THE BROOKINGS INSTITUTION

CULTIVATING A VIBRANT U.S. MARKET FOR BIOSIMILARS: A CONVERSATION WITH FDA'S SCOTT GOTTLIEB

CO-HOSTED BY THE USC-BROOKINGS SCHAEFFER INITIATIVE FOR HEALTH POLICY AND THE HUTCHINS CENTER ON FISCAL AND MONETARY POLICY

Washington, D.C.

Wednesday, July 18, 2018

Keynote Address:

SCOTT GOTTLIEB
Commissioner
Food & Drug Administration

Panel Discussion: Pharmaceutical Market

DAVID WESSEL, Moderator
Director, The Hutchins Center on Fiscal and Monetary Policy
Senior Fellow, Economic Studies, The Brookings Institution

LEEMORE DAFNY
Bruce V. Rauner Professor of Business Administration
Harvard Business School

JOSHUA OFMAN
Senior Vice President, Global Value, Access and Policy
Amgen Inc.

ARTI RAI
Professor
Duke Law School

* * * * *

P R O C E E D I N G S

MR. WESSEL: Hi. Good afternoon. I'm David Wessel. I'm director of The Hutchins Center on Fiscal and Monetary Policy here are Brookings.

I'm pleased to welcome you, along with my colleagues from the USC Schaeffer -- what is this -- USC Brookings Schaeffer Initiative for Health Policy. I think we should have an acronym. You might wonder why someone who is interested in fiscal policy is even doing an event on drug prices.

My colleague, Louise Sheiner, and I have decided two things. One is, if it's like over a billion dollars we consider it fiscal policy. And secondly, seriously, if you're thinking about the fiscal future of the United States you can't avoid thinking about health care prices and health care spending. If you're thinking about health care spending, you can't avoid thinking about prescription drug prices.

I'm very pleased that we have Scott Gottlieb, the commissioner of the Food and Drug Administration with us today. Dr. Gottlieb is a physician, but he actually majored in economics in college. Among other things, he was a resident fellow at our neighbor, the American Enterprise Institute. Dr. Gottlieb was deputy commissioner at the FDA from 2005 to 2007, and returned to the FDA as commissioner in May 2017.

He told me that means 15 months into the job, and according Gardiner Harris of The New York Times, the average tenure of an FDA Commissioner is 18 months. So, I hope this isn't your last.

When Dr. Gottlieb was appointed or nominated to be FDA commissioner there was quite a bit of criticism from people, many of them on the left, who felt that somebody who had done so much work with the drug companies wouldn't be an effective FDA commissioner.

I think a lot of people have been impressed with how much energy he's put into trying to spur competition in the prescription drug market, which is what he's going to talk about today, as well as what he's done with trying to reduce the use of

tobacco and other things.

So, we are very glad to have him with us today. He's going to speak, I'm going to ask him some questions, we'll offer you a chance to ask a few questions, and then because we have such intelligent design at Brookings we have a panel that consists of one economist, one lawyer and one physician to follow.

So with that, Commissioner Gottlieb? (Applause)

DR. GOTTLIEB: Thanks a lot. It's a pleasure to be here to talk about biosimilars and not to have to talk about almond milk. (Laughter) So, I appreciate the opportunity to be here. I want to talk about a plan that we are laying out today to try to instigate biosimilar competition.

Our ability here at the FDA to build a market of safe, effective biosimilar products is key for patients, and it's key for the nation's health care system. It's also a key to us to promoting access and reducing health care costs. And it's a key to advancing public health.

But we are worried, and I'm worried in particular, that the market for these products is still not firmly established. And the ability of these products to penetrate clinical practice, and gain acceptance in clinical practice isn't yet firmed up.

That doesn't mean that the future doesn't hold a lot of promise for biosimilars. It just means in my view that the future is uncertain, and the policy, and the regulatory decisions that we make, here in the present day, are going to have a lot to do with whether or not we realize the promise from this new category of products. Or whether we see the opportunities we once envisioned from biosimilars, go unrealized.

We know that biosimilars are used to treat many serious and life-threatening diseases, and they've become the mainstay for the treatment of cancer and autoimmune conditions, among many others.

They are also very expensive. While less than 2 percent of Americans use biologics, they represent 40 percent of total spending on prescription drugs. So,

enabling a path to competition for biologics from biosimilars is the key to reducing costs and to facilitating more innovation in this space.

And by enabling a path for competition for biosimilars, we also give innovators an added incentive to invest in further research that will lead to the discovery of even better drugs that deliver additional benefits to patients.

At the FDA, we are focused on advancing policies that make the process for developing biosimilars more efficient.

And to achieve these goals, I'm pleased to announce today that we are releasing what we are referring to as our Biosimilars Action Plan. This plan is important. It's an important piece of the Administration's overall blueprint to lower drug prices, and demonstrates the progress that we are making on delivering on the President's goals that we laid out earlier this year.

Our plans are aimed at promoting competition and affordability across the market for biologics and biosimilar products. And before I focus on some of the elements of the plan itself, I want to talk about some of the broader goals that we are focused on at the FDA.

At the Agency, we recognize the critical role that Congress has given us to make sure the U.S. maintains a robust market for new biologics innovation, while also advancing paths that promote timely biosimilar competition to enhance patient access and to reduce costs for patients in our health care system.

Preserving that balance between innovation and competition requires us to modernize our regulatory requirements to maintain efficient, predictable and science-based pathways for drug review.

Our aim is to reduce the time, uncertainty and cost of drug development while also supporting a competitive market through the efficient approval of lower-cost generic, and biosimilar and interchangeable alternatives after the expiration of patents or other statutory exclusivities.

This cycle of market-based innovation and competition has helped America's biopharmaceutical industry become the leader among its global peers across the world. And when patients with life-threatening diseases look for medical hope, they often look first to American research.

In many respects, America is the world's medicine chest. We've seen a lot of progress against vaccine diseases in recent years. But I believe we are at an inflection point in medical practice.

We are at the brink of an era that's comparable to the period just after World War II perhaps, when we first introduced effective antibiotics. That period was a period where we went from temporizing many ailments to curing them. And I think with the advent of new platforms like gene therapy, and more targeted drugs, we are at a similar point right now.

In the long run, these therapies are going to be very disruptive. They'll not only improve medical care, but they'll also lower health care costs, and they'll defray, or in some cases, even eliminate the labor costs associated with chronic, debilitating diseases that can lead to expensive hospital admissions. And they'll help more people escape a trap of long-term care in settings that can rob them of their independence and their dignity, and reduce their economic productivity.

But these costs and these cost savings may be less visible than a drug's sticker price. And they are an even greater drain, however, on our nation's finances and productivity. Yet we know that these cost savings tomorrow do not pay health care bills today. So we must learn how to deliver both cutting-edge innovation and affordable access to new treatments in the present time, and not decades after a product is introduced.

And that brings me back to the discussion of biosimilars. Biologics represent 70 percent of the growth in drug spending from 2010 to 2015, and they're forecasted to be the fastest growing segment of drug spending in the coming years.

To make sure that the next generation of breakthroughs remains affordable, and requires vibrant competition from biosimilars. But it also means that we need to consider new payment approaches, models that allow us to take advantage of the competition that biosimilars offer.

Our current payment system, which reimburses drugs based on their average sales price, was designed in a single-source world. It was a market with biologics where there's typically only one drug available in each category, and there wasn't a lot of therapeutic variety or therapeutic competition.

At the time, and I was there at the time, there was only one EGFR inhibitor on the market, and just one VEGF inhibitor. I was there when we designed this system, and implemented it at Medicare. And I can tell you that many of us didn't envision a world where there'd be so much competition in these therapeutic categories.

So that system was designed, that accepted the fact that government programs, like Medicare, would be price takers. We didn't have the advantage of drug competition to enable the development of formularies, bidding and market-based negotiations like we have in Part D, in the Part D prescription drug plans.

So the system we designed, and using the average sales price as a benchmark for reimbursement, was designed to help make sure that drug makers wouldn't be able to take big price increases once the drugs came to market. But it wasn't a system designed to take advantage of price competition, because we didn't foresee that there would be multiple drugs in these different categories.

That's not the case anymore. Now, with most of these biologics categories, we are seeing highly competitive markets with lots of different products aimed at the same target, yet the current payment system isn't taking advantage, or full advantage of this therapeutic competition.

And so we need to adopt a different approach to paying for these drugs. The ideal system, in my view, would reimburse biologics in a competitively-bid scheme,

where we would take full advantage of the multi-source competition. Even without these policy changes, right now savings estimates from expected biosimilar competition are large.

They range from $54 billion from 2017 to 2026 according to a study by RAND, to as much as $250 billion from 2014 to 2024 from just 11 biosimilars expected to be approved and marketed according to a survey by Express Scripts.

The assumptions and the timelines behind those estimates vary. But the fact is the biosimilar market isn't as competitive as many observers hoped it would be after Congress first passed legislative the Pathway. And so far, the real savings have been just a fraction of even the most conservative initial estimates.

You don't have to look very far to understand why. And while the FDA has approved 11 biosimilars through 2018, only three are now marketed in the United States. Competition is, for the most part, anemic.

It's anemic because consolidation across the supply chain has made it more attractive for manufacturers, and pharmacy benefit managers, and group purchasing organizations, and distributors as well, to split monopoly profits through lucrative, volume-based rebates on reference biologics, or on bundles of biologics and other products, rather than embrace biosimilar competition and lower prices.

It's anemic because litigation has delayed market access for biosimilar products that are, or shortly will be available in markets outside the U.S. several years before they'll be available to patients here. These delays can come with enormous costs for patients and for payers.

Let me give you one measure of those costs. At the FDA, we did an analysis of biosimilar competition across all OECD markets. We looked at what would have happened if all the biosimilars that the FDA approved in the U.S. were successfully marketed here in a timely fashion.

And we'll release the full details on this analysis soon, but I want to give

you some highlights of what we found. To measure the potential impact of this biosimilar competition, we assumed that the savings achieved in the U.S., in terms of price discounts, would have been on par with the experience enjoyed in the other OECD nations.

And based on these assumptions, our analysis shows that if Americans had the opportunity to purchase successfully-marketed FDA-approved biosimilar prescription drugs, they could have saved more than $4.5 billion in 2017 alone.

These are large savings. They're about half of the nearly $9 billion in total savings in 2017 from all of the 2017 generic drug approvals, according to earlier FDA analysis. And this analysis assumes that all of the biosimilars that the FDA approved were successfully marketed.

But we know that's not the case. We know that litigation has blocked a lot of these launches. Yet our study found that the entry of a single biosimilar product in a non-U.S.-OECD market lowers prices relative to the reference product by 30 percent; and the markets with three to four biosimilar entrants, they have prices 35 to 43 percent lower than their reference biologics.

Our savings estimates don't include additional potential savings from biosimilars approved in 2018. Estimated savings would therefore have been significantly greater than the 4.5 billion if these additional FDA-approved biosimilars were also marketed at or near the time of their approval.

Biologic manufacturers have a right to defend their legitimate intellectual property interests. And we want them to continue to offer the benefits of improved versions of originator biologics. These benefits might include biologics that target diseases in new ways, such as delivering a toxic payload directly to cancer cells, as we've seen in some recent innovations, or biologics that target multiple targets of disease simultaneously.

These benefits might also include new formulations of established drugs

that can improve delivery options. For instance: shifting from health care provider-administered infusions to products that a patient can self-administer at home, and therefore need less active physician monitoring for the administration of the drug.

Those types of innovations can deliver real economic and public health advantages. And the competition from new biosimilars might drive innovators to invest in these new opportunities. That's how biosimilars can help promote new innovation, just like with traditional generic drugs.

This is how the advent of biosimilar entry should also inspire entrepreneurs to invest in new technologies and develop new monopolies around better innovations.

But rebating schemes or patent thickets that are purely designed to deter the entry of approved biosimilars are spoiling this sort of competition in my view. Long-dated contracts are another toxin. The branded drug makers thwart competition by dangling big rebates to lock up payers in multi-year contracts right on the eve of biosimilar entry.

We are also concerned that volume-based rebates may encourage dysfunctional clinical treatment pathways. We've heard from multiple sources that some payers are requiring step therapy or prior authorization on the reference biologic before patients can access a biosimilar.

We see no clinical rationale for these kinds of practices, since a biosimilar must demonstrate, among other things, that it has no clinically meaningful differences from the reference product as a part of demonstrating biosimilarity.

The branded drug industry didn't build its success by being business naïve. They are smart competitors. But that doesn't mean we need to embrace all of these business tactics, or agree with them and think that they are appropriate.

Some of these tactics should be unacceptable to every member of the drug supply chain. Biosimilars may be relatively new, but manufacturers' tactics to delay

and frustrate Congress' legislative intent in this regard to promote competition in the drug pricing scheme date back decades.

These tactics were first honed in battles between branded companies and manufacturers of small molecule generics after the passage of the Hatch-Waxman Act in 1984. And these battles played out for a long time, but ultimately competition prevailed, and so did the benefits of small molecule generic drugs.

In 1983, generics accounted for only 13 percent of U.S. prescriptions. Today in 2018, it's 90 percent, and generics cost 75 to 90 percent less than their branded competitors.

Robust competition has led to generic drug prices that are often less expensive here in the U.S. than in other developed markets, in Europe and Asia. And the Association for Accessible Medicines, the trade group that represents the generic drug makers, estimates that generic medicines have saved the U.S. well over $1 trillion over the last decade.

The generics market that we see today, while not perfect, is robust in most respects. But it took about two decades, and longer probably, for it to develop. It took a long time for providers to grow comfortable prescribing generics, and patients to be confident in taking them. And it took a long time to work through legal tactics that were put in the way of competition. It took a long time for the coverage systems to be changed in ways that allowed for brisk, generic entry.

Sometimes it feels like we are seeing the biosimilars version of Groundhog Day with the brand makers replaying some of the same tactics, and all of us being too susceptible to many of the same misconceptions about biosimilars -- their safety and their efficacy relative to originator biologics.

We are falling into some of the same doubts and policy constraints that were used to deter competition for generics in the years after the passage of Hatch-Waxman.

But we are not going to play regulatory whack-a-mole with companies trying to unfairly delay or derail the entry of biosimilar competitors. We are not going to wait a decade for more robust biosimilar competition to enter the market.

Expanding access to affordable biosimilars and slowing the rise of health care inflation is an even more critical issue today than it was in 1984. The higher costs and longer timelines required to develop biosimilars relative to generics, means that these delaying tactics can make it uneconomical for biosimilar sponsors to postpone entry for extended periods of time.

And I'm worried that the biosimilar manufacturers may pull out of these markets altogether if the branded drug makers are able to lock up markets even in cases where there's a fully interchangeable biosimilar competitor.

Ultimately, this behavior is putting innovative drug development at risk by eroding public confidence in market-based pricing mechanisms. Too many people are now shooting at the branded drug makers, and the shrapnel isn't just going to tear apart the gaming tactics that we might agree are gratuitous and ill conceived. I'm worried that the shrapnel could also help to fray the fragile market-based rewards that support new drug innovation.

Our Biosimilars Action Plan applies many of the lessons learned from our experience with generic drugs, to accelerate biosimilar competition with four key strategies.

First, improving the efficiency of the biosimilar and interchangeable product development and approval process; second, maximizing scientific and regulatory clarity for the biosimilar product development community; third, developing effective communications to improve the understanding of biosimilars among patients, and providers, and payers as well; and fourth, supporting market-based competition by reducing gaming of FDA requirements, or other attempts to unfairly delay market competition to follow-on products.

I don't want to get into the details of the entire plan in my remarks today. We've issued that plan in its entirety. It lays out all of the discreet elements of the approach that we are taking. But I do want to highlight a few key actions that we are taking.

I believe some of these actions could be transformative for sponsors' ability to bring high quality biosimilars to the market.

As part of this effort, the FDA is seeking to strengthen its partnerships with regulatory authorities in Europe, Japan and Canada. Such partnerships can enable greater efficiency in developing safe and effective biosimilars.

For example, we are actively exploring, whether data-sharing agreements could give us better insights into biosimilars' real-world safety and efficacy and, in some circumstances, facilitate the increased use of non-U.S.-licensed comparator products in certain studies to support an application under Section 351(k).

We know that when those developing biosimilars use biologics sourced ex-U.S. as their comparator product, it can lower the cost of clinical studies since many of these products can be procured more easily and cheaply in European and Asian markets. In fact, about half the cost of conducing a biosimilar drug development program is the cost of acquiring the drug right now.

We'll also be updating the Purple Book and evaluate whether we can incorporate additional information into that resource to give product developers more transparency on issues like patents, and we are also going to be updating the guidance to provide additional clarity on how biosimilar manufacturers can carve out indications from the labels where a branded drug maker might still maintain (inaudible) pay. And we are going to describe how these indications can be efficiently added back to a biosimilar label, once that IP has lapsed on the branded alternative.

And we are going to be taking some new steps to challenge some of the gaming tactics I talked about earlier, and this includes new efforts to coordinate with the

Federal Trade Commission to address anti-competitive behavior. And we look forward to participating in additional forums with the FTC to jointly identify ways that we can deter anticompetitive practices in the space. So I hope you all stay tuned to what we'll be doing in conjunction with the FTC.

As part of our Drug Competition Action Plan, we made it a priority to ensure that Risk Evaluation and Mitigation Strategies, the (REMS), our safety programs, maintain their role in serving the public health and aren't used to delay competition from entering the market by refusing to sell the samples necessary for developing generic drugs. We are going to apply the same approach when it comes to our Biosimilar Action Plan.

One final important note that I'd like to stress from our experience with generics: the FDA can't do it alone. Effective market competition from biosimilars depends on additional actions from our public and private sector partners to align reimbursement and formulary design to encourage appropriate biosimilar adoption.

Competition requires all of us to shine a light on the anti-competitive impact of tying rebates and bundling biologics with other products to protect biologics' market share, and it requires us to educate providers and patients about biosimilars, and why people should have confidence in the safety and the effectiveness of these FDA-approved products.

There's active work under way on bold reforms, like shifting biologics from Medicare's Part B scheme into a competitively bid system like Part D, where we can take full advantage of price and therapeutic competition.

These types of approaches can delink physician reimbursement from drug prices and inject more competition into the market, while increasing the incentives to create the next generation of great innovation that's going to advance human health. And our new plan is aimed at laying the groundwork for these and other reforms, to make sure we are realizing these public health opportunities.

I appreciate the time here to lay it out with you all, and it's posted on our website. And I look forward to interrogation by David. Thank you for the opportunity to be here today. Thanks a lot. (Applause)

MR. WESSEL: Thank you very much. That was really interesting, and now I feel like I'm an expert on biosimilars, which I wasn't 15 minutes ago. So, I appreciate that.

I want to just probe you a little bit on your diagnosis, why there's a lack of not enough competition. You kind of divided it into two parts, one was kind of deals among manufacturers, PBMs, and others in the supply chains that keep biosimilars off the market make it hard for them.

So, just explain to me a little bit about what is going on there, and who has the responsibility for doing something about it; you, the FDA, the Federal Trade Commission, Congress, the Courts?

DR. GOTTLIEB: I think there are certainly steps that Medicare and FTC can take. I mean what I'm seeing is when the biosimilars come to the market they can only penetrate a portion of the market, it's only about 15 percent of the market is easily accessible to them.

What happens is that the incumbent biologics will often enter into long-dated contracts and offer big rebates right on the eve of biosimilar entry, they are, you know, astute competitors. And if the biosimilar wants to enter the market and come on to the formulary of a health plan or PBM, and maintain the formulary, what effectively will happen is that the health plan will lose all the rebates being paid on that incumbent product, because the contracts and the rebates are tied to being only a single drug on the formulary.

And so the biosimilar has the challenge of being able -- having to discount enough, and be able to shift enough of the market share from the incumbent product onto the biosimilar to offset those lost rebates, and that's nearly impossible.

Even with interchangeability it would be hard because there would be reluctant to switch among patients and providers.

And so the biosimilar literally can't discount to a point where they could offset the lost rebates, given the fact that when they come onto the market they're not going to capture a lot of market share day one.

And so that creates a real barrier to entry, and my concern is that if we see a number of failed launches in this space, if we continue to see failed launches, or very difficult launches you're going to see less people investing in this space, certainly, you know, the venture capital and some of the more entrepreneurial endeavors are going to pull out these kinds of markets.

What could be done about it? To your second question; I think there's probably certainly aspects of this that the FTC is looking at, and can look at. There might be things you can do under Medicare with -- certainly on the Part D it would be difficult to set rules of contracting because you would potentially pierce the Non-Interference Clause so you can't mandate that Part D plans -- contract in a certain way, but under Medicare Part D you might be able to put in place provisions that prevent these long-dated contracts, and --

MR. WESSEL: In Part D you can do it, or Part B?

DR. GOTTLIEB: In Part B, Part B -- excuse me -- that prevent these long-dated contracts so they allow for more flexibility in the market. I suspect that that would be scored as costing money. I think in the long run it would end up saving money because you'd have a more dynamic market, but there might be an impediment in that, the actuary or CBO might score that as actually costing money in the near term.

MR. WESSEL: So the other thing, the other piece of it where you mentioned litigation, ways that the original biologic innovator uses the court system to delay the entry of a biologic -- of a biosimilar.

So, one example that Members of Congress have called attention to, and

I can talk about that later with Josh from Amgen, is this deal that, for Humira, where the maker of Humira entered into a settlement with two biosimilar companies, Amgen and Samsung.

And under the agreement, as I understand it, this is according to Grassley and Klobuchar, Amgen and Samsung will not be able to launch their products in the U.S. until 2023, but they can launch their biosimilars in Europe in 2018. Is that the kind of thing you're talking about that slows the use of biosimilars here?

DR. GOTTLIEB: Well, I don't want to get into any specific litigation. I'm certainly not an expert on legal environment but, you know, we see issues around patent thickets as well in this space where you can patent different features of the manufacturing process, that end up also delaying the ability to carve around IP.

I think that, you know, part of the challenge here is that it took many years for the litigation to work its way through on Hatch-Waxman, now you have a relatively well-defined legal framework around small molecule generic drugs, and you actually have both sides loath to reopen any aspect of Hatch-Waxman because the litigation is so well resolved around that, and its predictability.

The only people who would probably want to reopen Hatch-Waxman are lawyers, but the problem here is that things haven't been litigated, and so, you know, you're seeing precedent gets set in real time. I think the challenge we have is that, you know, we don't feel we have the time to allow that to play out in the same way that they would with Hatch-Waxman, because the drug cost issues are more acute now.

MR. WESSEL: So, both of these, both the practices in the distribution chain, and the litigation, are a way to kind of extend the exclusivity that an innovator has, right?

DR. GOTTLIEB: Well in --

MR. WESSEL: In practice?

DR. GOTTLIEB: -- in practice I think that, you know, in my view, the

litigation is going to get sorted out, it's going to get sorted out by the courts; it could potentially be sorted out by Congress, and the action the FTC takes. I think that the way to impact market entry more immediately might be through some of the busting up these contracting provisions especially when the government is a party to them. There's more immediacy to policy changes that could impact that.

MR. WESSEL: Do you think we should think about the period of exclusivity, and whether that's optimal for balancing the incentives for innovation and encouraging competition?

DR. GOTTLIEB: But that's being carefully looked at, and I'm not -- I'm not in a position to relitigate the economic analysis that went into the, you know, twelve or seven years, and the people were asked to (inaudible) the arguments around that. You know, there is -- it is the reality that the effective -- the actual exclusivity period on products has, if anything, declined over the years, the effective exclusivity around these biologics is longer because of the difficulty penetrating the market with competition, but patent terms have actually come down over time.

MR. WESSEL: One of the things that the Federal Trade Commission has beseeched the FDA to do is to change something that you didn't talk about your remarks, this business of adding a random suffix to the nonproprietary name at the end of each biologics, so like there's a four-letter thing that goes at the end, and the biosimilar doesn't have the same thing.

And the FTC claims that this may reduce price competition, may create unnecessary costs. That's something that's under the control of the FDA. Do you agree with the FTC, or are you --

DR. GOTTLIEB: I disagree. I think this is a bit of a red herring. I've had a lot of conversations with the FTC trying to inspire them to bring litigation in cases where we see anti-competitive practices. I wish that they would focus more on the illegal activity and less on a scientific nomenclature that we use (laughter) for pharmacovigilance.

But, you know, this is important for our own pharmacovigilance, you know, we still have an open question of whether or not we are going to apply a suffix, or do you change, alter the branded company's name as well. There would be a lot of costs to the system of doing that but, you know, the fact it's differentiated with a suffix and that is important for our pharmacovigilance, our post-market assessments of these products.

If there is a trade-off there it's a small trade-off, and I think the trade-off is worth it relative to what we achieve in terms of an added measure of safety. I think what some people would like, would be to have more inadvertent substitutions because everything would have the same name, and you wouldn't be able keep track of it in the marketplace.

I'm not in favor of inadvertent substitutions, I'm in favor of true substitutability of these products, and that's what we need to work towards.

MR. WESSEL: So, as I understand it, there's one standard to have a biosimilar, and that is that it has to have no clinically meaningful difference between the original biologic, and there's a higher standard for interchangeability where it can be substituted without doing harm to the patient, depends on state laws and stuff.

And as I understand it also -- no FDA-approved biosimilar has reached that interchangeability threshold. Is that important? How important is that? Or do you think it's less important than some of the others?

DR. GOTTLIEB: I think it's important, you know, it's not a higher standard, it's a different standard. You have to do an interchangeability study and demonstrate that you're not going to have adverse clinical consequences. You know, the most obvious being the development of neutralizing antibodies to the protein. And if you're dealing with a biosimilar that's, you know, an innate protein, or a replacement protein is something that's very important to sustaining life, you don't want to develop neutralizing antibodies to it, that you'll become dependent upon.

You know, if it's Epogen, you'll become dependent upon blood

transfusions, if it's obviously a monoclonal antibody in developing neutralizing antibodies that might be therapeutic alternatives. So, the amount of data that you'd require and the safety threshold would be different.

I think it's important to -- allowing the market to be more competitive for sure, but what surprised me is it seems to be less important to the manufacturers than trying to address some of these commercial barriers. Even with interchangeability they would still face a lot of obstacles gaining significant market penetration at the outset, and being able to move a lot of market share.

So, it's certainly a key ingredient, but it's not going to solve the problem on its own. And you look, we are looking at -- we are going to -- as part of this announcement today we are going to finalize the guidance and interchangeability, and we are going to do all we can to push the boundaries on trying to make that a surmountable hurdle for more products.

And so we'd like to see more products to be able to claim interchangeability in the market, but I don't think that alone is going to solve this challenge. For a while I did. I thought if you had interchangeability you could just move a lot of market share at the outset, and that's not what I'm being told.

MR. WESSEL: What changed your mind?

DR. GOTTLIEB: Talking to -- Talking to the manufacturers of biosimilars, and understanding the market.

MR. WESSEL: I see. Okay. I think we have time for some questions. We have some people with microphones and this is being webcast. So, no one will hear your brilliant question if you start talking before you get the mic.

I'd like to be sure that everybody who asks a question tells us who they are, and make sure it's a question. You can give speeches at the next FDA public comment period. I need to -- all right, get the mic. And let's start, we'll start with a couple of the panelists. Let's wait for the mic, it's coming. That one isn't on yet.

QUESTIONER: Okay. Great. Commissioner Gottlieb --

MR. WESSEL: And you are?

QUESTIONER: Alema Gatney, Harvard Business School. Thank you very much for your remarks. I'll have a chance to make a few of my own and some other comments, but I wanted to ask a question about what you just said which is, you said that you had thought interchangeability would make a huge difference, but you heard otherwise. And my question for you is: if there were a fix for the rebate trap which you described very well, would you then think the interchangeability was a critical element to getting the benefits of competition?

DR. GOTTLIEB: I think we would have more impact. I certainly do think we would have more impact if there weren't these commercial barriers to entry. So it's, you know, I don't mean to diminish it, it's a very important regulatory step that we could take to set up more marketing competition, but I think if we were to be more, you know, gratuitous in how we offered interchangeability right now, I think the biosimilar manufacturers would still face a lot of obstacles to gaining market share. So, it's not going to be the only ingredient given the commercial obstacles.

MR. WESSEL: And is this the big difference between the U.S. and Europe? That in Europe they don't have these locked up for three-year contracts with the --

DR. GOTTLIEB: Yes. They do. A lot of the countries there, it depends on which country, some are more aggressive than others, but they do nationwide tendering. And so they'll forcibly switch patients from one product to another, sometimes on an annual basis, and some countries are quite aggressive at doing that.

So, if we are looking for scientific evidence on whether or not forced switching has a clinical consequence, we have a great natural experiment going on in Europe right now, clinically we are collecting good data, which we are collecting data on that, because the Europeans are switching patients back and forth on some of these

products.

And they're doing it with some of the products that are innate proteins as well, where you'd have more concern that if you develop neutralizing antibodies and you can no longer maintain the protein in your system, you're going to become dependent upon something that could be far more intrusive.

MR. WESSEL: I'm glad the Europeans are experimenting on their population for it then.

DR. GOTTLIEB: Very nice of them to do that for us.

MR. WESSEL: Paul Ginsburg?

MR. GINSBURG: Hi. Paul Ginsburg from Brookings. The way that -- for Part B drugs, the way that Medicare and many private payers pay as a fixed percentage of ASB, it seems as though that would really be getting in the way of biosimilar used by physicians. How significant is the need to make changes in that, to open up the biosimilar market?

MR. WESSEL: Let me just -- I want to make sure on this. So, some drugs are paid for under to the Part D drug benefit of Medicare, the relatively young benefit, some are paid under Part B, those are often administered by physicians. And now the physicians get a fee equal to 6 percent of the average sales price. Was that the --

DR. GOTTLIEB: Yes, average sales price.

MR. WESSEL: Average sales price, so these drugs are really expensive, so 6 percent can be a lot of money.

DR. GOTTLIEB: Well I think this was largely addressed in the Affordable Care Act where the physician is largely held harmless for that 6 percent, because they are effectively paid the equivalent of what they would have earned on the branded drug for prescribing the biosimilar. I believe I'm right on that. So, you know --

SPEAKER: The 6 percent is on the accumulated --

DR. GOTTLIEB: Right. So the 6 percent is being paid --

MR. WESSEL: It's the same, the same amount of money if you used the expensive drug, or --

DR. GOTTLIEB: It's the same amount of money, so we are actually overpaying relative to the cost of the drug to administer the biosimilar, assuming the biosimilar is cheaper than the branded drug. So, they effectively fixed that, but it's kind of an awkward -- awkward fix because you're paying more than you should.

MR. WESSEL: Can you get the mic to Josh?

DR. OFMAN: Thank you. And thank you for your talk. I think that relates to another --

MR. WESSEL: Josh, can you identify yourself?

DR. OFMAN: I'm Josh Ofman, from Amgen. And my question to you is -- it relates to this point about payment and Part B. The vast majority of biosimilars that are being developed, and that will come to the market in the next five years, to seven years, are going to be physician-administered drugs. Those are not the drugs where you have this big rebate issue, traditionally.

In the market today I understand there's a lot of concern about the rebate issue, and it's all -- you know, it needs to be evaluated very carefully, but in the biosimilar space the big rebates are not in the physician-administered world largely.

DR. GOTTLIEB: But is that true -- and more than we are moving on to, as the PBMs buy these specialty pharmacies more than we are moving into that reimbursement space.

DR. OFMAN: That may change over time, you're exactly right, but at least in today's world when you see the competition that exists, and you see the molecules that are coming to the market, they're really not in that world. So I guess the question around reimbursement in the Part B space there was that leveling of the playing field that we just described. Is there any other thing that you think might be more

effective in the physician-administered area, than the rebate issue, because it just may not be that relevant at least for the next several years?

DR. GOTTLIEB: Yes. Look, I mean you also have the issue of the long-dated contract, and it's going on to Part B side and the specialty side, on the physician-administered side. And you also have a function where, you know, since you don't have a competitively bid scheme on the Part B side there's less incentive to try to negotiate real big price discounts, and use the biosimilar to opt to negotiate a better price, because you don't have formularies, you don't -- you don't (inaudible) the branded drug relative to an alternative.

So, I think if you're going to want to do something very disruptive on the Part B side, that's why I mentioned trying to move Part B into a competitively bid system, and it could be -- it could be moving into Part D, and using some of the savings to offset the increased out-of-pocket costs to the consumer, or looking at the competitive acquisition program in trying to reinvigorate it.

You know, the issues that come up with the logistical challenges of doing that make no sense to me. I think we've seen a lot of supply chain intermediaries figure out how to solve logistics, and at the end of the day the cost of goods here is relatively low, so if there is some lost goods in the process, the contracts could force the companies to eat that, because you're talking about -- unless you are doing gene therapy, or CAR T, the cost of goods is relatively trivial.

I don't know if you disagree. You're shaking your head like, I can't figure out -- we won't ask him. (Laughter)

MR. WESSEL: In fact, I'm going to ask him later.

All right. All those kind of changes to Medicare, could those be done on CMS and --

DR. GOTTLIEB: I think it can be done under CMMI, I mean you would --

MR. WESSEL: You don't need legislation?

DR. GOTTLIEB: Well, thanks to the prior administration, they created a vehicle to obviate all forms of congressional interventions --

MR. WESSEL: So, I see. You now want to -- you want to now take advantage of the provisions of the ACA that you've criticized when the Bill was passed?

DR. GOTTLIEB: Well, I didn't criticize that, I think the people who wrote that never thought that they wouldn't be the ones using it.

MR. WESSEL: I'm sure that's true. Okay. I'm going to take like, there's a woman in the back and then, well, I'm going to take three questions, and we'll get answers to two of the three.

MS. WILLIAMS: Hi. This is Deb Williams of Pfizer. I have to say on your comment about the 6 percent add-on, what we've seen from competitors who are biosimilars is them advertising to the physicians that they still lose money, with that I'm sure we could be happy to send you that material, but it is interesting. I'm not quite sure how they -- I'm not quite sure what their rationale is, it could be because of the discounts to high-volume practices, but it is an issue. Thank you.

MR. WESSEL: Okay. There's a gentleman on the aisle here? I've got it, why don't you give it to this woman, here.

MR. CHERRY: Hello. My name is Tyler cherry, I'm from SKDKnickerbocker. Thanks for being here. And thanks to Brookings for hosting.

So, as you know, Senators Grassley and Klobuchar recently wrote to the FTC noting what they've done in the past the last two decades to address anti-competitive behaviors, lawsuits, working with Congress. I know you said, stay tuned, but can you give a preview of what you see the FDA's role in this new partnership with the FTC will be to address these anti-competitive behaviors?

MR. WESSEL: Let me just get one more here, and then we'll -- okay, go ahead.

MS. WOOLLETT: So, my question came around in the --

MR. WESSEL: You are, please?

MS. WOOLLETT: Gillian Woollett with Avalere Health. My question was around interchangeability and the reason -- and I am both a European and American, so I cover both sides of the Atlantic.

MR. WESSEL: We guessed that.

MS. WOOLLETT: At a recent meeting in London Medicines for Europe, FDA explained to the audience that for the purposes of physician prescribing FDA already agreed with Europe that the biosimilars approved by FDA were interchangeable. Is that something you could help the broader community understand by having such sources on your website, because I think as a primary source, FDA does carry that extra weight?

DR. GOTTLIEB: Yes. We are undertaking as part of this, and we've started already, an education campaign around biosimilars, and we have some dedicated resources, substantial resources to doing that, and this is something we've done in this small molecule world for some time.

As far as the partnership with the FTC, we have worked with them to provide information where we think that there's anti-competitive behavior as well as -- I don't want to say instigate certain scenarios -- but certainly when certain scenarios seem to be unfolding, working in concert with them through the activity to make sure that they have transparency on what's going on.

And I think we've handed them some pretty good set of facts in the past. I'm going to be meeting with the FTC, the new FTC Commissioner really soon, and being with some of the individual commissioners as well, to talk about what more we can do here. So, I don't want to get too far ahead of myself, but I think that there are places where we can help identify information that can help them bring actions.

MR. WESSEL: My impression with -- often through an antitrust legislation is that the lawyers are reluctant to bring cases because they feel the case laws

against them, and that their odds of winning are slim. Is that the problem here is there something else?

DR. GOTTLIEB: Well, I think generally speaking prosecutors are reluctant to bring cases that they don't think are airtight. I think policymakers sometimes think from a policy standpoint it's important to test the boundaries of where your authorities are in these regards. If there's an overriding, you know, public health prerogative, and then if you're wrong that's a role for Congress to step in and decide whether or not you need additional authorities and legislation.

So, you know, I don't have to be the one who will lose the case in court, but I think that there's probably some more cases we potentially could be bringing.

MR. WESSEL: Okay. I'm going to do a couple more. There's a gentleman here in the front, and the gentleman in the aisle. Helen, can you give this gentleman here -- can you raise your hand so we can see you? And then, over here, yes, please?

DR. HAUSFELD: Hi. My name is Jeff Hausfeld, I'm a retired surgeon, now the chief medical officer and chairman of the Board of BioFactura, a company in -- a biotech company Maryland that produces biosimilars. I do feel like we are reliving history because in the 1980s I was one of those docs that used to write, you know, "do not substitute" on my prescriptions. Here we are again doing the same thing over and over again. So, I applaud your efforts, but it is going to take a significant educational push, because before I got into this business, I had no clue as to what it really meant to manufacture drugs, and most, 99 percent of physicians out there also have no idea of the restrictions, of the analytics, of the quality that has to go into manufacturing a drug. We need to teach them so they can feel comfortable in utilizing these drugs for their patients.

Secondly, so right now I'm in the middle of writing a protocol for my Phase 1, for Ustekinumab biosimilar, and I'm going to ask you: what should I do? Do I need a three-arm study, or do I need a two-arm study, because I can just use the EU

reference drug and not have to have the U.S. reference drug which is two-and-a-half times more expensive.

And lastly, what is going to be the FDA's stance on, if you have a successful IND submission, with a successful Phase 1, what does Phase 3 look like?

DR. GOTTLIEB: Well, I think I'm the first question, this is what we are going to try to clarify in some of the upcoming guidance in terms of, you know, what you need to do, what the bridging study needs to look like, and whether or not -- whether or not we can use the knowledge that the U.S. reference listed product, and European reference listed product might be manufactured in the same facility.

Right now, you know, we literally have situations where if you wanted to use the European product even if it was manufacturing in the same facility as the U.S., you could do that, but then you'd have to do a bridging study to the product in the U.S., even though we know full well that they are the exact same product, because they're, you know, manufactured in the same facility.

So, so we are literally exposing patients to drugs in a clinical trial just because we can't acknowledge something we know. You know, we are going to see whether or not there are ways that we can acknowledge that knowledge, and it might even be through data sharing arrangements with the EU now.

You know, the companies the branded companies are going to feel that that represents CCI, and as they are protected --

MR. WESSEL: What is CCI?

DR. GOTTLIEB: Commercial Confidential Information, it's they are protected information, but I think that there's a public health product here, at least ask that question, and see how we can address it. So, those are the kinds of things we are going to be looking at as part of this process.

MR. WESSEL: And the last question?

DR. GOTTLIEB: I'm not quite sure I quite understood the question.

DR. HAUSFELD: What does it take to have a successful Phase 1, and what does Phase 2 look like? What is your expectation for Phase 2 and (inaudible)?

DR. GOTTLIEB: I think it's I think it's going to be variable, and it gets back to also the question you -- the issue you raised at the outset with respect to, you know, physician acceptance of these drugs. I think physician acceptance of these drugs and probably the regulatory requirement is going to be titrated based on whether or not you're dealing with curative therapy, or chronic therapy.

A product where, if the product does have some differences in its clinical performance, it's detectable to the physician over time, and you can intervene versus, you know, if it's a product being used as curative therapy in a short course for the treatment of advanced cancer, that's something where there might be different clinical requirements, and there's probably going to be greater physician reluctance to use that product.

MR. WESSEL: And the last question. I hope it's a short one.

MR. SPIEGEL: I'll try. Andrew Spiegel from the Alliance for Safe Biologic Medicines. Thank you for all you're doing to get safe and effective biosimilars to patients. My question follows up on the naming discussion that you had, and I want to thank the FDA for continuing to keep patient safety at the forefront by requiring unique names, and that's the suffix that the gentleman was talking about earlier.

But last week I attended a meeting here in Washington that we hosted, including a number of FDA senior leadership, WHO and Health Canada on the naming issue. And there was general agreement around the room for the reasons that you articulated that a global naming harmonization policy should be in effect.

And what we heard back from the WHO really was that there's going to have to be a call from the regulators for that to happen. And so Health Canada, the U.S., and other regulators that support this, are going to have to band together and put pressure on the FDA to get other regulators together to push this Patient First Policy

forward. And I wondered if you could comment on any steps that you would take as FDA Commissioner to help push that global policy forward?

DR. GOTTLIEB: I was involved in these discussions 10 years ago when that convention was established under the WHO, and I think it was -- I think it was unfortunately influenced by people who wanted to have substitutability without having to demonstrate it in scientific process. So, at least some of the folks who were involved in a discussion, I don't want to -- I don't want to cast aspersions at everyone who was involved in that debate but -- and I think the Europeans got what they asked for.

They got a system where it's very hard to track which products patients are on, so doing post-market pharmacovigilance is challenging. I'm not sure how, I'm now sure what opportunity we have to re-litigate that. This has already been solidified by the Europeans. I'm looking at my FTA colleague, so there might be some forums that I'm unaware of, but we did have this debate in a robust fashion about a decade ago, and I'm not sure our point of view prevailed globally.

MR. WESSEL: Okay. With that, thank you very much, Scott, for your time and your candor. (Applause)

And if I can invite my panelists up? So, I'm very pleased -- come on up, I'm going to be efficient. If you have a name, sit on it, and if there's no name, sit nearest to this one. Great! If we were more organized, you would have come up in the order in which we seat, but not organized. So, as I've said, we have the great fortune of having an economist, a lawyer and a physician here.

The lawyer is on my right, immediate right, Arti Rai. She's the Elvin Latty professor of law. I always think of a given name, the chair, like once in a while someone should give the name.

MS. RAI: Yes. It's a real person; he was one of the founding deans of the Duke Law School.

MR. WESSEL: Okay. The Elvin R. Latty professor of law at Duke Law

School, where she works on intellectual property issues, innovation policy, administrative law and health law. She's taught at a number of prestigious universities. She spent a year or so as the administrator of the Office of External Affairs at the U.S. Patent and Trademark Office. And although she's a lawyer, she majored in biochemistry and history, and did one year of medical school. I don't know what happened to the following years.

Josh Ofman is the physician on our panel. He's the senior vice president for -- great title -- for global value and access and policy at Amgen. He's been at Amgen for 15 years. Amgen is a very large pharmaceutical company that both innovates in the biologic space but also makes biosimilars. He also has a master's in health services, and I think I looked at -- I think you majored in history and the philosophy of science, I just want to --

Leemore Dafny, is the Bruce V. Rauner professor of business administration at Harvard Business School.

MS. DAFNY: We know who that is, right?

MR. WESSEL: Yes, we do. And Leemore is sort of narrow, she majored in economics, and got a Ph.D. in economics. Before she joined Harvard in 2016, she taught at the Kellogg School of Management at Northwestern. And she spent some time in the government as the deputy director for health care and antitrust at the Federal Trade Commission, which we learned from Scott Gottlieb, is not aggressive enough in bringing lawsuits.

So, Arti, maybe I can just start with you. I think it would be useful, Scott Gottlieb laid out a fairly ambitious agenda with some serious rhetoric about improving the market for biosimilars, and making that space more competitive. And I'm just curious do you believe him? Are they doing enough? Or are they touching the right buttons?

MS. RAI: So, he has a challenging position because his agency does not control the demand side, the CMS to some extent does but obviously only to some extent, and the FTC can intervene but maybe doesn't intervene enough. So, I think the

demand side is very difficult and, you know, the antitrust issues that are being raised already by the demand side, it seems to me the Humira deal that you mentioned is really worth looking into.

We may not have a reverse payment going on. I don't know what we have going on, but only the FTC can really get under the hood of that, and determine whether there are some sorts of incentives put in place, so as to delay, in this case, biosimilar entry that are not too dissimilar from some of the incentives that may have been struck down by the Court and FTC versus activists, and that's Supreme Court decision.

So, I think it's really important to get under the hood of that and figure out what's going on. I also think that there's a fair amount to be done on the patent side which, again, is not his jurisdiction. But fortunately I think there will be -- we'll continue to be the institution that -- to just boast a little bit here -- I helped to set up in 2011, the Institution at the PTO that allows a challenge to bad patents, which I think Senator Hatch has said on a variety of occasions, should not apply to biosimilar patents.

I don't think Senator Hatch is going to get his wish, and I think that's good, because it seems to me there are a fair number of bad patents in the biologic space as well, just as there are in any other space.

And I can say that because I worked at the PTO and, you know, the PTO does its best, but it's inundated by about 600,000 patent applications every year, so not everyone that gets out the door is -- not every patent that gets out the door is going to be perfect.

So, yes, I think that -- you know, there's stuff that he cannot do that's outside his jurisdiction. I did want to, however, commend Dr. Gottlieb for doing a bunch of things that you may not think that I, as a lawyer, would be so excited about, but I did spend that year in medical school, so there are a few things, and they're related to intellectual property, believe it or not in some respects, and so I am very excited about

the ways in which he is really interested in making sure that we improve the efficiency of the biosimilar development process.

That's got so many components to it, there are so many ways that the efficiency could be improved. As many of you may know, it takes like about $5 million to develop a generic drug, whereas it takes about 100 million to 250 million to develop a biosimilar.

Well, why is that? A lot of that -- one big reason has to do with the fact that we can't fully characterize the end product biologic, at least with our current scientific tools, and so as a consequence what the biosimilar company does is try to reverse-engineer the process that the originator came up with, because it's a trade secret, and they have to reverse-engineer it, and they probably won't reverse-engineer perfectly, so what they'll have to do ultimately to convince the FDA that they had the biosimilar product, is possibly do some clinical trials, which are really expensive, and you never have to do that in the context of generics. You never have to do clinical trials.

And what he's trying to do, I think, with this agenda that focuses on state-of-the-art analytic techniques -- and here I apologize for getting a little weedsy -- is to really reduce the need to do clinical trials, which I think is great. I think that's exactly what needs to be done, and this is something that I believe could really move the needle significantly.

Similarly relying upon, and I know that Gillian Woollett asked a question, and I can then give a shout-out to her paper, “Relying on a Global Reference Comparator for Biosimilar Development,” that will move the needle.

That's going to be controversial because they could involve trade secrets again, but I think it's really, really important, and really could move the needle. And so, in general, it seems to me that to the extent that we can really reduce the cost from 100 to 250 million to something much, much lower, maybe not in that order of magnitude lower, but something much, much lower. That's something he can really do, and do totally

within his jurisdiction. FDA has a lot of discretion there.

MR. WESSEL: Okay. Leemore, I know you wanted to respond to Dr. Gottlieb's comment, so I'm just going to let you respond, because I do have some other questions, but --

MS. DAFNY: Okay. I appreciate that. So, first of all I also want to agree with Arti and, although he's not here, and I don't often spend time to do this, I think it's pretty amazing that he's devoting so much energy to promoting biosimilar competition and competition in general.

It's not, in my view, an area that we've seen that much engagement by the FDA in the past. So, under his leadership they're doing a lot, and I think that's great.

But then when you give a little, of course you're going to want to ask for more, and there are a couple areas where I'd like to see more, one was on the naming which you brought up. My understanding is that the four letters nonsensical suffixes, according to very large purchasers, are completely unnecessary for pharmacovigilance, they aren't used abroad, as we know.

And moreover, even if it isn't costless, even if there were some benefit to being able to track in this way, although buyers are telling us they don't actually need it, on the other side you would have the transparency for the prescribers and for the patients, and knowing that the nonproprietary name is the same, it's just like. It isn't just like small molecule bioequivalent generics, but for the purpose of the buyer if we want to get the benefits of biosimilar competition, it ought to appear that way, and then the informed prescriber can be educated about what differences there may be.

And these are products that are approved on the basis of being clinically equivalent. Okay? So, I take the point on the four-letter suffix, but I still say that you have to put on the other side the benefits.

The other thing I wanted to -- I pushed a little bit on in my question, was interchangeability, and this is where you could automatically say substitute. If you

wanted it to be automatic, you could also have it be conditional on the prescriber, not writing -- dispense is written, or having a conversation, but the FDA has yet to, intends to release guidance on the interchangeability.

And what I would say here is that some of the initial guidance released suggested that they might require standards that the reference biologics themselves wouldn't achieve. So there's a lot of, you know, batch-to-batch variability in these products, and if within the reference biologic they wouldn't pass to be biosimilars of each other, right, then if you're not going to require that of them, how do you require that of the biosimilar?

And also would the biologic that was approved five years ago, passes to the biosimilar, to the one today because there are so many production process changes over time. So, more generally holding the would-be rival to standards that are tougher than you hold the innovator seems like a way to prevent us from getting the benefits of biosimilar competition. So, those are big-picture two things I would have liked to --

MR. WESSEL: Josh, I want you -- I guess you respond to whatever you want to, and then I have some questions, but I think you deserve a chance, since you've been invoked about six times already.

DR. OFMAN: Sure. Ah, where to begin! So, maybe I can just respond to a few of your thoughts first, and then maybe give some more general comments. I think big picture here you invoked the purchaser, you know, multiple times and I think what we have to do when we are thinking about biosimilars is focus on the patients.

And the issue around naming is one example where this is all about patient safety, and so if you can imagine a world where there are innovative products, and multiple biosimilar products, and the safety, and you mentioned things like drift, and other things, that this is very complex in terms of how biologics evolve over time, and how they compare with one another.

If you are unable to know at any point, the purchasers may not care, but

for patients, and for the FDA they care quite a lot, as do we as manufacturers about what is being infused into any given patient at any given time that could result in some level of immunogenicity or toxicity.

So, we think -- you know, when you're thinking about these broader topics it's a more general comment, we have to level set, that this is not a small molecule generic world. We all have to think about the complexity of biologics, their manufacturing, how they change over time, and really level set, because I think if we think that this marketplace should evolve the way the generic small molecules evolved, we are all going to be very disappointed, and when they do things as a result of that disappointment that won't make sense scientifically, or on behalf of patients.

MR. WESSEL: But other countries which seem to be -- care about their patients, the Australians and others, right, they've gone a different direction on this naming thing, so --

DR. OFMAN: Well, some have, and some have not. Some have also adopted different systems in those markets, they have lots of different ways of tracking patients, in medicine, so it's very -- I couldn't go through each country and how they do it, but rest assured that is a major issue for all of those markets as well.

On a more general point, I really do want to agree with you and Commissioner Gottlieb on what he's doing, what he's focused on. He's taking a very scientific approach trying to focus on patient safety, and develop a robust market place. As Amgen, we are at the same time the world's largest biotechnology innovator company that's independent, and we also hope to be among the largest manufacturers of biosimilars.

We have 10 of them in development, and so our interest is to make sure, for the long term, that we have a very robust and sustainable biosimilar marketplace.

And what does that mean? Well, first it means that we have to have great confidence in the FDA, and in their robust regulatory standards, and while many of

you have mentioned we can stop doing trials, and we can, you know, streamline everything, as a manufacturer of biosimilars we think the regulatory standards are appropriate.

We don't see those trials as big barriers or hurdles, we think of them as completely necessary to establish biosimilarity, but also the safety of being able to switch among biosimilars; so, we are very -- those regulatory standards with that focus on safety; is a prerequisite for a good market because it will provide confidence.

Secondly, competition and a level playing field. There is a lot of competition going on, I think it's much too early for anybody to look at 3 biosimilar launches in the United States and conclude one way or another how competition is working. There is vast competition, we know this from our own personal experience, where most of the biosimilars are against Amgen products, and they've gained dominant market share, prices have come down dramatically.

So, there's enormous tools about how to be competitive, and a level playing field is what's important, not a playing field that will tilt the balance one way or the other, and introduce either perverse incentives, or kind of instabilities in the market as we are trying to develop it.

Finally, as Dr. Gottlieb mentioned, lots of education is going to be needed here, and manufacturers with a lot of experience in biologics will be very helpful in that regard, as will the FDA, and the pharmacists.

And then finally, a reliable supply; as the world's leading manufacturer of biosimilars and biologics, you know, we are confident in a reliable supply of these medicines, but that's not always been the case outside the United States where there has been reliable supply. All of this will result in a robust, stable market where physicians, institutions, hospitals have great confidence in the standards with which these drugs have been approved, in the rationale for their use, and in the safety, and how we use them and track them for individual patients.

Because we have to remember the patients that use biologics are the sickest 3 to 4 percent of the patients in this country. And they have serious diseases, mostly cancer, and most of the biosimilars that are going to be coming out in the next five to seven years will be for these very, very serious illnesses.

MR. WESSEL: Right. Well, I'm willing to posit that everybody who is involved in this debate, whether they say it explicitly or not should, if they don't, have the patients' interests at heart.

DR. OFMAN: I hope so.

MR. WESSEL: But I'm just -- one of the things that just strikes me as so unusual about this space, is that we are used to thinking, I think there's actually some evidence that's no longer true, that Europe is where they regulate everything to death, we are the Wild West, and stuff.

And so you have the situation where there are -- that Europe -- I mean, you make the good point that we don't want to draw conclusions from three biosimilars, although it does make you wonder: why are there only three biosimilars on the market?

So, I wonder if each of you can talk about: what's the difference between Europe and the united states here, and what is it that we should as a -- I'm not an investor in drug companies, I'm neither a lawyer, an economist or a physician, so I guess I would call myself a potential patient, God forbid. What should we learn from the European -- and a tax payer -- what should we learn from the European experience that's relevant to us, and what's just different? Maybe you could start, Arti?

MS. RAI: Sure. So, I mean one thing frankly is patents. So, 11 biosimilars have been improved by the FDA, eleven, there are three on the market, and one launched at risk which is pretty -- a pretty aggressive move to make because if you're found to violate the patent, your damages are going to be astronomical.

So, biosimilars have been approved that can't be marketed because of patent litigation. These patents are not the primary patents on the compound because

those would have expired a long time ago. A lot of these biosimilars have been around for decades. Patents, on average, are supposed to last about 12 to 13 years post the marketing of the drug.

So, those main patents have all expired, and we are talking about all these ancillary patents that just -- you just have to get through the thicket of, and we don't usually talk about thickets when we talk about drugs, but this is really a thicket problem, it's --

MR. WESSEL: They don't have patents in Europe?

MS. RAI: They don't have the same sorts of ring fencing in Europe, that's my understanding of it, and/or perhaps some of these markets are smaller, and so the threat of assertion is lower, that it's a very interesting point that we are reaching because you can -- unlike the generic drugs where it's very difficult to launch at risk because you're very under-capitalized as a generic firm. Amgen is a biosimilar firm, and yet it can't launch at risk, or it feels like it can't launch at risk.

MR. WESSEL: At risk means, where you're going to run into a lawsuit?

MS. RAI: A patent thicket, yes. So, that's one thing. And I do think that the second point, and this is where, you know, I should of course put in the caveat, that I only went to one year of medical school, is that it does seem that all of the risk aversion that we are seeing it in the U.S. is not something that the EU feels with respect to all of this.

So, you know, the problem with risk aversion is of course doing nothing is doing something. So, if you don't approve a drug, or if you approve a drug that's completely inaccessible cost-wise, that's doing something, that's making sure the person who doesn't have access to the drug, will die. So, I mean risk aversion is a real problem.

MR. WESSEL: So, Josh, you do business on both sides of the Atlantic.

DR. OFMAN: Yes.

MR. WESSEL: What's your analysis?

DR. OFMAN: So, I think we have to remember first of all that in Europe there's a perception, and I'm hearing it in the room today, that somehow the U.S. is lagging way behind Europe as it relates to biosimilar. The facts simply don't bear that out. Let me -- let me just remind everybody, and biosimilars were approved in Europe in 2004, and they were approved to the Pathway in 2010 the United States.

From the time of the approval of the Pathway for the next four to eight years we are on about exactly the same trajectory as Europe was in terms of the numbers of approvals, and the numbers of marketed products. So, it's not that we are way behind we are behind it in time; there was great conservatism, and in fact fear, early on in Europe when biosimilars came, because there had been some devastating safety problems related to biosimilar manufacturing in Europe.

I don't know if people remember in the early 2000s, and so there was a lot to overcome, in terms of fear and conservatism, in both the agency. So, I think about 13 to 15 biosimilars were approved over an eight-year period in Europe.

And so I think that, you know, again these are very ill patients, with very serious diseases, using very complex biologic medicines, and we need to have very clear regulatory standards, and very clear expectations about what manufacturers need to do. And I think that the other lessons from Europe, obviously, enormous amount of education with the physicians.

MR. WESSEL: So, Commissioner Gottlieb argued that these long-term contracts, where the maker of the original biologic kind of makes a deal with the health plan, I don't know, whoever, that that is providing the creating what might be an insurmountable hurdle to biosimilars because they just will never get a piece of the action. And you pushed back because you said that, well, but most of this is going on in Part B, and there's the rebate things that aren't going on there. So, do you think this is just not an issue, these long-term contracts?

DR. OFMAN: Well, I think it will be an issue, if things stay as they are

today, as more and more biosimilars are in the retail setting or the non-physician buy-and-bill setting, those rebates do come into play. And I know beyond biosimilars there's enormous work going on in Health Policy right now about how to address that issue with the middleman and where all the money is going.

So, that's an issue that's going to be addressed, whether it's about biosimilars or not. There, I think what Dr. Gottlieb was probably referring to is the Remicade and Inflectra biosimilar issue. Again, a complex one, about complex bundled situations.

I don't know enough about that to comment, but I can tell you I can't see an issue like that happening in the physician-administered world, because those types of rebates are generally, those don't exist with the payers for physician buy-and-bill. There are some rebates but the kind of rebate discrepancies that caused that problem about -- around patient access, typically do not exist in the physician.

MR. WESSEL: Wait a minute. But his basic point was Amgen is not going to be able to succeed in the biosimilar space given our current regime, because the biologic companies are making it hard for -- so he's worried that you'll give up. So, should I worry about that? Or you don't worry about it?

DR. OFMAN: We believe -- look, we have great expertise in the field of biologics, of the providers who use biologics in the institutions, and we believe that we are going to need to make the best, most-reliably supplied biosimilars out there, and compete.

And what does competition look like? It looks like providing the suite of services that those providers and institutions expect around reimbursement support, patient copay support, around education, and around training, and around reliability, and of supply and expertise.

And we expect to compete, we expect to get competition, and there are so many tools in the marketplace today that are market based that we don't believe it is

necessary for the government to intervene to create new areas of competition, because we have so many tools at our disposal.

It might be different in intellectual property, that's not my area of expertise, or in other areas of anti-competitiveness I simply don't know, but from a commercial competitiveness perspective we are ready to go.

MR. WESSEL: Leemore, I had the sense from your eyes that you were ready to jump in there.

MS. DAFNY: Well, I mean what is it -- with all due respect, but what does a player in the industry want? They want less competition if they're already in it, so the incumbents have a lot to lose. That's just frankly how it is. The U.S. is a very rich pharmaceutical market, innovation, pays off, we want to encourage innovation, but once these patents expire we really want to have the benefits that accrue from having multiple competitors.

So, I would say that in my view, the pace at which we are adopting, and I don't agree but it's perfectly reasonable the BPCIA was passed in 2009; guidance on what to do came out in 2015. Don't ask me what happened to all those years, but in the business school where I operate, six years of uncertainty is a lot of uncertainty.

And same on the guidance that we are waiting for. So, I'm not really trying to point fingers, except to say that it matters for the pace at which we get this entry. And one thing businesses will tell you is, even if the rules are not good for us, say this four-letter thing, which by the way, if you really want to know exactly what someone is taking, it's hard for me to believe that four letters will do that, I think you're going to need to scan and barcode, and the four letters could confuse. But basically you're going to, you know, need to try something else here.

MR. WESSEL: And do you think this long-term contract thing is a big a deal as Gottlieb said?

MS. DAFNY: I think it can help. And I suspect that he's alluding to the

success that some European countries have had by putting out for exclusive bid, their biologics.

And I thank my former colleague at the FTC for sending me some slides, Elizabeth Jex, for sending me some slides from the FTC's excellent biosimilar panel in the fall, where the Head of the Norwegian Medicines Agency put up some statistics showing how far and how fast their prices had fallen, because they have annual contracts where anybody who is active that year, who is ready can go up and take a bite at the apple. And if you have three-year contracts they would have to wait longer, and that would just slow the adoption and focus.

MR. WESSEL: Well, we all know that if only the United States were more like Scandinavia everything would be wonderful, right, (laughter) in this sphere and everything else.

So, Arti?

MS. RAI: Mm-hmm.

MR. WESSEL: I know you've written something about something I don't really understand, so help me along with --

MS. RAI: (Laughter) Probably everything I've written somebody doesn't understand, yes.

MR. WESSEL: Well, that's true, but I'm -- so, you once wrote about the difference between patents and trade secrets.

MS. RAI: Mm-hmm.

MR. WESSEL: And you raised the question that, if we make the patents harder to get, then companies will rely on trade secrets, and if it's a trade secret, that no one gets to go to the Patent Office and read it, and no one will know anything. So, is that relevant in this -- in this space or not?

MS. RAI: I'm so glad that you brought that up, because usually people don't like to talk about IP, but this was an article where I think that there is a conundrum

here. Look, so I've been talking about -- and I should note by the way that -- and I can say this again because I worked at the USPTO. The USPTO standards for issuing patents are lower than Europe, so Europe it is said, is really tough, maybe too tough, but as a consequence there are fewer patents in Europe; so, just to answer that question.

But to the point about the patents and trade secrets' intersection, so this is a really interesting conundrum with respect to biologics because patents, at least in theory, are supposed to show you how to make and use the invention, none of the patents that biologics originators file really do that in any meaningful way. So, does that mean that the patent bargain, which we always talk about, or I always talk about to my students, is not being fulfilled? Maybe.

So, why aren't all these patents invalid? Well, a bunch of them could be, may be, but it's hard for a variety of really weedsy reasons to really invalidate them. Some of it has to do with the way the law is set up, some of it has to with the fact that it's -- all of us would have to go to a jury that would be bored out of their mind talking about how one goes about determining how to do the manufacturing process for a biologic.

But these patents don't really disclose much, but at the same time they disclose a little bit at least, and if we made the patents harder, much harder to get, or if we really require the innovators to disclose everything about their manufacturing process, so that's -- that manufacturing process information is the, you know, absolute treasured gold information that is submitted to the FDA but under complete trade secrecy. If that were required to be disclosed in the patent, I think they would move away from patents.

DR. OFMAN: Could I?

MR. WESSEL: Please, yes. And then, please be ready with your questions. So, yes.

DR. OFMAN: So, that's very helpful to have that a little better explained. I think that we have to just remember the distinction. I think the distinction, what's happening in the generic world is quite unique, and there's all kinds of games and things

being played to delay patents and pay off delays.

We have to think about that very differently than what's happening in biologics right now. Those are very different activities, I think that an innovative company, you know, the patent exclusivity is the life blood of our industry. And we have strong patents in our industry, people will defend those patents.

There are examples where there are so many patents, where it becomes not worth trying to fight them all, and therefore, for example, Amgen entered that we licensed the patents from AbbVie, and we actually think it's a good thing because it probably is going to get biosimilars to market sooner than otherwise would occur.

But it's not those same types of pay-for-delay types of things that you hear about in the generic market, they are just completely different. And I think it's important to keep that in mind.

MR. WESSEL: What's the rational (inaudible), that you can sell this product sooner in Europe than in the U.S. on that?

DR. OFMAN: The patents are completely different.

MR. WESSEL: I see.

DR. OFMAN: Patents expire at different times for all of our products. The patent length is different, the actual patents are different, the numbers of patents are different. It's completely different.

MR. WESSEL: Okay. Your turn; so, the gentlemen over here, Helen, and there's someone on this side?

DR. MILLER: Thanks. Mike Miller, I'm a Physician and policy wonk. And if this question is to weedy, please just tell me, I don't want to get the last --

MR. WESSEL: I don't know, if you have to say that I can -- (Laughter)

DR. MILLER: It gets to the point of what's disclosed in a patent versus what's a trade secret, because it's my understanding having a patent from many years ago, it's not supposed to include things that are obvious, it's supposed to be non-obvious

things are patentable.

So, in the manufacturing process it's not going to be how you, you know, make normal saline to grow cells in, that's obvious, but the specific manufacturing process of how the cells are grown and the whole process for that which I presume is a trade secret, but if that's put in a patent, then that becomes protected, and then the biosimilar has to figure out how to get around that not infringe on the patent.

So, where's the balance going to be? Maybe that's between the U.S. and the EU, in what's put into the patent versus what's allowed to be kept as trade secret.

MR. WESSEL: I thought that -- correct me if I'm wrong -- I thought the point about the trade secrets, like the recipe for Coca-Cola, you never disclose it.

MS. RAI: Right. So, from a business point of view, if you think that no one will ever be able to reverse engineer your knowledge, then you don't seek a patent on it, because patents only last from time of filing 20 years, whereas, you know, trade secrets can last forever.

And so one of the challenges is, a lot of this information that we all think will be important for biosimilar development, is currently being held as trade secret information, and maybe that's okay, but maybe there's also a role for openness, at least in the public sector in some ways.

And so again I'll give a shout-out to my colleague -- not my colleagues -- my former colleagues at NIST, the National Institute for Standards and Technology, they're trying to come up with standards for manufactured processes that would be publicly available.

QUESTIONER: Can we just clarify that there'll be no unusual or unexpected adverse events with any biosimilars in Europe? The point was made about there being a problem in Europe with biosimilars. I think that's been conflated with the Epogen/Eprex problem.

DR. OFMAN: The biologic, yes. Yes, it's the biologic --

QUESTIONER: Which was pure red cell aplasia, it was a comparability problem of an originator making a manufacturing change. Not to say it's not serious of four in 10,000, but it wasn't anything to do with biosimilars.

DR. OFMAN: No. But again, it's a manufacturing change which is what would occur with the biosimilar manufacturing --

QUESTIONER: With an originated patent -- which is important, don't get me wrong, but it wasn't biosimilars.

DR. OFMAN: Absolutely.

MR. WESSEL: The gentleman over here, in the pink shirt.

QUESTIONER: Bobby Pestronk, a potential user of some of these drugs, hopefully not.

MR. WESSEL: Not soon, I hope.

QUESTIONER: Not soon, right, and not now. What is it that patients should know about this debate? And how is it that they can be better informed so that the prices that they may not see, and may not have an effect right now on them, become something that they do understand, and they are more knowledgeable about whether new drugs coming to market, generic or otherwise, are ones that they should want, seek, ask for and help create a better market for?

DR. OFMAN: I mean, my perspective is a great deal of education. My hope is that we and, you know, Commissioner Gottlieb and the FDA, and other scientific organizations produce great educational materials for patients. It's critically important that patients understand more about biologics, and also more about biosimilars so that you can know exactly.

I mean we are infusing large proteins in large volumes into humans, and that's serious business, and it's critically important that patients fully understand what we are doing, when switches are made, the automatic substitution or changeability debate ultimately gets to who's going to make the decision about what large proteins and what

amount go into you.

And our belief, firmly, is that those treatment plans need to be made between clinicians and their patients. And, you know, payers have a role in helping to rationalize formularies, but the treatment plan needs to come in a very personalized way, particularly as these biologics and biosimilars evolve in the more personalized approaches to care.

MR. WESSEL: And, Leemore, do you think this is a market in which consumers are really going to be the deciders, and that consumer education and co-pays are going to be what moves the market?

MS. DAFNY: Well, I think it's a case where consumers will rely quite heavily on their clinicians, but the financial component does influence whether consumers take their drugs, and also the financial hardship if they do take their drugs.

And it's my view that when there are multiple competing therapies, that the availability of coupons actually disables the mechanism that insurers have to try to negotiate good prices for a drug that they can do by saying, we'll put you in a favored copay tier, when manufacturers of these competing therapies say, our prices are really, really high, we'll pay your share of it until you get, you know, to a certain path for the deductible, and then your insurer will pay all of it.

Now, we have the situation that leads to price inflation. So, to answer your question, consumers do vote with their feet, their wallets, they are manipulated to do so, and to some degree to serve a profit motive that hinders access. So, I think there's a role there.

MR. WESSEL: If you watch ever, the network evening news you would think that the capacity of their commercials to take anymore prescription drug bills ads, is nil. They filled up all the space.

DR. OFMAN: Can I maybe just clarify, or amplify a point that you made that is critically important for everybody to understand. Remember patients who take

biologics are the 2 to 3 percent sickest that we have. Okay. It is those patients, those exact patients who are being asked to pay the largest share of their drug benefit, often 30 to 50 percent coinsurance for specialty drugs.

So, in effect our insurance designs have evolved to the place where we are asking our sickest patients to subsidize their health care, or at least the pharmacy benefit for the healthy. That is not right.

And until our insurance designs are more rational we, as Amgen, I as a clinician, believe that our ability to help someone like yourself get supported with copay assistance, through that high out-of-pocket exposure that your insurance company is placing on you for your drug benefit, I think it's critical that we are able to support our sickest patients through that.

And, you know, everybody can compete the right way, we can provide co-pay assistance, but it is simply not right that people are being punished for their biology. They're failing their generic therapy, they're failing their first line, second line therapy; they need to be on biologic: welcome to a 50 percent coinsurance payment. It's just not right.

MS. DAFNY: So what I would -- so, I would agree with you that it isn't right to have patients who have needs pay a higher share of actually -- I mean, I agree with that, but I spoke carefully. I said when there are competing therapies.

DR. OFMAN: Yes.

MS. DAFNY: If there's a single, that's a different story, but when you've got two competing therapies, and these therapies can make ratcheted price increases because there's no way for the insurer to try to steer its volume to one to get a price concession, we have price increases, we have drug price inflation.

That's different from saying that it's appropriate to make these patients pay more. No. It's appropriate to allow the buyers to use their buyer power to negotiate for lower prices. That's different.

MR. WESSEL: I think we have time for a couple more. There's a gentlemen here. Can stand up or raise your hand so that Helen can find you?

MR. HAWKINS: Is that okay, can everybody hear?

MR. WESSEL: Yes.

MR. HAWKINS: Jim Hawkins. I've spent the last 10 years as an investment banker, but my background is as a Molecular Biologist, and I've had occasion to create five early-stage biotech companies. So, it's that perspective that I would offer these comments.

First of all the -- I think the matter, and it has been an important matter in the past for small molecules that relates to intellectual property, I'm not sure it's as big a deal. First of all in terms of original -- companies that produce originator molecules in the biosimilar area, all of those biologics have been wildly successful. The current revenues as these things come off patents are in the billions of dollars, and I think we could count on one hand how many small molecules have been billion-dollar products in the last few years.

So, the patents work at the beginning. When you come to the end though the idea of either trying to be obstructive with the patent side of it, or to be clever, I think is not a good idea, and it's really based on what the young lady on the left-hand, my left-hand side said. That fundamentally, every batch of an originator molecule that is made is by definition a biosimilar.

So, there's no way to have both sides of the argument. You can't say, well we have to make this, the criteria so strict that will keep biosimilar companies out, or that will make it so loose that we will have problems at the patient level.

So, I think that's going to work itself out. I think that where I would have concern though is later on where with the tremendous abilities that the pharmaceutical companies have to market things. And some of these other areas we've talked about, how do you kind of get around things, with payers, and things like that, that's where the

thing is going to, I think, become very competitive, and it won't have the protection of intellectual property or anything like that.

Maybe I could raise one more issue here that hasn't been covered, and that has to do with the sort of perspective of an investment banker. Biotech companies have been very useful in originating and building innovator molecules, and many of the big companies, even Amgen that's a very innovative company itself, are dependent on this flow of ideas, and compounds, and so on from these little companies, if you will.

And they are traditionally financed, as somebody else said before, by venture capital. To make a biosimilar, to become an independent biosimilar company is a totally unique challenge.

It is a challenge that no venture capitalist, even as portfolio managers, will ever take on, it's way too much money, it's way too much risk, 100 to 250 is not an exaggeration.

So, by definition it becomes something only in the province of very, very wealthy pharmaceutical companies who can convince themselves that it's worth taking those chances, which may happen because the rate of the profit fall off for biologics, for biosimilars, is not at all like for small molecules. So, it's worth being in that space.

But what I'm trying to say is, nobody in that space is going to be a small company. So, it's, whereas there's tremendous promise here, and biosimilars, and biologics, the rate at which these things can be brought to market is not -- or brought through development is not the same as for little companies bringing originator molecules forward, which are inherently more risky, longer, and more expensive. So, I leave you with that observation.

MR. WESSEL: Thank you. So, Josh, can you just respond to this one thing that's come up a couple of times. So I don't -- I'm probably oversimplifying but, so the claim has been made that even if you're the original biologic maker, each batch may be different so that, as the gentleman put it, you're producing your own biosimilars. Is

that the right way to look at it?

DR. OFMAN: Well, I think what -- it's an interesting way of phrasing it. I think, you know, what everybody has to understand is that biologics are produced in living cellular systems, it's not like going into your lab and pouring chemicals in a test tube and mixing it up and producing aspirin, these molecules are enormously large and complex, and they need to be produced in living cellular systems.

So the conditions under which those biologic proteins need to be produced have to be incredibly precise, reproducible, and when a biologic manufacturer produces a brand name product -- branded product there are quality standards, and when we make a change to manufacturing, we sometimes end up producing a different molecule, and we have to go back to the drawing board. This happens all the time.

So, I wouldn't go as far as saying every batch is a biosimilar, but quite honestly what you produce out of a bioreactor is a distribution of proteins that you then have to kind of winnow down into a very specific set of (inaudible), it's a completely different process. It's painstaking, it's expensive, it can take seven years and cost $200 million to do it, that's about what it's taking us right now to do it. And we are really good at this.

And we, as the best, largest manufacturer have produced molecules that are different many times, and that's a big problem.

I would say one thing to you which I think is very interesting. The point he's making, one of the points he's making is that the opportunity for companies to succeed in a biosimilar market is challenging. And so things like crude payment policy approaches, or things that have been done in the generic market, those can create distortions that can make the market very unstable which will push away the smaller manufacturers of biosimilars which is not good, because we want a robust biosimilar market.

A biosimilar marketplace we share, at Amgen, the goals that

Commissioner Gottlieb does, we want to introduce biosimilars to lower health care costs, and lower health care spending that will not happen, unless multiple biosimilar entrants in each therapeutic class are in the market, and that will only happen if we have a stable, robust, level playing field that these companies can rely upon.

If there's distortions in the market, if there are payment policies that don't make sense; as an example, CMS put a payment policy in place that put all biosimilars in the same code, a few years ago. They recognized that that was something they did with small molecule generics, they wanted to apply it to biosimilars, after talking to hordes of biosimilar manufacturers, they recognized that that was probably not a good idea, and they changed it.

And that's going to keep happening. There are a lot of ideas being floated around about how to pay for biosimilars at a higher rate than for the innovator drugs. Why would we want to spend more? The whole idea of biosimilars is to lower health care spending. So we need to think very carefully about those types of policy approaches.

MR. WESSEL: So, let me ask you each, one quick final question. If we are sitting here five years from today and we read, as our text, Scott Gottlieb's remarks, what would you want to see that would lead you to say that this effort, his effort that he laid out today really succeeded? Do you want start, Leemore?

MS. DAFNY: Sure. I'd like to see those drugs in market having penetration rates above 30 percent, and prices having dropped about that amount as well.

MR. WESSEL: And what are the odds that you think that'll happen?

MS. DAFNY: I'm a little bit of a pessimist.

MR. WESSEL: Josh?

DR. OFMAN: I would agree. I think success looks like a very rational scientific set of regulatory standards that are very transparent and clear with great

guidance, adequate and effective pharmacovigilance, with naming that allows that to happen. A marketplace that's robust and stable without distortions, and competition.

And I think when all of those exist with multiple biosimilars in the same class, so that you get price competition, and I think you've seen we -- you know, we have -- we make a drug called Neupogen, the Neupogen Biosimilar was one of the first biosimilars in the market, it's already got dominant market share, and I mean -- so things are working.

Even in the area that Dr. Gottlieb said wasn't working, with the Inflectra and the Remicade, the ASP, the selling price for the innovator is down over 30 percent already, even though the biosimilar has very little share. So, it's going to happen on price, it's going to happen on share, the competitive dynamics are going to make this market run, so I have great confidence.

MR. WESSEL: Highly confident this is going to work out?

DR. OFMAN: Oh, yes.

MR. WESSEL: Okay, your turn.

MS. DAFNY: In five years you said?

MR. WESSEL: What?

MS. DAFNY: In five years you said.

MR. WESSEL: Five years?

DR. OFMAN: Well, ell I think it's -- I think it's happening now. We have -- we only have three in the market, two more coming, and there's what, 11 approvals. And I think some of the intellectual property issues certainly need to be worked out.

MR. WESSEL: Okay, your turn.

MS. RAI: Thank you for teeing me. Yes, so I'm not -- having spent too much time laboring in the intellectual property fields, I'm not optimistic about that particular piece of it. I think it will be a huge thicket, and we'll just have to slog through it, and continue to slog through it.

So, yeah, my optimistic view would be -- and the definition of success would be similar to Leemore's. I'm not necessarily optimistic we'll get there. I guess the other thing that I would add is that I do hope that, as we talk about biologics and biosimilars, we recognize of course biologics are not just one thing, there are simpler biologics, and there are more complicated biologics.

And so I really do hope that once we get more scientific understanding, we'll begin to say, okay, these simpler biologics are not these *Wild West* things where every batch has to differ from every other batch, I mean, and there has to be drifting. You know, Filgrastim should just not be that hard. It's a very -- it's a relatively small biologic.

And so one thing I would like to leave everyone with, especially if you're not a scientist is, you know, when somebody tells you biologics, you should start asking: well, what exactly kind of biologic are you talking about? Are you talking about monoclonal antibody, or are you talking about something else? You know, because these are all different and not everything is as scary as everything else.

MR. WESSEL: Not everything is as scary as everything else? (Laughter) I want to thank the panel for, you know, one of the things we've been trying to do at Brookings is bring rational conversation with disagreements into civil discourse, which makes us unusual I'm afraid, in Washington.

I want to thank our panelists for helping me achieve that goal.

(Applause)

* * * * *

CERTIFICATE OF NOTARY PUBLIC

I, Carleton J. Anderson, III do hereby certify that the forgoing electronic file when originally transmitted was reduced to text at my direction; that said transcript is a true record of the proceedings therein referenced; that I am neither counsel for, related to, nor employed by any of the parties to the action in which these proceedings were taken; and, furthermore, that I am neither a relative or employee of any attorney or counsel employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.

Carleton J. Anderson, III

(Signature and Seal on File)

Notary Public in and for the Commonwealth of Virginia

Commission No. 351998

Expires: November 30, 2020