So dictionary meetings may not be as important as what people are likely to understand.

Suppose a claim is not false? How do you establish whether it's misleading? This is relevant if a claim is ambiguous and it has potentially true and potentially false meanings, much of the stuff that we've been talking about here.

The question is what message does a

reasonable consumer receive? This is usually done through surveys of the relevant consumers, and the rule of thumb is that if 15 percent or more of consumers, the net of some control, receive a message, then the plaintiff is relatively likely to prevail.

When is this empirical evidence of consumer reaction necessary? It's not in literal falsity cases. Literal falsity is presumed to reach a substantial number of reasonable consumers, but surveys are basically always required in misleadingness cases.

There are a couple of exceptions. If there's an intent to deceive consumers, then that can substitute for evidence of consumer reaction. Sometimes direct testimony from deceived consumers can substitute but probably this is not a great scenario for that just because you can always find someone who's confused about something. So if you have a really broad range of consumers, the survey is going to give you a better idea of what's going on.

I did want to mention, and I do have a slide from this because I think it's hilarious, there's a Seventh Circuit case, Eli Lilly versus Arla Foods. If we could get the image up. Eli Lilly sued over images from an organic producer portraying RBST, which is a hormone given to cows to increase milk production. So it's being portrayed as a scary-toothed monster with electric fur that will shock you if you touch it.

The Seventh Circuit finds that there's nothing in this ad that is literally false, but that it is still misleading and enjoins it without any evidence of consumer perception, basically because of the disparagement. When you look at this, it is obvious that they are telling you, well, it's complicated but RBST is scary, which is a very relevant case for this scenario that we find ourselves here.

The court says the use of monster imagery, weird stuff language, and child actors combined to colorfully communicate the message that responsible consumers should be concerned about RBST-derived

dairy products, so I think this case is quite on point to some of the claims that we've seen.

The other thing that is clearly of relevance that we haven't really talked about is the relevance of the First Amendment for the regulation of these claims. In Lanham Act cases, courts generally say that the Lanham Act false advertising cause of action raises no constitutional issues at all. By definition, it targets only false or misleading commercial speech that can constitutionally be banned.

According to Supreme Court doctrine, when it comes to direct government regulation of speech, there is a distinction between inherently or actually misleading versus potentially misleading. So whether the speech can just be banned or whether instead a disclosure must be added to try and draw the sting of the misleadingness, this distinction is not well worked out. Maybe we can address it in the questions.

It's largely been done by courts guessing, or worse, about what's inherently or actually

misleading versus what is only potentially misleading. There's a lot of room here for presenting courts with facts about misleadingness. It is not the same distinction that's made in Lanham Act cases, where misleadingness is actually just one category distinct from falsity.

This leads to a related issue, which I hope we'll discuss, which is the relationship between private and public enforcement. Courts in private litigation regularly do defer to the FDA's factual findings about what is true, but without a lot of explanation about why they're deferring or with general references to the FDA's expertise.

The First Amendment may start to bear on the question of the review of these agency determinations, so what are the medical facts and what our consumers' perceptions of the messages that they receive?

Those are both actually facts about the world, but the level of deference that they receive may differ because courts may have their own sense of how good they are at figuring out whether

deception is going on. So as a practical matter, I would expect more deference to agency findings about safety and efficacy itself versus findings about deceptiveness, even though both really are subject to the ordinary mechanisms of proof.

So that is my lightning tour of the relevant concepts from my perspective, and hopefully we can now add some richness to that.

Panel Discussion

Randall Weinstein and Richard Cleland

MR. WEINSTEIN: Professor Tushnet, in the Lanham Act, those are actions brought by competitors; is that right?

DR. TUSHNET: Yes.

MR. WEINSTEIN: What about like a consumer? Where's the ability of the consumer to bring an action for disparagement?

DR. TUSHNET: Really, it would be relatively difficult, although one can imagine a consumer class action saying that the disparagement deterred a whole bunch of people from trying this drug. It could be done. I think as Professor Carrier will

talk about, the real possibilities for consumers here probably do lie in the realm of antitrust.

MR. WEINSTEIN: And is that because there's just no good law under which consumers have standing to bring a claim?

DR. TUSHNET: Consumers have standing under their state consumer protection acts, but there are just a lot of barriers to a successful class action at this point, not the least of which are the contracts that you might likely sign when you buy something. So depending on how the medication is transmitted to the consumer, they might actually have waived their rights.

Courts are also very tough on claims that not all consumers may have seen. So if the advertising is not actually on the package, then it's going to be hard to sustain a class action. So in this space, I think the false advertising issues are really Lanham Act issues.

MR. WEINSTEIN: Thank you.

MR. CLELAND: Let me follow up on the First Amendment issue with just one question here. You

mentioned the difference between inherently deceptive and potentially deceptive. One of the things is, for example, in the Palm case, where the D.C. Circuit said we've now determined that these claims are deceptive; there go [ph], no First Amendment issue.

If the fact-finder first finds deception or a misleading, the potentially deceptive part of that equation should go into what kind of relief is ordered, not whether the court can ban the claim that is found deceptive; right?

DR. TUSHNET: I think that's a completely logical way of looking at it. My only caution is that courts have been very far from logical in the order in which they approach these issues. I think that's completely right, but sometimes courts get a bee in their bonnet about the order of operations here.

MR. CLELAND: And in terms of the materiality prong on the Lanham Act cases, that's materiality for the competitor.

DR. TUSHNET: It's actually materiality for

the consumer; that is it has to be likely to affect a reasonable consumer's decision, and then the materiality to the consumer then produces the negative effect on the competitor. And again, you're not looking for it to affect everybody's decision. As long as a substantial number of reasonable consumers are likely to be affected, then we can see an effect on the market.

MR. CLELAND: But given, in this particular market, usually it's the physicians that are making or at least having a great impact on the decision, how does that affect materiality?

DR. TUSHNET: I think the best answer is that it's actually open to the plaintiff to show either the patient or the doctor. As I'm sure you're all aware, there's plenty of evidence about the impact that patients have on doctors when they're asking for a specific medicine. I think you could readily show actually either group being a relevant market actor, especially given that the standard is substantial number rather than uniform effect.

MR. WEINSTEIN: Turning then to the antitrust framework, Professor Carrier, can you walk us through the current framework for evaluating disparagement as an antitrust violation?

DR. CARRIER: Sure. So the big picture here is we're talking about monopolization, which is Section 2 of the Sherman Act. We're not talking about mergers. We're not talking about agreements among rivals. For monopolization, you have to show monopoly power and exclusionary conduct.

The first piece is monopoly power. You can either show it indirectly or directly. Indirectly tends to be through a share of the market. We usually see at least 90 percent of the market, although you could see perhaps lower, maybe 70 percent, together with barriers to entry. For direct monopoly power, we tend to see price increases or the price maintained at a high level or output reductions.

Do we have that sort of power here? I think that we do. It's clear that biologic products are a generally very expensive product. So even if the

biologics are not as much in terms of the biosimilars, in terms of the number we see, the amount of money is a ton.

You look, for example, at one case, Pfizer sued J&J, Pfizer claimed J&J increased the price 10 percent and still has 96 percent market share and 90 percent of producers refused to stock their product at all. In these cases, there tends to be such power, there are very few substitutes. So I'd say monopoly power is not something that we spend a lot of time on.

Then the question is what about exclusionary conduct, and courts here have fallen into one of three buckets. The first bucket is that there is no liability at all for something like disparagement; the second bucket is assuming that the harm is de minimis; and the third bucket is a case-by-case approach.

So the first bucket as shown by the Fifth and Seventh Circuits is that there's no liability at all. These courts say that false statements enhance competition in advertising markets; that

business torts are different than anticompetitive conduct; and that false statements set the stage for competition in the advertising market.

In short, they basically say there is nothing to do about false statements. I think that that is wrong. I have an article forthcoming. Professor Tushnet and I also have an article forthcoming in which we both think it's wrong. You can't say that there's no liability at all when you engage in this conduct. It's certainly possible to get or maintain monopoly power by engaging in this behavior of disparaging your rivals. It's certainly not something that the rival can fix. It certainly can have a significant effect on the overall market.

So we would say that this approach is wrong. Nonetheless, if a court were to adopt it, then there's no liability because that's just what courts say following this approach.

The second approach is a de minimis approach. It's followed in the Second, Sixth, Ninth, Tenth and Eleventh circuits. Basically,

it's presumption that the exclusionary effects of disparagement are de minimis. That presumption can be rebutted if the plaintiff could show six things. The case law is not clear as to whether or not you have to show all six, but those six are that it is a clearly false statement; it is clearly material; clearly likely to induce reasonable reliance; made to buyers without knowledge of the subject matter; continued for prolonged periods; and not susceptible of neutralization.

So again here, the bar is too high. This case arose in the leading treatise, or the framework is taken from the leading treatise, the Hovenkamp treatise in antitrust law. It was adopted at a time that the standards of false advertising really aren't clear, and there is something to say; that not every instance of false advertising is monopolization. Certainly, there are lots of instances that are not monopolization, but the cases that we're worried about, the cases in which biologics are disparaging biosimilars, are ones where there is monopoly power.

How would this test be applied? Well, we start off saying that it is de minimis, then you look at the factors. So the first is clearly false. And if we've learned anything from the day so far, it's that you can have deceptive and misleading statements even if they're not clearly false. So I would take issue with this factor. And if we expand it a little bit to what's deceptive and misleading, then, again, that is what we've talked about for hours, saying, oh, they're not identical; they're not interchangeable; they don't work the same way, these are deceptive and misleading.

The second factor, is it clearly material? Of course it is. This deals with safety and health. What's more material than that?

Third. Does it induce reasonable reliance? Yes, relatedly. Doctors and patients and payers are going to care a lot about the assertions that are made.

Fourth, buyers without knowledge of subject matter. Here, there's a lot of emphasis on the

drug companies and what the drug companies are saying, so this factor shouldn't apply as much.

Fifth, lasting for prolonged periods. Yes, these are monopolies. The monopolies, as we saw in one slide, go on for years, so certainly that is satisfied.

Finally, the plaintiff can't neutralize it. It's hard to neutralize. Once the biologic company says we have some real safety problems here or maybe you'll go to the ER, it's tough for you to say, "Well, we're not going to go to the ER." It's really tough to rebut.

So applying the test, the first factor of clear falsity I'd say is too high a standard, but that one you could argue if you were to have deception or misleading, and I'd say all the other factors are satisfied. So even if it starts off with a presumption that it's de minimis, I'd say that the factors can be rebutted.

Then finally, the third bucket is the case-by-case approach. This is followed in the Third, the Eighth, and the D.C. circuits. Here,

for example, in D.C., the court said there are too many forums. It's too dependent on context to enumerate all of the varieties. The multiple courts say the false statements could be so unfair that they constitute an unreasonable restraint. Courts have looked at things like whether false statements lead to inflated financing costs and whether they lock in decision-making.

So how would all of that apply here? Because it's case by case, we have a lot more flexibility. Just on those two last factors that I mentioned, the first is financing high expenses. It's really hard for a biosimilar to get the financing it needs if it's subject to all of these inappropriate claims. In terms of decision-making, that's locked in as well.

Then we step back and see the regulatory situation. It was so rewarding to hear FDA Commissioner Hahn, just like FDA Commissioner Gottlieb before, talk about things like shenanigans. These are not appropriate types of behavior.

It certainly is wonderful to see the FDA and the FTC working together and this is incredibly important, but it's possible that the agencies might not be able to solve this problem completely on their own. As we've seen for the past several decades, drug companies think it's in their bottom-line interest to play these games, to get away with a slap on the wrist, and to keep their monopoly power for years.

So there could be a role for courts to play a role here in terms of the different barriers to entry. I'll just mention, as we saw before, the cost of development is extremely high. We haven't talked about trade secrecy and the manufacturing processes that the biologic companies do not want to share with their rivals. We've seen that there are patent thickets that make it extremely difficult.

Settlements could be a good thing, but pay-for-delay is not. The Supreme Court and activists said you cannot pay your rival to stay off the market. So while we want settlements in

this case, we don't want one company paying another to stay off; that's not right.

Third, the bundling, exclusive dealing, and rebates we've heard about, and finally established patients are unlikely to switch. So in some of these cases there's bundling with the established patients and the new patients, which makes it even harder for the new patients to consider the biosimilars.

So you put all of these barriers to entry together, and you see it's really hard for the biosimilar to enter the marketplace. There are so many barriers already there. Then on top of that, for the few new patients who could consider a biosimilar, you threaten all of these safety concerns, it's going to be extremely hard.

So I'd say following the case-by-case approach, which I think is the most justifiable of the three approaches, I think there's a strong antitrust case that could be made.

MR. WEINSTEIN: Thank you, Professor Carrier.

Let's back up and maybe just ask at a high level, do we need a disparagement cause of action arising in antitrust? I guess on the one hand, is there a regulatory or a policy fix available that might accomplish the same thing or is the enforcement of private or public framework we have in the consumer protection context sufficient standing alone?

DR. CARRIER: I'd say yes to all three; yes to antitrust; yes to consumer protection; and yes to regulatory things that we're talking about today. It certainly is wonderful to see the FDA and FTC getting together using their complementary expertise to go after this conduct, which is subtle in nature.

Is there a role for antitrust? There is a role for antitrust because no matter what the agencies can do, there's always the possibility that some bad actors will cross the line and commit an antitrust violation.

The benefit of antitrust law is that it focuses on market-wide effects. There could be

increased price and reduced output that antitrust is uniquely able to deal with. Antitrust offers treble damages; it offers attorneys fees; it offers injunctions; and it offers the chance to consider all of this conduct in combination.

For example, you have a case involving Suboxone where you have a grab bag of anticompetitive conduct. You have citizen petitions, product hopping, and sample denials. The court on the sample denial piece said, "Well, this is pretty nuance stuff."

So standing by itself, it's not a violation, but as part of the overall course of conduct, it could be, and that should be on the table here. These biologic companies are not just doing one thing; they're doing a whole a bunch of things. So putting antitrust on the table is one way of dealing with all of that together.

MR. WEINSTEIN: Now, earlier, Professor Tushnet mentioned that perhaps a private class action claim in the consumer protection context would be hard. What about in the antitrust

context? How would you characterize the distinction between public and private enforcement from a normative perspective?

DR. CARRIER: Well, I think it also would be hard here as well. Courts are not always receptive to class actions, and then the question is who's going to organize a class when the conduct is really nuanced? Saying, well, it's not identical, that's a bit nuanced.

So I think there's always a role for the government to play. The FTC uniquely has power under Section 5 to go after unfair methods of competition and unfair deceptive acts or practices. That gives us a little more leeway than antitrust law. So I think there's a crucial role for the FTC to play.

MR. WEINSTEIN: With the disclosure that I may have had some insight into your forthcoming article, have courts correctly evaluated disparagement in either of these three circuit-split options? If not, is there a better

approach?

DR. TUSHNET: The fundamental problem with the majority approach is we have one branch of competition law that presumes correctly that false advertising harms competition; it poisons the communicative environment; it makes it harder to understand and compare products and services; and it is anticompetitive in the most basic way.

In the majority approach, we have competition law that presumes that false advertising is fine and maybe even good. Those things both can't be true, and false advertising law is right about the harms of false advertising to competition.

We think that false advertising law has had the chance to develop a lot of thinking about how you prove falsity and how you prove that it affects consumers. These are tools that are available and should be used both in Lanham Act cases and where relevant in antitrust cases to show that, in fact, the market did move.

Right now, there's a situation where you can

be put into a heads-I-win/tails-you-lose position. There's a case in the Fifth Circuit that is really reflective of what happens, involving Becton Dickinson. Basically, there was a bunch of false advertising, but it seems to have harmed all the competitors in the market.

The Court of Appeals first said, "Well, you can't win a false advertising claim because you can't show which of the sales were lost to you because it harmed everybody else in the market," and then the court says, "And there's no antitrust claim because it's false advertising, which can't harm the market," and does not seem to appreciate the -- that just can't be right.

So I think we do need a rethinking, and hopefully at least the circuits that do a balancing or a case-by-case approach at least have the better idea of it.

MR. WEINSTEIN: So if you were the king of the world, if you were, or perhaps just the one crafting all of the laws of the United States, what would be the cause of action?

DR. CARRIER: Again, Professor Tushnet and I have an article where we lay out what monopolization should look like. So we presume that there is an anticompetitive effect if you have a monopolist engaging in false advertising. The presumption is appropriate because we're only talking about monopolists.

If you go back and look at the treatise, it's worried and it doesn't want to have every instance of false advertising become a case of monopolization. And that's fair, but that is implicit in what we're doing because our test only applies to monopolists. So if you have 1 percent of the market, go do whatever you want. If you have a monopoly, however, there are certain things that you can't do.

What we do, as Professor Tushnet pointed out, is we take the learning from false advertising law. We don't think it's appropriate for antitrust courts to say there's no role at all for antitrust. We don't think it's appropriate to say let's just assume the harm is de minimis.

False advertising has built up a well-developed body of law. So if we can show, or if the plaintiff can show, that the conduct is literally false or misleading; if it is material; if it deceives or is likely to deceive consumers; and if it causes or is likely to cause harm, then the elements of false advertising are met and the presumption is that there is monopolization. And the defendant could always come back and show that the false or deceptive conduct is ineffective; that somehow it lost market share or wasn't able to put away its rivals.

So we think that is appropriate with thinking about false advertising. It ensures that false advertising is limited to the place where it can do the most damage, and we think it makes a lot more sense than what some of the courts are doing today.

MR. CLELAND: Can I follow up with one question? If I'm understanding this correctly, the more penetration that the biosimilar makes in the market, the less compelling the antitrust argument

becomes.

DR. CARRIER: Certainly. If the biosimilar is able to enter the market to the extent that a generic has entered the market, where you see the price fall dramatically and the penetration increased significantly, then that would be a less strong case; correct.

MR. CLELAND: So it's 20 percent or 25 percent?

DR. CARRIER: Well, in generic space, you see the generic taking 90 percent of the market and having the price fall dramatically. I'm not sure if we'll ever get that sort of penetration and discounting given how expensive biosimilar development is. So we'd have to think of something in between, to have more competition than we've had now, but maybe a little bit less might be okay as compared to generics.

MR. WEINSTEIN: How do we establish competitive harm here, harm to competition? Is it enough to show that we can prove deception? Is that sufficient, or that folks were misled?

DR. CARRIER: Yes. For a biologic company that has monopoly power, I think that's the case. You see this sort of behavior. You see that biosimilars are injured. You also see the regulatory scheme in which this is not like any other industry. We have biosimilars that are supposed to play a crucial role in lowering price. They haven't done it like they should. So the fact that competitors are harmed means that consumers are harmed, and then you supplement that with high price and lack of market share, and I think that you still have an antitrust case.

MR. WEINSTEIN: An earlier panelist today mentioned his belief that it would be hard going forward to deceive at least the prescribing physicians or the folks working in hospitals that biosimilars were not as safe or effective as the reference product. If that's true, is there still a role here for harm to competition, at least for the patient and the consumer?

DR. CARRIER: Absolutely. The markets that we're talking about here are unique because we have

what's been famously called by the Federal Trade Commission, decades ago, the price disconnect because it's not like any other market where the price quality determination is made by one party.

So you have the doctors that are making the decision as to what to prescribe. You have the payors or the insurance companies that pay for it. So there is a lot of room for anticompetitive conduct going here, not just the doctors -- and I'm not sure that that problem has been completely solved -- but the patients as well, and the insurance companies, and the PBMs with the big rebates. I think there's a lot of room for anticompetitive conduct here, so that's why I wouldn't rest on our laurels yet.

MR. WEINSTEIN: Professor Tushnet, you mentioned that there was a body of research -- I don't want to mischaracterize you -- describing the role that patients have in their own prescribing decisions. I'm curious what your thoughts are in this context, where perhaps the physician is not persuaded by some disparaging comment but the

patient is.

DR. TUSHNET: From my perspective, as somebody who mostly thinks of this from the Lanham Act perspective, I think it's just a matter for proof what is actually going on in the market, and when we figure that out, we will know. I do think that you can infer something from the fact that companies are trying to reach patients directly. They wouldn't be trying to reach patients directly if they didn't think that it had some chance of moving the market or keeping the market where it is in this case.

MR. WEINSTEIN: Thank you.

Is there any case law currently that exists that supports this -- I don't want to mischaracterize it -- what I'll call a reinterpretation of how we should think about these kinds of cases?

DR. TUSHNET: Certainly from the Lanham Act perspective, this is actually a pretty straightforward Lanham Act cause of action. It's just a question of what are the elements and can

you prove them. Certainly, I wouldn't expect the originators to roll over and agree that all the elements have been met, of course not, but at least it's straightforward about what needs to be done to prove the case.

Then from the antitrust side, there is this case-by-case approach, which at least is open to hearing about the anticompetitive effects, the harm to the market. Especially in a very small market, by the way, of course harm to one entrant may well be harm to the market if that's all you have, which in some of these cases is what you have.

MR. CLELAND: Are you aware of any pending cases raising the antitrust for disparagement of biosimilars, other than I think Johnson & Johnson-Pfizer?

DR. CARRIER: I'm not aware. But I would say, going back to the last question, that antitrust, as Professor Tushnet points out, certainly does take the common-law approach. The big picture here is we're talking about the pharmaceutical industry. Pharma is basically

giving us whack-a-mole all the time. Every time you think you've figured out what's going on, there's another mole to whack.

Just a couple days ago, we saw the judge denied most of the motion to dismiss in the Gilead case, in which there's a new combination of settlements and product hopping that we haven't seen before. Go back a little while, once you thought you figured out everything that pharma was doing, they transferred patents to a Native American tribe to avoid review at the patent office. We couldn't see that coming, but again --

(Laughter.)

DR. CARRIER: -- it comes with the territory.

So this is just the next stage, and there are so many different hurdles here, that it's really clear that this is part of the game, and antitrust is certainly well equipped to deal with these, as we've heard about, shenanigans.

MR. WEINSTEIN: One of the other possible options would be some sort of a rulemaking.

Commissioner Chopra, FTC Commissioner Chopra, has stated that he wants to see the FTC make broader use of its rulemaking authority. Is this an area where FTC rulemaking might be useful?

DR. CARRIER: Sure. As I said to a previous question, yes and yes; yes for rulemaking and yes for enforcement in the courts. Rulemaking could shed light on the problem here, and I think the guidance that FDA has offered is really helpful. Why not have the FTC offer similar guidance; just to make clear that you can't hide behind this fig leaf of clear falsity and that there's a lot of deception and misleading conduct that is going on?

So I'd say sure. Rules could make a lot of sense, but certainly not at the effect of enforcing the antitrust laws because we need to do that, too.

MR. WEINSTEIN: What about the distinction between this claim as a private versus a public cause of action? What are some of the incentives that should motivate the government versus the private sector, either the consumers or competitors?

DR. CARRIER: I think an argument for the government to act is that sometimes this conduct is pretty nuanced. And again, imagine that it's not clearly false but we're raising some sort of safety intimations that maybe it's only similar to. That's pretty nuanced and, to me, that sounds like an ideal recipe for effective FTC enforcement.

DR. TUSHNET: The other thing that I would say, too, is it's always an enforcement decision. Government agencies have limited resources. There is definitely a role for private companies. If they think that they're losing millions of dollars, they really at some point should put their money where their mouth is and go to court and fight about the money that they are losing.

So there's a reason that the FTC's discretion is often limited, where markets are deconcentrated and where we don't think that there's some private interest that will actually fulfill consumer interest by going after its own interests. But at a certain point, when the consumer harm is great enough, if for various

reasons private companies aren't acting, then, yes, there's definitely a role for the government, too.

MR. CLELAND: Forgive me. I'm not as familiar with all of the players in this area as others. Obviously, the cost is a big barrier for private rights of action. Are the companies that are suffering the most really in a position to litigate those rights and assume those costs?

DR. CARRIER: It certainly is possible. We've seen with biosimilars these are really big companies. Pfizer suing J&J, we don't usually think of Pfizer as the little guy plaintiff. To just enter the market, or try to enter the market, as a biosimilar, you need to have a lot of resources. So, yes, I think they could litigate.

MR. WEINSTEIN: So if there are no other questions, let me just offer Professors Tushnet and Carrier an opportunity to make any final remarks.

DR. TUSHNET: I just think it's great that we're having this conversation. The law of false advertising is actually pretty good at grasping the realities of the market. I hope that also when we

think about antitrust, we can think about being better at empirics, which antitrust prides itself on in many other categories, and then for false advertising has just decided to pretend that there are no empirical effects of false advertising. That's weird. Hopefully, we can create some change on that, and then be realistic about market harms.

DR. CARRIER: I just want to say how promising it is that the FDA and FTC are working together on these issues. This is such important stuff. It's so nuanced, and the FDA and FTC have such unique skills and experiences that they can bring to bear, that I really think it's helpful because the pharmaceutical industry knows how to play these games, and sometimes we need the government agencies working together to counteract these games.

So I think it's a wonderful development to see the agencies working together on such important issues.

MR. WEINSTEIN: Thank you. I hope you all will join me in thanking our panel.

(Applause.)

Open Public Comment

MS. IKENBERRY: We have some folks eager to get started on the public comment portion of this workshop. Again, my name is Sarah Ikenberry. I'm a senior communications advisor in the Office of Therapeutic Biologics and Biosimilars.

For the open public comment session, we have I think 17 speakers registered. I'm not sure if they're all here. But each of them will have 4 minutes to present. If a speaker finishes early, I will ask if the members of the panel have any questions for the speaker. If the speaker and/or if the questions from the panel do not take the full allotted period, we intend to move on to the next speaker.

For the speakers. You can see where she is putting up the microphone, so that is your place. We have timer lights to guide you. You can see them right here on the top of the podium. The timer will give you a 2-minute warning before the red light goes on. If you have not concluded your

remarks by the end of your allotted time, I will ask you to do. Please don't make me do that.

(Laughter.)

MS. IKENBERRY: We have a lot of people registered to speak, so please be mindful of your time and courteous to your fellow speakers. Also, please remember that the hearing is being transcribed, so please be sure to use the microphone with speaking and introduce yourself so that your name will be included in the transcribed remarks.

I will now ask the panelists to introduce themselves, starting with Eva.

MS. TEMKIN: Hi. I'm Eva Temkin. I am the acting director for policy in CDER's Office of Therapeutic Biologics and Biosimilars.

MS. GRAY: I'm Caty Gray. I'm the supervisor for the advertising and promotion policy staff in OPDP.

MS. DUTTA: I'm Antara Dutta. I'm an economist at the Bureau of Economics at the FTC.

MS. BLACK: Hi, everyone. I'm Armine Black.

I'M an attorney in the healthcare division of the Federal Trade Commission.

MS. IKENBERRY: Alright. Thank you, everyone.

With that, our first speaker is Juliana Reed from the Biosimilars Forum?

MS. REED: Good afternoon. I'm Julie Reed, the vice president of global corporate affairs at Pfizer, but also the president of the Biosimilars Forum. The Forum really appreciates the opportunity to provide our perspective on the need to discourage false and misleading communications about biosimilars and to deter anticompetitive behaviors that interfere with efforts to establish a competitive marketplace for all biologic drugs.

The members of the Forum represent the majority of the biosimilars approved and marketed in the U.S. to date as well as those under development. The Forum is committed to ensuring that patients and prescribers have complete truthful and non-misleading information about biosimilars.

As my colleague, Hillel Cohen, mentioned in his remarks, we are very concerned that there has been and continues to be a pattern of negative information about biosimilars to patients, healthcare professionals, and others who have a role in adoption of biosimilars in the U.S. Continued misleading information about biosimilars will have a negative impact on the U.S. healthcare system, physicians, and patients, ultimately leading to ongoing lost of cost savings and uptake of biosimilars in the U.S.

But we know misleading information is not the only barrier. As all of the speakers have said today, there are multiple barriers that are preventing the success of this marketplace. The members of the Forum have spent hundreds of millions of dollars to bring each biosimilar to the market. Pfizer alone has 8 approved biosimilars in the U.S., but we all know the market is not working, and it is not working for the patients we are here to serve.

We are grateful to the FDA for your

incredible work to date over the years. We're also grateful for the FTC and your incredible work over the years to help support biosimilars. What we need now, though, is every other stakeholder to join us in this fight and to get engaged to proactively support policies that will remove these barriers.

We need not only the FDA and the FTC to be engaged and be proactive when you walk out of the door here today to get this done, but we also need Congress, CMS, payers, patients, and others to start to proactively support the uptake of biosimilars in this country.

This is about cost savings and it's about cost savings to patients and the healthcare system. This is about innovation in the future so that we can all afford the innovation that is coming, but ultimately this is about the patients we're here to serve and that the members of the Biosimilars Forum are here to serve. Thank you.

MS. IKENBERRY: Thank you.

Our next speaker is Philip Schneider from

the Ohio State University College of Pharmacy.

DR. SCHNEIDER: Thank you, and thank you for the opportunity. My name is Philip Schneider. I am a professor of pharmacy at the Ohio State University where I've been on faculty for almost 40 years, as well as the chair of the Advisory Committee for the Alliance for Safe Biologic Medicines, which I've done for 11 years.

I'd like to make a statement, first of all, correcting misperception, a true and misleading communication related to my quote in the Washington Post. That relates to a quote I made about supporting the FDA's role in assuring the safety of the medication supply in our country.

ASBM has been involved in working with regulators around the world, including FDA, on policies that focus on safety, including distinguishable non-proprietary names and an interchangeability classification for biosimilars. In no way do we feel that is anticompetitive, and I want to correct the perception that ASBM is spreading misperceptions and that I did that

personally myself.

Today I'd like to address my comments on what we think to be an incorrect assumption underlying the proceedings today, namely that biosimilar uptake in the U.S. is strongly linked to low physician confidence levels in biosimilars and physician confidence has been depressed because of anticompetitive practices.

Last year, ASBM conducted a survey of 579 physicians in six Western European countries: France, Germany, Italy, Spain, Switzerland, and the UK. We surveyed physicians in 10 different areas of practice, including rheumatology, gastroenterology, oncology, dermatology, and neurology. All of these physicians prescribe biologic in their practice.

What we found is these physicians were very familiar with and confident in biosimilars. This is not perhaps surprising because European physicians have had 13 years of experience with biosimilars.

Depending on the country, between 82 and

93 percent of prescribers consider themselves familiar or very familiar with biosimilars. Between 80 and 99 percent would feel comfortable prescribing a biosimilar to a new treatment-naive patient. Between 46 and 76 would be comfortable switching a patient from a reference product to a biosimilar even if they were stable on the current medicine.

In spite of that, if we look at the biosimilar market share in the six countries that we surveyed, there's very wide variation among biosimilar adoption in each of these countries. For example, market share for the epoetin biosimilar ranges from 6 to 84 percent. There are similar ranges for other biosimilars.

Clearly, there are other factors besides physician confidence, which is uniformly high across the countries. These factors are likely to include differences between each country's payer policies; differences in the length of time a biosimilar has been on the market; the number of biosimilars in a given product class; the discount

each product receives relative to the originator product; and other factors.

Healthcare professionals here in the U.S., as in Europe, are not antisimilar. It is inaccurate to suggest that negative perceptions are holding up biosimilar development and commercialization. We are enthusiastic about biosimilars and want to see them as much as anyone else, and we are pleased to see how far the U.S. has come in a few short years. We urge the FDA and FTC to continue their work to build a strong and sustainable biosimilars market. Thank you for the opportunity to comment.

MS. IKENBERRY: Thank you very much.

Madelaine Feldman, Alliance for Safe Biologic Medicines.

DR. FELDMAN: Thank you. As you said, my name is Madelaine Feldman. I'm a rheumatologist in private practice in New Orleans. I'm also president of the Coalition of State Rheumatology Organizations and the founder of the Rheumatology Alliance of Louisiana.

ASBM is an organization of more than 140 patient advocacy groups and physician societies. The work includes sharing the perspectives of pharmacists, patients, and physicians with regulators and other policymakers at the state, national, and international level. I'd like to speak on a couple of issues regarding biosimilars.

The first is that misinformation continues to affect the objectivity of physicians and make us essentially antibiosimilar. Perhaps rheumatologists are a different lot. I just presided over a national rheumatology meeting this past weekend and polled the entire group coming from around the country if anyone felt that biosimilars were inferior to originators. No one said yes; everyone said no and that they all thought they were not inferior; and then would anyone have any hesitancy in prescribing a biosimilar, and no one had any hesitancy.

So at least for that group of rheumatologists, which was quite representative, there appeared to be at least no negative feelings

in that regard. But I have to admit, clinicians are generally more cautious and conservative regarding new treatments and are hesitant to change, particularly when it comes to changing a stable patient.

Because it can take years to months and months to years to stabilize the rheumatoid arthritis patient, rheumatologists have been sensitized to non-medical switching by payers, wherein that they are told the medicine that finally stabilized our patient will no longer be paid for.

By changing formularies often to a higher priced drug that cost the patients more to solidify the formulary profit margin, middlemen can legally switch patients in the United States and switch their medicines every six months. This could involve switching back and forth between originators and biosimilars, which wouldn't be horrible, but they even switch patients, and this has happened, to completely different biologics. So yes, physicians are leery of a great American

switching experiment.

Speaking of incentives in our supply chain on the pharmacy side, formulary placement, hire list prices, and higher market share are the ones that are preferred. That puts biosimilars behind the eight ball from the get-go once they've been launched. If incentives are implemented for biosimilars, any cost consideration should be directed to the patient because incentives that monetarily benefit the physician could actually undermine the patient's trust in their doctors.

Finally, repeating what everyone has said, considering the perception that U.S. lags behind Europe, thinking that at 5 years out from biosimilar approval in Europe, there were 11 products approved, in the United States we have 26. The FDA deserves credit for their support in building a biosimilar market so quickly without compromising on safety or efficacy standards.

Physicians are enthusiastic about biosimilars and the benefits they can bring in

terms of therapeutic offerings and true cost savings, and through price reduction to our patients in the larger health system and not merely increasing middlemen-pocketed-fees and price concessions.

The most important strategies to continue the process in the U.S. are strong FDA educational programs for healthcare professionals and patients, along with pharmacovigilant programs, particularly in light of the payer's ability to frequently switch patients every 6 months. This will allow clinicians the opportunity to learn from real-world experience with biosimilars and to gain confidence in using them. Thank you for allowing me to -- and I have no time for questions.

MS. IKENBERRY: Thank you.

Our next speaker is Sundar Ramanan, Biocon.

DR. RAMANAN: Hi. My name is Sundar Ramanan, vice president and head of global regulatory affairs for Biocon Biologics, a fully integrated biosimilars company. Our goal is to transform health care and transform lives by

bringing affordable high-quality biosimilars to the U.S. patients. We're also an innovative company, and we intend to transfer the value of innovation to the health systems and patients. We thank the agencies for setting up this public workshop and working towards a fair and balanced marketplace for biosimilars.

The things that I'm going to cover fall under five buckets. Number one, insulin guidance. We applaud the agency for issuing a draft guidance for insulin. The draft guidance is science-based and patient-focused. Despite the expected opposition that has come from few companies, we urge the agency to finalize the guidance.

In addition, for molecules like insulin with high financial unmet need, we request the agency to consider a shorter time frame for the review process once the filing is made. The agency already has precedence in the generic space. This is another critical component to bringing these much needed products to insulin patients faster and fostering competition.

Number two, interchangeability. With the abundance of real-world evidence and frequent marketplace driven switching demonstrating the safety of biosimilars globally, we request the agency to reconsider ON/R [indiscernible], and evaluate the need for multiple switch studies for interchangeability.

Furthermore, we ask the agency to reconsider the need for any distinction between the evidence requirements for biosimilarity and interchangeable biologics. Any regulatory requirement must be based on science and evidence and not based on fear. Needless to say, we collectively must put the patient's safety first.

The immunogenicity data requirement for biosimilarity already satisfies the data requirement for interchangeability. No new or additional information will be gained from multiple switch studies, however, it only results in time delay and wasted resources in bringing interchangeable products to patients.

From a practical point of view, either due

to the use of exclusive formulary replacement in retail pharmacy or through institutional buying practices, interchangeability is the de facto practice in a large number of cases. Practically speaking, though, the regulatory distinction ends up giving an opportunity for originators to create an incorrect perception that biosimilarity standard is not necessarily adequate for safe and effective use while not having a meaningful impact on actual usage.

Number three. Disincentivize anticompetitive behavior on the part of reference product manufacturers and provide positive incentive for biosimilars. The biosimilar market is at the critical juncture, and the steps taken to encourage it now will be critical to ensure its viability.

There have been multiple instances where biosimilar products have not been encouraged, but have been actively excluded from insurance coverage. It is critical that positive incentives such as ASP plus 8 percent reimbursement and steps

like additional biosimilar or specialty tiers in Medicare Part D be provided in order to avoid originator behavior intended to discourage entry of biosimilars and reduce long-term competition.

Delays and cost to frivolous patent litigation and patent thickets should also be disincentivized. We also request the agency to take strong action against misinformation campaigned by the reference product manufacturers. Allowing innovation in the biosimilar development with regards to evidence required, related to immunogenicity, there is little clinical relevance of immunogenicity in oncology settings and general immunosuppressant status.

For drugs with less frequent dosing, say, for example, every 6 months, the need for switch studies is not value-added. Scientific rationale should be encouraged based on the risk of immunogenicity.

With regard to sample size determination, the methodologies need to evolve further to keep in time with the times. Specifically, we request the

agency to utilize Bayesian statistics for residual uncertainty. We also request the agency to allow for mathematical models in PK/PD for extrapolation of indications.

Lastly on naming, we request the agency to consider, with significant experience in the marketplace, the need for suffix for biosimilars. We have additional comments, and we'll be submitting to the docket. We thank you for the opportunity to present.

MS. IKENBERRY: Thank you.

Next, Andrew Spiegel, Global Colon Cancer Association.

MR. SPIEGEL: Good afternoon. My name is Andrew Spiegel, the executive director of the GCCA, and today I am proud to not only represent that organization but also the Alliance for Safe Biologic Medicines, an organization which I am a founding member for more than 10 years ago. We have advocated for patient-centered policies regarding biosimilars since then.

To that end, I have testified numerous times

before the FDA in support of approving biosimilars and before state legislatures all across the nation in support for updating pharmacy practices to facilitate biosimilar substitution. We have also worked and held three joint meetings with the FDA, Health Canada, and the World Health Organization, all with the goal of advancing a harmonized international standard for biologic naming to improve global pharmacovigilance for all biologics and biosimilars.

I can assure you as a founding member of ASBM that no ASBM member has ever suggested that a patient went to the emergency room as a result of switching to a biosimilar. Those patients are here and can tell you their own story later, but I can assure you that not only did that not happen, but ASBM has never advocated or suggested that a biosimilar is inferior to a biologic originator product, and to the contrary, we've been fierce advocates for biosimilar uptake all around the world.

It's also been my privilege to serve in a

number of leadership roles in the international patient community such as the International Alliance of Patient Organizations and now chairing the World Patients Alliance. We know that biologic medicines have helped more than 800 million people worldwide, and in the case of colorectal cancer, in my organization, which has 49 members around the world, we've seen these medicines help triple the life expectancy of the most advanced colorectal cancer patient. We're talking about a life expectancy from 10 months to now 3 years thanks to not only these new treatment options but also getting these treatment options at a reduced cost, and we're hoping that biosimilars will help expand access to these therapies.

With respect to the U.S. marketplace, first and foremost, speaking as the head of an international patient organization, let me be clear that I'm unaware of any attempt to undermine confidence in biosimilars, either in the minds of the public, or in the patient community, or among physicians.

To the contrary, I am encouraged by the extremely positive reaction biosimilars have had in the United States thus far, and patients, physicians, and healthcare providers have all seemed to accept biosimilars as a part of standard medical care, and they recognize what an important tool it can be in containing healthcare costs.

Just as a few days ago, I chaired a panel at a biologics conference in San Diego, where a number of people who are here today were at, and that included chairing a panel where we had one of the largest reference companies, as well as a representative of one of the largest biosimilar companies on that panel. I was very encouraged that both agreed that the U.S. biosimilar market thus far is very much a success story, and both agreed that the future looks very positive.

This great enthusiasm and confidence surrounding biosimilars is in no small part due to the phenomenal work that the FDA has done in approving so many biosimilars in a relatively short period of time, almost half of those approvals

happening within the last year, and the FDA doing so without compromising on its standards for safety and efficacy.

The heart of the U.S. health system, like any other country, has its own unique challenges different from those in the EU, Canada, Australia, or places where we work, but nevertheless, there are things that we can learn from other countries' successes, particularly those of the EU countries who enjoy a robust biosimilars market.

The one thing that we've seen across Europe is that more and more biosimilars are launched in a given product, that more competition drives prices down where discounts increase substantially and biosimilar market share goes up, and we know what to expect and what things to look for, and thankfully we're seeing that happen here in the United States.

Here, we had a biosimilar that launched with a relatively low 15 percent discount over its reference product, and today with increased competition, that product has gained a majority

share in the U.S. market with 55 percent. We have every reason to believe this pattern will continue as we see it becoming routine for 3, 4, 5 biosimilar approvals for a reference product. And as these come to market, manufacturers will continue to compete on price, going from relatively low discounts to higher discounts.

Speaking as a representative of the broader patient community, we of course want more biosimilars approved and available, but our enthusiasm is tempered by the understanding that with anything of this scale and where people's lives and health are at stake, it's not an instantaneous process.

Simply put, the system is working, a little slower than some would have hoped. But just as we don't want biosimilars or any other medicines rust through the approval process, we urge our regulators to be mindful not to unnecessarily and possibly counterproductively interfere with a young but steadily growing biosimilars market.

MS. IKENBERRY: Thank you.

MR. SPIEGEL: Thank you very much.

MS. IKENBERRY: Thank you.

Our next speaker is Kim Caldwell, Pharmaceutical Care Management Association.

MS. CALDWELL: Good afternoon. I am Kim Caldwell, a registered pharmacist with more than four decades of experience throughout the practice of pharmacy. Included in this time is more than 12 years as a member of the Texas State Board of Pharmacy and a year with CMS as a leader engaged in the creation of the program rules for Medicare Part D. I appreciate the opportunity to be here today on behalf of Pharmaceutical Care Management Association, PCMA.

PCMA is a national association representing America's pharmacy benefit managers, which administer prescription drug plans and operate specialty pharmacies for more than 270 million Americans with health coverage through Fortune 500 companies, health insurers, labor unions, the Medicare and Medicaid programs, the Federal Employees Health Benefits Program, and health

insurance marketplaces.

PCMA commends the FDA and the FTC for their collaboration to enhance competition in the biologic products marketplace. We also commend and strongly support the many important steps the FDA has taken to facilitate greater availability of biosimilar and interchangeable products, including its final guidance on interchangeable biosimilars, the 2018 Biosimilars Action Plan, in its comprehensive campaign to educate clinicians about the benefits and savings possible through these innovative therapies.

We are encouraged by the FDA's more recent efforts to reduce barriers to achieving interchangeability, including final guidance limiting the cases in which switching studies were required. The agency also has designed an approval pathway allowing manufacturers to use comparative products not approved in the U.S. for biosimilar development.

These are encouraging steps. Now, we urge the agency to sustain this forward progress by not

adopting unnecessary barriers as it finalizes industry guidance relating to licensure and labeling

Another encouraging development is FTC's commitment to address manufacturer tactics used to block biosimilar entry with anticompetitive patent settlement agreements. Increasing competition through the approval of biosimilar and interchangeable products is key to lowering the prescription drug costs for consumers, employers, and public programs.

We appreciate the collaboration between the FDA and the FTC, which has argued that tactics aimed at gaming FDA rules may be anticompetitive and unlawful, and we urge consideration for further action when manufacturers employ tactics using anticompetitive patent settlements and patent thickets to delay widespread use of lower costs and biosimilars.

An important and necessary next step to further facilitate a competitive biosimilar marketplace is for FDA to promote the therapeutic

substitution of lower cost, interchangeable biosimilars for the reference products. Additionally, we recommend the FDA provide clear direction to states in favor of product substitution without burdening barriers such as notification provisions.

Patients and clinicians need expressed clarity that these therapeutic substitutions are really and truly interchangeable. For many patients and clinicians alike, these therapies are new, and there may be a degree of uncertainty around switching and substitution.

As the FDA's voice is the gold standard for safety and efficacy, when the FDA has approved a product for interchangeability, it should be labeled and marketed as such without conflict or confusion. Anything short of that clarity would reinforce caution with patients and clinicians, and thus impede the ability to achieve a truly competitive biosimilar market. Thank you for the opportunity to provide input. I'll welcome your questions. We have 25 seconds.

(Laughter.)

MS. IKENBERRY: I'm not sure I could get a whole question in 25 seconds.

MR. SPIEGEL: Oh, go ahead. We have time.

MS. IKENBERRY: But you mentioned in your statement some guidance considerations around licensure and labeling, and I would encourage you, to the extent that you intend to submit written comments to the docket, to spell those out a little bit because I didn't quite follow what you were saying.

MR. SPIEGEL: We do and we will. Thank you very much.

MS. IKENBERRY: Thank you

MR. SPIEGEL: And just so you know, that was a lot of words for a guy from Texas to say in that time period --

(Laughter.)

MR. SPIEGEL: -- and I really wanted to say whack-a-mole, but I didn't know if I could get that in. Thank you.

(Laughter.)

MS. IKENBERRY: Yeah, shenanigans and whack-a-mole are two of the nice words of the day.

Next is Andrew Greenspan, Janssen Immunology, vice president of medical affairs.

DR. GREENSPAN: Good afternoon. My name is Dr. Andrew Greenspan, and I'm the vice president of medical affairs for immunology at Janssen, the pharmaceutical company of Johnson & Johnson. At Janssen, we have more than three decades of experience with biologic development, manufacturing, postmarketing safety, and promotion. We pioneered biologic therapy with the first ever approved monoclonal antibody, Remicade, or infliximab, a TNF blocker for which there are currently four approved biosimilars.

From the beginning, we have led in advocating for a biosimilar pathway. We have seen patients struggle for years with chronic progressive disease before getting diagnosed and finding a biologic therapy that finally brings them relief.

We are deeply committed to helping patients

remain healthy and safe throughout their treatment journey and have affordable access to the therapies that they and their doctors decide on. We are also committed to reducing overall healthcare costs and believe that these goals can and must be accomplished together.

With this perspective in mind, we'd like to ask FDA and FTC to consider four points. First, as you collaborate to spur biosimilar adoption, continue to uphold the critical role of the patient-doctor relationship and individual treatment decisions. Many patients endure long and painful journeys before achieving clinical control of their disease. They need valuable information about their options to make informed treatment decisions with their doctor.

Second, we heard many perspectives today on interchangeability. We believe patients and their doctors deserve clear and complete communication on the interchangeability status of a biosimilar. For treatments that require multiple administrations, such as infliximab, patients and doctors should

have relevant data on alternating back and forth between products before deciding to do so.

Implying that a biosimilar is interchangeable when it has not been approved as such is misleading. To ensure that patients and their doctors have clear and complete information on the interchangeability status of a biosimilar, communications on a biosimilar should disclose its interchangeability status.

Third, we urge the FDA to clarify that communications on biosimilars to payers and formulary committees continue to be governed by the FDA guidance on manufacturer communications with payers, formulary committees, and similar entities.

Fourth, we would like to underscore that biosimilar policies are delivering on the promise of the BPCIA with lowered costs for the system and will continue to as long as there is a level playing field for biosimilar and reference products.

The Remicade and infliximab biosimilars experience shows that competition is bringing down

prices for the reference biologic and its biosimilars alike. Since the introduction of infliximab biosimilars, Remicade's average sales price, or ASP, has fallen by 31 percent. Remicade is now the market's lowest priced innovator anti-TNF therapy with annual costs less than half of other innovator TNFs.

Because of Remicade's price competitiveness and uptake of biosimilars, the system has seen over $4.8 billion in savings in the past three years. Additionally, it is important to note that biosimilar development continues to expand with 19 biosimilars in FDA's biosimilar product development program in January 2013 to 63 as of last year.

In closing, as the FDA and FTC look to spur biosimilar adoption, we call on you in parallel to 1) take a patient-centric approach in your policy decisions; 2) ensure interchangeability status is disclosed to patients and providers; and 3) safeguard the competitive market dynamics that are dramatically bringing costs down. Thank you for the opportunity to speak.

MS. TEMKIN: Can I squeeze in one question? The red light just went on.

You said that communications on a biosimilar should disclose interchangeability status. Do you have something specific in mind or can you expand on that a little bit?

DR. GREENSPAN: Sure. As explained earlier, as the market dynamics may lead to switching as frequently as every 6 months with a chronic therapy like infliximab, we think the patients and providers will have questions about the possibility that they may be switched as frequently as twice a year from the products.

My area is immunology where we market infliximab, which is a highly immunogenic molecule, and we think the interchangeability standard was created by the FDA for a very valid reason. I think the point made by a speaker this morning is very valid, that the interchangeability standard should consider specific characteristics of molecules. Some are more immunogenic than others, and that's why it's more important for particular

molecules like Remicade, for example.

MS. TEMKIN: Thank you.

MS. IKENBERRY: Our next speaker is Kathleen Arntsen, president and CEO of Lupus and Allied Diseases Association.

MR. GREENBLATT: Hi. I am not Kathleen Arntsen. My name is Corey Greenblatt.

FEMALE VOICE: I think Steve Lucio is next on the --

MS. IKENBERRY: Oh, I'm sorry.

MR. GREENBLATT: Okay, back up.

MS. IKENBERRY: Steven Lucio, Vizient.

DR. LUCIO: Thank you. To the members of the workshop and to all esteemed employees of the FDA and FTC, my name is Steven Lucio, vice president of the Center for Pharmacy Practice Excellence at Vizient, the largest member-driven healthcare performance improvement company in the U.S., on behalf of Vizient, I'd like to express our deepest appreciation not only for this forum, but also for all the enduring efforts that have been made to enhance competition, thereby improving

patient access to safe and effective biologic molecules.

Vizient provides solutions for more than 50 percent of the nation's acute care providers, including 95 percent of the nation's academic medical centers, a wide array of leading integrated health systems and pediatric hospitals, and more than 20 percent of ambulatory providers in the U.S.

Vizient has focused its array of expertise of supporting health systems evaluation and adoption of biosimilars to lower pharmaceutical expenditures and to maintain or improve patient care. Still more work is required to alter the trajectory of pricing growth for many biologic drugs. Therefore, Vizient would like to offer three key insights and recommendations to advance the desired competitive landscape related to the approval process, education, and payer decisions.

First, Vizient would like to thank the FDA for its efforts at improving the understanding of the approval process through the publication of regulations and guidance documents. The additional

clarity is essential for perspective manufacturers, as well as the population of providers that will ultimately be prescribing these medications.

Vizient would like to note the FDA's decision regarding the clinical immunogenicity considerations for biosimilar and interchangeable insulin products, specifically the decision not to require comparative clinical immunogenicity studies in the approval of these agents, and scientifically substantiated efficiencies and approval will decrease the investment expense required to develop competing molecules.

We encourage FDA to continue evaluating the opportunity for similar decisions to be applied to other biologics. For example, the European community has identified certain molecules and/or product classes where comparative effective studies have been or could be waived, and we would ask that FDA continue to evaluate additional opportunities to streamline approval requirements up to, and including, and eliminating the need for comparative effectiveness studies where scientifically

justified.

We would also like to commend the FDA for increasing the level of education provided to improve the understanding of foundational concepts of biosimilar licensing. We especially thank FDA for increasing the timeliness of access to approval documents for approved biosimilars, even those not subject to an advisory committee hearing.

This information, even the more detailed aspects of analytical characterization, has been invaluable as we have worked to educate pharmacists and physicians on the fundamental differences between the approval methodology of biosimilars as compared to new molecular entities.

Vizient would ask FDA for additional information concerning biologic production. Right now, given the tremendous desire for increased transparency in pharmaceutical manufacturing, including the origination source of API due to our lingering history of drug shortages, as well as the concerns about coronavirus outbreak, while these issues are not primarily impacting biologics, there

is additional transparency that would be helpful addressing any lingering concerns about biosimilar quality and safety.

One of the biggest gaps we found regarding biologic manufacturing understanding is the fact that all biologics, originator or biosimilar, demonstrate variability. In Europe, where this information is disclosed, the content referring to the clinical literature has been very informative in educating pharmacists and physicians. Therefore, we would ask if the FDA could provide information on manufacturing changes related to U.S. biologics. It would further the understanding that the monitoring of biologic variation through analytical means is not novel to the biosimilar experience.

As has been discussed today, there are challenges associated with payer reimbursement decisions, which impact providers and most importantly patients. Beyond educational issues and messages questioning the validity of the approval mechanism, biosimilar adoption continues

to be delayed due to variable coverage and payment policies. It is one of the most substantial hurdles facing the market and will continue to require appropriate attention and focus, and we would appreciate any guidance from either agency on ways to further conversation regarding this hurdle with the appropriate audiences.

We appreciate FDA's and FTC's leadership and working collaboratively to support a more competitive approval landscape for biosimilars. Thank you.

MS. IKENBERRY: Thanks, and sorry for the mix-up.

Next is Kathleen Arntsen.

MR. GREENBLATT: Hello. My name is Corey Greenblatt, and I'm representing Kathleen Arntsen from LADA and ASBM. Before I begin, I just want to say I have no disclosures to make today regarding my comments on behalf of Lupus and Allied Diseases Association.

Good afternoon and thank you for the opportunity to provide our unique patient

viewpoint. Biosimilars hold tremendous promise and therapeutic advantages for people like us, just as biologics have revolutionized treatment for millions of individuals living with life-altering diseases.

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. There is no cookie-cutter approach to treat intricate patients like us, and it requires access to the entire arsenal of treatments and open and transparent communication between us and our providers.

In order for biosimilars to reach their potential and improve stakeholder engagement, education, and access, we need to ensure confidence that biosimilars are as safe and as effective as the reference biologic products among patients, healthcare providers, pharmacists, payers, and other stakeholders while prioritizing patient safety and affordability.

We are pleased that the agency has finalized guidance for interchangeable biologics by clarifying safety, efficacy, and immunogenicity methodologies by requiring manufacturers to conduct vigorous multiple switching studies that alternate between a biosimilar and its reference product. We are also thrilled that the FDA supports robust pharmacovigilant mechanisms for postmarketing safety monitoring of an interchangeable in order to not diminish efficacy and patient safety. Developing an aggressive postmarketing tracking system will also help to guarantee stakeholder confidence and facilitate market uptake while establishing a longitudinal electronic medical record.

We suggest that you consider adopting methods such as apps on electronic devices and patient-reported outcomes to monitor real-world events. Engaging patients and teaching them to be more proactive in their care will be empowering and can help diminish any lack of trust.

Biosimilars have the potential to promote

greater price competition among biologics, and we hope that they are more affordable, but the variance in terminology when referring to biosimilars is both confusing and a hindrance. Stakeholder adoption of more uniform language such as the FDA's would foster more confidence.

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 impact provider ethical obligations by requiring them to follow a set course of care regardless of their best personal judgment.

As an individual who is harmed by step therapy, I am concerned that patients who are stable on any drug will be switched for non-medical reasons, and in particular those doing well in a biologic will be switched 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, stating that switching of stable patients should only be determined by the treating provider and the patient, and facilitating dialogue among multistakeholders, including payers. We ask you to reach out to other federal agencies and work with them to develop sound policies that address such issues.

In closing, I want to reiterate that we are unwavering in our 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 safety must be first and foremost in choosing the most appropriate therapies for any person with complex medical conditions.

We have faith that we can advance biosimilars while still allowing physicians to make decisions in the best interest of their patients. Sometimes that decision is to keep a patient on a successful biologic throughout their therapy; sometimes it is switching to a biosimilar or

starting a naive patient on a biosimilar.

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. We need to work together to make that happen. We thank you for the opportunity to share our perspective and applaud the FDA for continually recognizing the importance of the patient voice during the regulatory process. Thank you.

MS. IKENBERRY: Thank you.

Our next speaker is Ian Orekondy, AdComplyRx.

MR. OREKONDY: Hello. Thank you for the opportunity to comment today. My name is Ian Orekondy. I'm the founder of AdComplyRx. We work with industry to monitor prescription drug advertising and identify ads that appear to inadvertently infringe on FDA guidance so that firms can fix them. Currently, we have a focus on digital ads and search engine marketing.

My input is specific to the draft guidance for promotional labeling and advertising

considerations for prescription biological reference products and biosimilar products. Earlier we heard about Dr. Google and the importance of patient education and healthcare professional education around biosimilars. Dr. Google is often the number one driver of traffic to a prescription medication's website where patients can learn about a specific biosimilar or biosimilars in general.

We also note that there was an FDA warning letter issued last month that was specific to search ads on Google, so our request is that the final guidance documents specifically get into how this biosimilar guidance would apply to internet marketing platforms with character space limitations; for example, Google and Twitter. Additionally, how would this guidance apply to, quote/unquote, "brand-connected ads," that is ads that do not mention any brand within the ad itself but then link directly to a brand.com website.

These are important questions that impact virtually all prescription biologic and biosimilar

brands. We can elaborate on the specific scenarios where we believe more specific guidance would be useful when we submit our comments via the public docket, and we thank you again for the opportunity to comment in person today. Thank you.

MS. IKENBERRY: Thank you.

Our next speaker is Gregory Schimizzi, Coalition of State Rheumatology Organizations.

DR. SCHIMIZZI: Yes, hello. My name is Gregory Schimizzi, and I'm a board-certified rheumatologist with 39 years of experience in private practice. I'm speaking on behalf of the CSRO, which is a national organization composed of state and regional rheumatology societies in the U.S. and Puerto Rico.

To date, some rheumatologists have experienced occurrences of adverse effects or decreased efficacy of biosimilars, but the vast majority of rheumatologists do not believe that biosimilars are inferior. We also have not observed noticeable deceptive marketing practices or received disparaging information on biosimilars

in our offices, at educational meetings, or seen them in journal advertisements. Therefore, we do not believe that these are responsible, to a meaningful degree, for the impaired patient access to these products. We do see significant access issues developing as a result of other marketplace player activities.

Increasing patient access to these medications can only be achieved if cognitive distortions in the marketplace are addressed. Developing remedies that disregard and ignore manipulations designed to maximize profits from fees, rebates, and other schemes that greatly impede access may not be successful. We believe these activities, which are at the core cause of formulary design, far outweigh the impact of deceptive marketing on patient access.

Formulary changes are rarely, if ever, based on comparative clinical outcomes, or studies, or safety, or tolerability, or even wholesale acquisition costs, but rather on profitability to the insurer, the large pharmacy, and PBM entities.

The preeminent access barrier to address is the control of an overly consolidated industry of unregulated middlemen with unfettered power, demanding ever-increasing tolls from patients, community pharmacists, and manufacturers, almost always to the detriment of patients' and physicians' therapeutic options and the quality of health care. Described earlier as one of the bad barriers, these are also a major driver of rising medication costs.

This should not be allowed to continue. It is gratifying to hear that the FDA and FTC are aligned with our own goal here. We urge addressing these reprehensible and egregious insurance and PBM behaviors, much of which exists due to overconsolidation. These abuses need to be addressed either through existing authority or by requesting additional authority where needed and/or petitioning statutory solutions.

We must end the profiteering inherent in the current formulary design process by insurers, large pharmacy, and PBM conglomerates. These are the

main barriers to a fair, robust market of biologic medication access and indeed to all medications. Thank you very much.

MS. IKENBERRY: Thank you.

Next, Laura Brand, Biosimilars Global Commercial Lead, Amgen.

MS. BRAND: Good afternoon. My name is Laura Brand, and I'm the biosimilars global commercial lead at Amgen. Thank you for allowing me to share Amgen's perspective on a topic of critical importance to the future of our nation's healthcare system.

As a manufacturer of both innovator and biosimilar products, Amgen shares a deep commitment to the FDA's and FTC's goal of promoting a robust-to-competitive marketplace for biological products, including the adoption of biosimilars. Although the U.S. market for biosimilars is still maturing, it is competitive.

The FDA has approved significantly more biosimilar products in the first nine years since the U.S. pathway was established compared to other

regions such as Europe, and there are currently over 80 biosimilar programs enrolled in the FDA's biosimilar product development program. Amgen believes this reflects robust manufacturer interest in the current market opportunity under current payment and coverage systems.

Patients in the U.S. healthcare system have benefited from considerable cost savings as a result of biosimilar products already in the market. Competition in the marketplace is likely to yield additional savings as more biosimilars are launched throughout 2020 and the coming years.

Cost savings are just one benefit of biosimilars. Biosimilar manufacturers can also benefit the market by offering improved patient choice by competing on delivery devices and improve reliability of supply. With this portfolio of 10 biosimilar products and development, including four approved by the FDA, Amgen is committed to delivering potential savings and expanded treatment options to patients.

In Amgen's experience, a level playing field

that encourages competition, not only with innovator products but also among biosimilars, creates a robust and sustainable marketplace. This head-to-head competition drives meaningful cost savings and also supports continued innovation to expand biologic treatment options for providers and patients. Our experience demonstrates that the current regulatory and reimbursement policies for biosimilars are working to promote competition.

Amgen has faced competition from biosimilars for innovator products since 2015. Currently, three of our innovator products, Neupogen, Neulasta, and Epogen, compete against multiple biosimilars. Biosimilars of Amgen's Neupogen product together sell more units than Amgen, and a Neupogen biosimilar competitor has obtained preferred status over Neupogen with several formularies, even though this competing biosimilar does not have an interchangeability designation.

In 2019, Amgen launched the first therapeutic oncology biosimilars in the U.S. The list prices for both products are markedly lower

than the average sales price of the respective reference products, generating significant cost savings for patients and payers. Amgen's two biosimilars are gaining adoption quickly, having each secured approximately 20 percent share of the market in just over six months as recently reported by the Bernstein report.

These examples demonstrate the current policies, for example separate coding, are supporting biosimilar uptake and encouraging price competition. At Amgen, we believe the long-term viability of industry depends on a competitive marketplace in which patients, providers, and payers have a real understanding of and confidence in biological products, including biosimilars.

We share the FDA's and the FTC's goal of promoting stakeholder confidence in biosimilars through scientifically accurate educational outreach. Such educational initiatives are crucial to preserving patient choice, driving uptake of biosimilars, and supporting a sustainable marketplace.

In summary, competition is robust, biosimilar market share is increasing, and prices are coming down. Amgen remains fully committed to the success of biosimilars within the U.S. healthcare marketplace. Thank you.

MS. IKENBERRY: Thank you.

Our next speaker is David Balto, Coalition to Protect Patient Choice.

MR. BARLOW: Hi. Good afternoon. This is Andre Barlow on behalf of David Balto, a public interest attorney and the founder of the Coalition to Protect Patient Choice, an entity that advocates on behalf of consumer and patient advocacy groups. We're also speaking on behalf of consumer action.

We are appreciative of the opportunity to provide comments today and we commend the FTC and FDA's efforts to work together to promote biosimilar competition, which will hopefully result in patients having increased access to more affordable drugs. Biologics are essential for the treatment of serious debilitating and

life-threatening diseases.

While fewer than 2 percent of all prescriptions are for biologic drugs, they account for almost 40 percent of all drug spending. In other words, biologics are extremely expensive, and they are the fastest growing segment of drug spending in the United States. The expectation 10 years ago was that a robust biosimilar market would substantially lower the price of biologic drugs. It has been estimated that biosimilars can save U.S. consumers $54 billion by 2026.

In Europe, where biosimilars have entered the market, biologics such as AbbVie's branded blockbuster Humira has been discounted by 80 percent. Unfortunately, biosimilars have faced numerous obstacles in obtaining commercial success in the United States. There are a number of anticompetitive behaviors, or shenanigans, including sample blockage, patent thickets, pay-for-delay agreements, and rebate walls. We would like to highlight rebate walls because we do not believe that they're getting enough attention.

We believe the agencies need to use their enforcement muscle to prohibit rebate contracting practices that block biosimilars from competing on drug formularies. There is increasing evidence that rebates actually raise the cost of prescription drugs.

What is important to understand about these rebates is that they are not discounts for patients. Because the rebates go to PBMs and plans rather than to consumers, payers have perverse incentives to negotiate higher list prices so they can secure higher rebates without regard to patient well-being or patient cost. These rebates actually increase patients' cost because the patient's coinsurance is based on the inflated list price of the branded drug. If the patients had access to lower cost biosimilars, their co-insurance costs would go down.

How does a rebate wall work? A rebate wall or trap is erected when an incumbent manufacturer uses existing market power to secure preferred formulary access for its drug by offering

volume-based rebates to PBMs and plans on the condition that they deny or limit the formulary access of rival drugs.

The rebate is bundled across multiple products, indications, and/or therapeutic specialties, the breadth of which cannot be matched by a new rival. The rebate wall, a manufacturer with a dominant incumbent drug, can prevent entry of a newly approved biosimilar even if the biosimilar is offered at a greater rebate or for free. That's because the new biosimilar has few prescriptions, if any, so even a larger rebate will not overcome the potential loss of the rebate dollars from the market-leading product. Biosimilars lose because they can't get on a formulary. Patients lose because they do not have access to lower cost drugs.

A related practice that keeps patients from detaining access to biosimilars is step therapy, also known as fail-first policies, whereby patients are forced to try a drug preferred by the payer before being approved to use a drug originally

prescribed by their doctors.

Remarkably, most health plans have instituted fail-first policies for new biosimilars, meaning that a patient must fail on a more expensive branded product before the plan will cover a biosimilar of that same branded product. This is noteworthy because, historically, generics which are less expensive than branded drugs have been the first option on the fail-first policy. One explanation for discrimination against biosimilars is that PBMs and health plans secure significant rebates from branded drugs.

In short, the FTC needs to prioritize investigations of rebate walls and step therapy rules, which can be used to foreclose biosimilar competition, which limits patients choices and raises patients costs. Thank you.

MS. IKENBERRY: Thank you.

Our next speaker is Jocelyn Ulrich, deputy vice president at PhRMA.

MS. ULRICH: Hello. Thank you. My name is Jocelyn Ulrich, deputy vice president of medical

innovation policy at PhRMA. I appreciate the opportunity to represent PhRMA and our member companies at today's Workshop on a Competitive Marketplace for Biosimilars.

PhRMA represents the country's leading innovative biopharmaceutical research companies, which are devoted to discovering and developing medicines that enable patients to live longer, healthier, and more productive lives. Consistent with that mission, PhRMA is dedicated to advancing policies that promote innovation and competition in the biologics and biosimilars marketplace.

While the BPCIA is less than a decade old and biosimilar development is significantly more complex and expensive than generic drug development, the benefits of the BPCIA on innovation and competition are already being seen. As of today, there are 15 biosimilars on the market competing against 7 innovator biologics, with an additional 10 approved by the FDA coming to the market over the next several years.

In addition, the upcoming transition of some

products to licensure as biologics and the recently enacted change to the definition of biologic will provide additional opportunities for more biosimilar applications and patient choice.

Publicly available data on the current U.S. market has shown that in every case where a biosimilar has entered the marketplace, both the average sales price of the biosimilar and the innovator biologic have decreased, and as noted by the FTC, basic economic principles support that this indicates the competition is indeed leading to lower prices, increased consumer access and choice, and innovation.

PhRMA supports FDA's efforts to implement a science-based approach to regulating biosimilars that both ensures patient safety and facilitates a robust biosimilars market, and we believe it is critically important to ensure the long-term stability of the BsUFA through financial transparency, efficiency, and accountability.

We also support many aspects of the FDA's biosimilars action plan. In particular, we concur

with FDA that physician education and experience with biosimilars will be critical for fostering biosimilar uptake, and we applaud continued efforts to develop effective communications to improve understanding of biosimilars among patients, clinicians, and payers.

PhRMA believes that FDA and FTC have a robust set of authorities available to them to continue to foster competition and encourage the maturing biosimilars market. To further support the market, we believe policymakers and stakeholders should take the following additional steps. First, we should increase transparency for certain patents on biologic products consistent with what is currently available in the FDA Orange Book for drug products.

Second, to the extent there were issues with access to samples, the recent enactment of what had been previously referred to as the CREATES Act may facilitate access to samples, which in turn will facilitate biosimilars entering the market.

Third, we believe that policymakers should

address barriers to appropriately structured alternative payment models, particularly in Medicare, that have the ability to increase competition among innovator and biosimilar products. And finally, policymakers must advance meaningful rebate reform that would remove barriers to biosimilar uptake and promote access and competition.

In enacting the BPCIA a decade ago, U.S. policymakers rightly sought to balance increased competition with policies that support the United States' leading role in finding new treatments for patients. By allowing the market to continue to evolve and enacting policies that support this evolution, we'll continue to see biosimilars' benefits for patients and society. Thank you.

MS. IKENBERRY: Thank you.

Next we have Corey Greenblatt, manager of policy and advocacy, Global Healthy Living Foundation. Hi, again.

MR. GREENBLATT: Hello, again. Before I begin, I just want to disclose I have no

disclosures to make regarding my travel here today. The Global Healthy Living Foundation accepts grants and charitable contributions from pharmaceutical companies, the federal government, private foundations, and individuals. The organization has received scientific briefings from pharmaceutical companies as well as our independent medical advisory board.

Good afternoon. My name is Corey Greenblatt, and I'm the manager of policy and advocacy for the Global Healthy Living Foundation. On behalf of GHLF, I want to thank this committee for allowing me to speak. GHLF is a 20-year-old 501(c)(3) organization representing chronically ill patients and their caregivers across the country. GHLF works to improve the quality of life for patients living with chronic disease by ensuring their voices are heard and advocating for improved access to care.

The barrier for entry in the U.S. biosimilar market has been too high for too long. Despite the Biologics Price Competition and Innovation Act, the

U.S. is about seven years behind Europe. Not having a robust biosimilar market is a failure in U.S. health care. Patient and provider education is one reason for this failure; economics is another.

Patients understand generic versus branded drugs, but they do not understand biosimilars, especially in the aggressive context in which they are presented by insurers. Even many healthcare professionals don't understand when to use biosimilars and what the positives and negatives of biosimilar use are. They are instead instructed when to use them by insurers.

Switch biosimilar patients are required to abandon a medication that works with little or no explanation, education, or counseling. The healthcare provider gets a letter in the mail telling them to switch the patient or the patient will pay the full retail price of their current drug. This is obviously not the way to sell the benefits of biosimilars to patients or physicians.

Government is being asked to favor one group

of manufacturers making biosimilars over another which doesn't, with complete opacity to the patient. Our hope is that the agencies will work to create a transparent environment for the patient, one that does not show a bias for biosimilars or biologics, allows the patient to directly benefit from generic-like lower price, and feel positive about switching to or starting on a biosimilar. We believe that only then will a robust biosimilar market emerge for chronically ill patients.

GHLF, the FDA, and other patient groups can handle the education issues around biosimilars if you can clear up the economic inequalities. To the patient, biosimilars are generic biologics. Your job is to create the market that allows them to be priced this way. We need a system that allows therapies to compete based on clinical outcomes and costs to the patient, not a system that allows anticompetitive practices such as rebates, rebate walls, favorable pricing to physicians, access-restricting formularies, co-pay accumulator

adjusters, and step therapy.

Non-medical switching needs to be defined. Patients and physicians should be able to voluntarily non-medically switch drugs when it benefits the patient, not only the insurer and the PBM. If a patient can save money and their healthcare professional does not object, they should be allowed to switch brands, whether it's a biologic or a biosimilar.

Forced non-medical switching, which occurs now, offers no quantifiable financial benefit to patients, only profits to insurers. The patient is the only one who shows up to the table with a checkbook but no power. Everyone else shows up with varying degrees of power that are used to protect profits. It is nearly impossible to identify any other market where the person paying the bills has so little influence on the price of the product or the product itself.

You can change this by recognizing the need for strict regulation of insurance practices and market-based price lowering incentives to

biopharmaceutical companies. If there's no financial relief for patients from what to them is a generic drug, then biosimilar growth will continue at its slow pace compared to other generics and biosimilars in other countries.

We thank the FDA and the FTC for emphasizing the value of the patient perspective through public meetings, and we will continue to mobilize our patient communities and create a better life for those who will benefit from biosimilar therapies. Thank you for your time and attention. It is greatly appreciated.

MS. IKENBERRY: Next is Fouad Atouf.

DR. ATOUF: Good afternoon. My name is Fouad Atouf. I'm vice president of global biologics at the United States Pharmacopeia, USP. I appreciate the opportunity to present on behalf of USP our comment on the competitive marketplace for biosimilars. USP is an independent scientific non-profit organization dedicated to improving health through the development and dissemination of public standards for medicines, foods, and dietary

supplement.

Through a long-standing collaboration with the FDA, we have worked continuously to benefit public health by facilitating broader access to quality medicines. USP supports FDA's and FTC's effort to foster access to biosimilars and to pursue initiatives that facilitate increased competition to biological products. Furthermore, we believe that our public standards serve an important role in fostering a competitive marketplace.

First and foremost, USP public standards help ensure quality medicines. For example, USP's quality standards for insulins have been used by manufacturers for a decade to meet quality expectations. Additionally, USP standards provide valuable information to biological manufacturers to support early development of new or biosimilar products and address common quality issues. These standards can add flexibility by offering choices of analytical approaches.

Furthermore, studies indicate that public

standards help foster a more competitive marketplace for medicines because the standards provide transparency on the quality expectation for medicine, which helps new manufacturers bring new products to the marketplace.

USP standards are developed in an open transparent process. They're established by independent experts and scientific experts, and development of the standards takes into account public input. The expert who works with USP will collaborate closely with stakeholders and government agencies such as the FDA.

USP is committed to ensuring that our approach evolves with the science of biologics and the needs of stakeholders by developing solutions that support the adoption of emerging analytical tools for biological product innovation and competition. We are currently developing standards that are broadly applicable to classes and families of biological products and also working on tools to address quality of raw materials with an overall goal to support analytical testing throughout the

product life cycle.

USP is a convener and will continue to convene stakeholders to identify areas of needs and improvement for development of biological products. In recent years, we hosted a series of roundtables to address and discuss with the stakeholders the common quality challenges and to develop together a set of solutions that address biological products throughout the product life cycle.

We will continue that convening role and we plan to hold in the next coming month a series of roundtables to address topics like ensuring quality of biologics globally, but also ensuring quality of insulins and other topics such as the role of genomics analysis and personalized medicines.

We are very much interested in hearing from the FDA and FTC any additional topics you would like to discuss with stakeholders and would be happy to facilitate those discussions. Thank you again for the opportunity to present, on behalf of USP, our perspective. Thank you.

MS. IKENBERRY: Thank you.

Laura McKinley, director of regulatory policy, Pfizer.

DR. McKINLEY: Hello. Thank you. I am Laura McKinley as she said, director of regulatory policy at Pfizer, and we appreciate the opportunity to present here today and applaud the FDA-FTC collaboration to support appropriate adoption of biosimilars.

The introduction of biosimilars in the U.S. was intended to increase competition by providing additional safe and effective biologic treatment options, thereby reducing healthcare costs. This goal will not be realized if patients and healthcare professionals receive incomplete or misleading information.

In August 2018, Pfizer filed a citizen petition requesting that FDA issue guidance to help ensure communications by sponsors concerning the safety and effectiveness of biosimilars are truthful and non-misleading.

In this regard, Pfizer appreciates the important steps FDA has taken to address

misinformation, including the publication of draft guidance that specifically notes that reference product promotional materials should avoid representing or suggesting that a biosimilar product is less safe or effective than its reference product because it has not been studied in all clinical indications and/or is not licensed as interchangeable.

The Federal Register notice seeks input on promotional materials for interchangeables. Pfizer believes it is essential to avoid inaccurate perceptions of the safety and effectiveness of biological products based on their licensure pathway. Therefore, we encourage FDA to also address interchangeable biosimilar labeling and promotional materials to help ensure these to avoid representing or suggesting that a biosimilar product is less safe or effective because it has not been licensed as interchangeable.

Pfizer fully supports the rigorous evaluation standards that FDA applies to all products, including biosimilars, but believes

further opportunities exist to optimize the approval process for biosimilars without compromising scientific standards.

For example, FDA has indicated they intend to review and act upon supplement-seeking licensure for an additional condition of use in a 6-month review time as opposed to the 10-month review time frame outlined in the BsUFA II goals letter. However, the BsUFA II goals letter is limited to supplements with clinical data.

We think consideration should be given to reduce even further the review time for supplements seeking licensure for additional indications supported by scientific justification of extrapolation in the absence of additional clinical data. This would avoid unnecessary delays in patient access to biosimilars.

It would also be beneficial to have further guidance regarding the post-approval process for adding safety information to biosimilar labels. In particular, Pfizer urges the agency to consider biosimilar safety labeling updates that are

consistent with the risk information in the reference product labeling as a CBE-0 submission. Treating such updates as CBE-0's will help ensure important risk information is being disseminated to healthcare providers and patients in a timely manner.

Finally, Pfizer is concerned about anticompetitive contracting practices by which a biologic manufacturer undertakes systemic efforts to maintain unlawfully a monopoly in connection with its reference products. The practice of withholding significant rebates for both current and future patients, unless insurers agree to biosimilar exclusion contracts, effectively block coverage of biosimilars. Without such coverage, providers are reluctant to stock biosimilars.

Further, anticompetitive contracts effectively conditioned on the providers not purchasing biosimilars in exchange for discounts on the reference or other products prevent physicians from trying and patients from accessing biosimilars. Pfizer again thanks FDA and FTC for

convening this workshop and for the opportunity to speak.

MS. IKENBERRY: Thank you. That was our last registered commenter. So with that, I will turn it over to Caty for final remarks.

Closing Remarks - Catherine Gray

MS. GRAY: I have the best job of the day.

On behalf of FDA and FTC, I'd like to thank all the speakers and panelists and everyone in the audience for participating in today's workshop. Whether you attended in person or via webcast, we greatly appreciate your attention and your interest in today's sessions and presentations. I'd like to also send out one last acknowledgment to the many folks at FTC and FDA who worked tirelessly in preparing for this meeting. Thank you for your persistence.

As a reminder, we strongly encourage you to submit your comments to the docket, which will be open until April 9th. If you would like any details on how to submit your comments to the docket, we have placed copies of the Federal

Register notice announcing this meeting at the registration table just outside the meeting room.

A transcript from the workshop should be posted to the workshop website within 30 days. We will provide copies of today's presentations upon request and contact information about getting those copies is also available at the registration table.

On that note, I'm closing the workshop. Thank you again for participating and have a safe trip home.

(Applause.)

(Whereupon, at 4:18 p.m., the workshop was concluded.)

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