FTC Understanding Competition in Prescription Drug Markets: Entry and Supply Chain Dynamics Workshop
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Segment 2: Panel 1
Transcript

SUZANNE MUNCK: Perfect. Well, my co-moderator is working with Dr. Gottlieb. So maybe we'll give her a minute to join us. In the meantime, I'll do the quick introduction for the panel. So as you heard in the morning, concern about rising drug costs has caused policymakers to question whether there are obstacles to generic entry that prevent competition from keeping prices in check. I'm pleased to introduce our first session, which will explore generic drug markets, including considerations that may preclude entry after relevant products, or after relevant patents have expired.

We're going to begin with 10-minute presentations from each of the panelists, after which we will enter into a roughly 40-minute moderated discussion. I'd like to introduce shortly our panelists. All of their bios can be found in the materials. But first, you'll hear from Dr. Kesselheim, who I'm pleased is joining us. He is an associate professor of medicine at Harvard Medical School and a faculty member in the division of pharmacoepidemiology and pharmacoeconomics in the Department of Medicine at Brigham and Women's Hospital.

Chester Chip Davis is the president and chief executive officer of the Association for Accessible Medicines. Ronny Gal is the senior analyst at Bernstein covering global specialty pharmaceuticals and biotechnology. Maarika Kimbrel, my co-moderator, is deputy chief of staff at the Food and Drug Administration. Michael Carrier is distinguished professor at Rutgers Law School and the author of the leading IP Antitrust Treatise, IP and Antitrust Law, and Analysis of Antitrust Principles Applied to Intellectual Property. And Dr. Schondelmeyer is a professor of pharmaceutical economics in the College of Pharmacy at the University of Minnesota. So with that, let's begin, and I look forward to your presentations. Thank you.

AARON KESSELHEIM: All right, well, thank you very much, Suzanne, and thanks to everybody for coming here. So as you said, my name is Aaron Kesselheim, and I am going to get us started today talking a little bit about the generic drug market. I am the director of the program on regulation therapeutics and law at Brigham Women's Hospital and Harvard Medical School. Portal is an interdisciplinary research group focused on intersections between pharmaceutical development, and law, and regulation. And there, you can see some of our research funding as well. I don't have any important conflicts of interest to disclose.

OK, so I think it's useful to step back for a second and to think of-- when we're talking about the prescription drug market, to also step back and think about prescription drug spending in the US to give a little bit of overall perspective. But prescription drug spending rose 12% in 2015, 6% in 2016, and now accounts for about $450 billion, about 20% or so of overall health care spending. And this far exceeds per capita comparisons for the US as opposed to other countries. Now, the high drug spending in the US is mostly due to high cost brand name drugs, which make up about 10% of prescriptions, but about three-quarters of spending overall.

And this these high drug costs have important implications for patients, which I think we'll also come back to a lot throughout the day. In particular, David Mitchell is going to be up here later to talk about these kinds of things. But one survey found that 20% of patients reported not being able to fill a prescription due to cost. And patients prescribed costly brand name drugs rather than more affordable generic alternatives adhere less well and have worse patient outcomes. That's why it's so important that we have a vigorous generic drug marketplace because generic drugs and generic competition is the only type of competition that consistently and substantially reduces prescription drug costs.

And this is because of the combination of the facilitated approval process that requires a demonstration of bioequivalence and state drug product selection laws that allow for automatic substitution at the level of the pharmacy so that when even when a physician writes for a brand name medication, pharmacists are emboldened to be able to automatically substitute a generic product, which leads to substantial competition, price competition, and because the generics do not distinguish themselves from each other. And as you can see here, these are some data that we have that are currently in development and are coming out in a journal soon.

The average relative price declines based on how many generic drugs are in the market and providing that competition starting at about 15% to 20%, dropping substantially after the third generic is on the market, and falling substantially down after nine or 10 are in the market to about less than 20% of the brand name cost. However, there are a number of factors that can limit generic drug use. And I want to go through some of them in my comments, in my introductory comments today. So one of them might be advertising and promotion. And so you can see that there are advertisements out there from brand name drugs that try to distinguish, and the use of a brand name drug from a generic drug.

Even though there is no clinically, plenty of studies show there are no differences between brand name and generic drugs. Here is another advertisement for writing dispenses written for a physician to write a note on the prescription to prevent automatic substitution of the generic product. So this advertising and promotion by brand name manufacturers can limit generic drug use. Another factor that limits generic drug use is skepticism about generic drugs on behalf of patients and physicians. And we've done a series of studies showing that skepticism in this realm, while it has improved-- so these were some studies that were done in 2007 and 2009 about whether patients consider generic drugs to be as effective as brand name drugs.

And as you can see, the numbers have increased over time. There is still a strain of skepticism among both patients and physicians about the interchangeability of generic drugs as well. And this leads to important outcomes. And so you can see this is part of the survey as well. We asked patients if they've asked a doctor for a brand name drug rather than a generic. And there is still a substantial minority of patients who are requesting brand name drugs, even when there is no clinical difference. And the fact that they are less expensive means that patients are more likely to take them.

And then, of course, the big conversation, the big focus of discussion today is the cost and availability of generic drugs. And the availability of generic drugs, and the delays, and the various hurdles that brand name manufacturers put up to try to prevent generic drugs from

coming on the market by patenting parts of these secondary parts of the pill, like the coating, or metabolites of the pill, or the distribution system, limit is preventing sharing of samples needed for bioequivalent studies, other things to try to-- other strategies that they use, product hopping and other things to try to delay generic entry. My carrier and leader on the panel is going to talk a lot about some of these in detail.

But it's also relevant to think about the cost of the product itself. And the cost of the generic product is in large part due to the amount of, as a said, amount of competition that is available. And so we did a study looking at the competition that is available in the generic drug market and found that of all the drugs that are off patent there is a substantial-- about 15% of them had no generic competition at all, and about a third of them had three or fewer generic manufacturers on the market, which led us to recommend that the FDA accelerate approval of drugs for three or fewer products, which as you heard from Dr. Gottlieb, they recently did do.

And so this is reflected in the actual spending and cost of products. And so if you take this anti-parasitic medication, Albendazole it was available for $6 per daily dose. But because it's used for a such a small population, many of which are refugees, there was not a big market for it, and no generics had entered. And so another manufacturer bought the US marketing rights and raised the price to $120 per daily dose. And then once a second medication, Albendazole was taken off the market by its manufacturer, the spending and prices on, and patient use of Albendazole rose up. And so these are data from Medicaid showing that after the company raised the price and this other potential competitor came off the market, costs and spending in this area rose quite substantially.

Another factor that contributes to high generic drug prices is consolidation in the marketplace. And so we saw in the case of a drug called digoxin, there were eight manufacturers. And after a few years, those manufacturers had fallen off to more like three, and the price increased 600%. This is another study that we did looking at consolidation across the market in general that was published in Analyst of Internal Medicine earlier this year, finding that there is a direct correlation between the consolidation that's in the market and the ability of generic manufacturers to raise the price. And so a higher HHI index indicates a more monopolized market. And you can see that the generic manufacturers working in a more monopolized market are able to raise prices over the course of the study period much higher than manufacturers in a much more competitive marketplace.

OK, so niche patient populations that don't provide sufficient requirements or opportunities for competition, complex manufacturing processes that might limit the number of generic manufactures available, consolidation in the market can contribute as well to high prices. And then finally, another potential contributor are drug shortages, which can lead to the same kind of consolidation and monopolies in these off patent products. So we've done a study looking at the associate-- what are some of the factors that contribute to drug shortages and found that there is an association between the price of the product being offered and the drugs being at risk for a shortage, and that the drugs that have the lowest prices overall may be more likely at risk for shortages in part because manufacturers may be more likely to leave the market in those circumstances.

And then you can get results that look like this. This is what happened when there were shortages in a drug called BCG, which is a treatment for bladder cancer. And these are two other treatments that are used in bladder cancer. And you can see that in the course of-- when there were two different shortages that occurred for this medication in 2012 and 2014, manufacturers of the alternative treatments used those as opportunities to raise their prices. OK, so what are some of the solutions that we might think about in this area to address some of these issues? Closer scrutiny of advertising practices to make sure that they are providing truthful and non-misleading statements about the effectiveness and utility of generic drugs, better education of patients and physicians to try to overcome the skepticism that continues to exist in the pharmaceutical, in the market about generic drugs.

One other thing that I would add to the list of suggestions that Dr. Gottlieb posed, which I thought were great, is that we might also consider a more systematic policy to import off patent drugs from other countries, where they've already been approved by highly regulated, high level regulators over there as well, and thus increasing the market size across borders. Right now, this is legal, but there are not systems set up to ensure the safety of the product. But the FDA already does this in cases when there are shortages. And so if we develop systems to try to address the jumps in drug prices by importing drugs from other countries where the generic products are already approved, than we can more effectively address those hikes in prices.

Finally, applying greater regulatory attention, better funding of generic drugs science, and some of these to address some of these complex manufacturing issues to bring more manufacturers into the market, and the FDA offices and better funding the FDA Office of Generic Drugs to reduce delay times are important, as well as I already talked about expediting the review of priority generic applications. And then I'd be remiss if I didn't also mention the concept of follow-on biologics and the application of all of these rules to follow-on biologics. And so I think hopefully we'll get into that as part of the discussion later on about the extent to which we can try to get effective competition for follow-on biologics, which might involve looking at the way that they're named ad the way that they're reimbursed. So hopefully we can cover that as part of the discussion. So thank you very much.

SUZANNE MUNCK: Terrific. Well, thank you very much, Dr. Kesselheim. And now I'd like to introduce Chip Davis.

CHIP DAVIS: Thank you, and good morning, everyone. Let me start on behalf of the Association for Accessible Medicines by thanking both Suzanne and Maarika for the opportunity to participate in this distinguished panel today. And I look forward to the discussion. I would also be remiss if I did not thank Chairman Ohlhausen, Commissioner Gottlieb for their respective leadership on this issue, and the work of FDA and FTC staff. So it is a privilege to be here today, and I look forward to the discussion. I'm going to start by just setting a little bit of context on behalf of the Association for Accessible Medicines.

By way of background and context, we were formerly the Generic Pharmaceutical Association. We represent the interests of generic manufacturers as well as bio-similar manufacturers here in the United States. Our members manufacture 89% of all prescriptions dispensed here in the United States and do it for an amazingly low percentage of total costs, as you see here. I think

our statistics align very well with some of the figures you saw from Dr. Kesselheim within his presentation. Our core mission is to improve the lives of patients by advancing timely access to affordable generic and biosimilar medications. That level of prescriptions, at that level of costs enabled the generic and biosimilar manufacturers to save the US health care system $253 billion between government, private pay, and cash pay in calendar year 2016.

There is truly nothing else like this sector in health care, meeting almost 90% of the demand for slightly more than a quarter of the total cost. Generics actually operate in a deflationary market, not an inflationary market. Consider that in the past 12 months prescriptions for branded drugs have decreased by approximately 7%, while the revenue has climbed by 5%. By contrast, generic prescriptions have gone up by 2% year over year, while revenue has declined by 13%. This is due primarily, as you've heard from the previous speakers today, to the robust level of competition that in many ways has defined the historical value proposition of the generic marketplace.

And while that value proposition, driven by robust competition, has ensured that hundreds of millions of patients, if not billions of patients, the world over here in the US, as well as all over the world have been able to access the medicines they need, the current reality is this. The future of a sustainable competitive supply of lifesaving and enhancing affordable generic medicines is very much at risk. And that risk is being driven by the three factors on this slide. One, a demonstrable increase in the level of anti-competitive behavior and abuses that are seen in the market, some of which you've heard about already today, particularly from Commissioner Gottlieb, that are designed to delay or forestall generic and biosimilar competition, two, significant market consolidation, particularly on the buyers side of the generic market, and three, a series of public policy missteps or failures.

I'll touch on each of these briefly, and then I'm happy to expand as appropriate during the panel discussion. With respect to the issue of anti-competitive abuses, I know several of the other panelists are going to be speaking of this, so I will be brief. Whether it is the exponential increase seen in the filing of late-stage suspect patents, or conscious efforts to ensure that generic and biosimilar manufacturers cannot obtain the samples needed to do the necessary pharmacovigilance, increased product hopping, and even the recently well-publicized case where a company went so far as to pay a Native American tribe to run its sovereign immunity.

Barriers to entry for generic and biosimilar manufacturers are without question on the rise. So the question to all of us here is why is that the case? Well, simply put, despite all the public outcry and rhetoric over the cost of prescription drugs we have had and continue to have, a political environment here in the United States that not only tolerates these types of business practices, but because of failures to take action and remedy some of these actions, an effort to ensure a fair and level playing field for competition implicitly encourages these types of behaviors, not just to be sustained, but to proliferate.

It's important to understand the differences between generic and brand marketplaces because it does have, as you've heard, a direct impact on the prices, and the affordability, and the accessibility of generics. Branded companies typically market a small number of high margin products as a result of the investment that they have made to bring innovation to the market.

Generic manufacturers often market hundreds of products with varying levels of profitability and loss. When generics enter to provide competition to a brand monopoly, payers typically shift away from rebate models of reimbursement and rely alternatively on distribution channels to effectively lower the price of medicine. Because the products are identical, commonly, the only leverage generic manufacturers have is the ability to lower price and guarantee volume.

This creates fierce competition amongst many generic manufacturers when the market is working as designed, which in turn causes prices to decline. So the reality is the markets for brands and generics are entirely different, monopolized versus commoditized, and these differences create vastly different incentives for all the stakeholders in the supply chain that you see on this slide. Unfortunately, too many policymakers in Washington and at the state level assume that it is a single market for the pharmaceutical ecosystem and that all sides are experiencing significant price inflation. The result can be misguided policies, such as the recently enacted Medicaid generic penalty passed as part of the budget agreement the fall of 2015, which creates, actually, a financial penalty against generic manufacturers, even in circumstances when no price increase has been realized.

On the market consolidation front, a bit of historical perspective. In 1975, there were over 200 wholesalers doing business for pharmaceuticals in the United States. By the year 2000, there were less than 50. Today, there are three large purchasing consortiums reflecting agreements between wholesalers and large scale pharmacy chains. They effectively now control approximately 90% of the generic drug market. As these purchasers are moving more and more towards single source contracts for generic drugs, it creates a dynamic where it is entirely conceivable that no more than three generic manufacturers, or only slightly more, may be able to successfully market any given product. This dynamic risks future competitive success in the generic market, as generic drug manufacturers may be forced to maximize economies of scale and consolidate themselves.

In 2004, FDA published a study that showed that a generic drug can cost as little as 20% of the reference branded drug when eight or more competitors have entered the market. This has generally been referred to as achieving commoditized pricing. Those days-- and Dr. Kesselheim, I think, had a slide that showed something along these lines as well. Those days are now behind us. As more recent data suggests, this is a degree of price erosion that happens much sooner in the generic marketplace, often when there is as few as three to four generics in a particular class.

So generics are launching lower, dropping faster, and bottoming out deeper as an overall market basket than they ever have before. This reality tracks with the consolidation of purchasers I just referenced on the last slide. And I am sure that this is seen as good news by many attending today's workshop, and to a degree, understandably so. This chart, however, does not reflect a good long term, sustainable business model for generic manufacturers. Simple economics dictate that over time you will not have 10, or 15, or even 20 or more generic manufacturers competing to supply three buyers that are increasingly moving towards single-source contracting. Market forces will increasingly require our members to consider the size and scale of their portfolios, including whether they ceased production in certain therapeutic areas, either low volume or low market, or low volume or low margin, and potentially look to consolidate.

This is not theoretical. It is real, and it is already happening. A few weeks ago in mid-October, on the same day that I had the opportunity to testify before the Senate Help Committee on the issue of drug cost, two of our leading companies publicly announced their plans to merge. Later that day, another top member announced that it will be shuttering one of its leading US manufacturing sites within the next year. Let me be clear. Our members are not the only ones who are raising the warning flags here relative to the sustainability issue. In the last 12 months, each of the three major wholesalers that now exists in the US market have at least one time where another downgraded their own earnings guidance, and have identified continuing price deflation in the generics sector as the primary or a primary reason why.

It is a bit ironic at a time when policymakers and the public are upset about high drug costs that the generic industry is experiencing an unprecedented level of price deflation. So most importantly and in conclusion, what does all this mean in terms of having an impact on patient access and health outcomes? Well, as the FDA has noted in the past, generic drugs are particularly susceptible, and as you've heard already today, to the issue of drug shortages, often related to issues around market incentives or lack thereof, as well as low reimbursement. And once again, we are in a period of increasing barriers to access and unprecedented price deflation.

So what can be done about all of this? Well, over 30 years ago, as you've heard, Hatch Waxman created a remarkably strong foundation designed to balance access and innovation. But that system can only function if there is robust competition amongst buyers and sellers in the generic marketplace. And that system can only work if generic companies can get access to the samples they need to do the pharmacovigilance and start the FDA application and approval process. And that system only works when generic medicines have the ability to enter the market when patents and other IP protections are actually supposed to expire and are not subject to additional increasing levels of delay and gamesmanship.

And ultimately, that system works when the public policy environment in the United States doesn't favor one end of the access versus innovation equation at the expense of the other. If moving forward-- and you see some of the recommendations that we have for both the FTC and FDA on this slide-- if moving forward these issues get the attention that they need-- and in many ways, historically, we would respectfully submit over the last several decades have not gotten the attention that they need-- it could go a long way toward stabilizing what is an increasingly de-stabilized market. And most importantly, I think one thing we would all agree on is a destabilized generic market is not good for patients, it's not good for payers, and it's not good for the US health care system. Thanks very much, and I look forward to the panel discussion.

[APPLAUSE]

SUZANNE MUNCK: Thank you, Mr. Davis. Now I'd like to introduce Ronny Gal.

RONNY GAL: Good morning, and thank you very much for having me here today. So I'm basically going to talk about two things. One of them, I'm going to echo some of the points that Chip has made about the overall pressure on the generic industry and the value chain. And then I want to point to a few points of anti-occurrence, of anti-competitive, of problematic competitive behavior that I'm seeing as a food for thought for the group. So this is just my very simplified

rendition of the value chain, with the patient on top, then comes what's called a principle layer, a layer of people which should take financial risk on the cost of health care, beyond them, other service providers, the PBM. And below those are the distribution channel and the pharmacies and then the wholesalers at the bottom of the generics.

The point that I'm trying to make on this slide is that really, we've seen a consolidation across the channel. It's both horizontal and vertical. We have now have a PBM group, which purchases drug. Essentially for a large group of buyers, and the wholesalers that do the same. And we've also seen the power shifting up the value chain. So Chip already discussed the relationship between the generic manufacturer and the buying groups. But there's also a shift away from the pharmacy chains towards the PBM layer and the principle.

And the reason there is that employers and at risk insurance are getting a lot more interested in the costs of drugs overall due to the reason-- Aaron have mentioned essentially drugs are now around 20%. When you begin to have this conversation about where we can take cost out of the system, the conversation immediately goes to the generics because that's probably the easiest place we can take cost out. The other thing that happened are vertical consolidation, essentially insurance now owns some PBMs directly or indirectly, PBMs now all essentially all mail order pharmacies. And those mail order pharmacies are now part of those three large buying consortia.

So what has happened is that pricing visibility is now available for the PBMs to know exactly or close to exactly what is the price at the manufacturer level. With that knowledge of price, they're able to exert pressure on the level below them demanding lower prices. And they've been very effective with this. This is typically done in the form of Mac prices. This is maximum allowable cost. This is what will pay for the drug at the pharmacy level. And then essentially transmits the entire pressure down. Now, because of their ability to limit access to limit the network of pharmacies they use, they've gained a lot of power versus the pharmacies, and are able to negotiate down those pharmacies.

The pharmacies negotiate against the wholesalers. And those profit warning we've seen for the wholesalers and the generics are the results of that. Three observations here. The first one is-- I've already mentioned the best price issue in the visibility. The second one is the consolidation on the value chains that Chip has mentioned. And I'll mention one more, which is that the top of the value chain is couple of step removed from actually seeing the price and the pressure at the manufacturer level. And that is the risk point, which is if the immediate layer negotiates with the layer below it and says, look, you guys probably cannot afford any more discounts, that's one thing.

If the pressure comes from the top, there is essentially a slower feedback loop before they realize the bottom of the value chain is hurting too much. And in economics, you see in those situations a lot of times the pricing could go below what is a fair economical value, stay there for quite a long time before supply and demand readjust, and prices begin to come up to the logical level. And the big fear is that this is what will happen here. This is like my rendition of basically making the same point that was made before, that generic prices are cheap. This is just IMS dividing revenue, dividing revenue by the number of prescriptions over time for the largest 20 products in the US market by volume.

What you're seeing is a pretty robust decline of drugs, which [INAUDIBLE] before and are essentially selling for under $4 for a prescription. So our drugs, generic drugs, the largest of [INAUDIBLE] drugs at least are sold at very logical prices. And when we get into problems of costs of generic drugs, it's usually around the corner, essentially marketed with lower competition, market with access is somehow limited. And as a result of that, almost economics dictate this is where the nice pricing would be.

The other problem we are seeing here is as those prices come down, we are seeing movement of the old manufacturing of those drugs off shore. Now, there's nothing wrong with drugs being made off shore. But as the volume of drug on off shore-- we are getting subsidies now from other markets where profits are better. So the Indian companies, who have been capturing a lot of share over the last decade, are companies that have very nice profits in their home markets, roughly around 30%, and roughly fixed.

So they do not mind so much selling in the US market for lower margin than that, but sometimes below what you might call very economical margins. When I talked to those companies, they think about 10%, maybe 12% as their pain point for margins for selling the drugs because they've got really nice subsidies in their home market. The question is what will happen with those subsidies in the home market goes away? India will not for always support the domestic industry at 30% profit margin. And this is where we could run into shortages.

Now, the other points I want to make here is that there are therapy areas with upfront large costs, and the consolidation of the layer just by the manufacturer is now already leading to companies to rethink their manufacturing. One common area now here for bad for manufactures around, respiratory drugs. Those typically require unique manufacturing, and investments of $200 or $300 million in a manufacturing facility. And if you think that you'll be the fourth or fifth player in the market, and there are only three large buyers, the question is do you actually want to do those clinical trials? Do you want to put the iron into the ground to make that drug, or should you accept that market?

So competition drives prices lower up to a point. At some point, you're going to have a withdrawal of the cycle. And I've mentioned a few other points that delay competition on the other side. I want to mention three or four quick points around the competition between generics and brands where we're seeing some problems. The first one has to do with markets with limited competition, typically market with only one generic companies. In those situations, the generic companies compete directly with the brand, OK? However, the PBM, which typically makes the decision in this case, they decide either to approve the brand or to approve the generic and step at it, the other, has mixed incentives. It guarantees its own clients both a generic fill rate of a certain percentage. But it also guarantees a rebate trade across its desired portfolio.

A branded drug, which competes on price with the generic drug, typically have rebate prices, which can go as much as 80% or 90% down. That's a wonderful thing to meet your overall branded rebate rate if you are a PBM. And sometimes the incentive goes that way. That's not a problem in a way the relation between PBMs and the insurers are more about whether their economics are. But the question, do you isolate the patient from differential co-pays as a PBM

might prefer a brand over the generic essentially drive down to the lowest price, but isolate the patient no matter what your product choice is.

A second problem that we have run into recently is this issue of biosimilars. So in the biosimilar market, especially the ones with buy and build products, we have a split between the provider and PBM. Essentially, the provider fills the drug, administers it to the patient. But the PBM has a veto rule, or the ability to have a veto rule, by arguing, by preventing the-- by essentially putting a step edit that requires it to use the branded product before you use the biosimilar. What has happened is that the first large chronic used bio-billed drug in the market, Remicade ran into this problem where the brand essentially put a step edit, or convinced the PBMs to put step edits in about half the market.

No if you're a large hospital, and half of the product has to be from the brand, well guess what? You're likely to use the brand regardless for everything, add to that some bundling to the providers across the various products. And what you end up with, a market where the biosimilar cannot really penetrate. This is just data providing the amount of step edits and blocks that we are seeing in the Crohn's market, which is one of the markets where Remicade is used. And you're seeing here. The bigger bar in red suggesting that most of the market is now blocking the biosimilar Remicade.

And this is the adoption biosimilar Remicade. The biosimilar's right there on the bottom somewhere. Several people have mentioned here already this issue of REMs, citizen petitions, and I'll add the delay of decision making at the FDA level. So I'm not going to belabor the problems, just three quick suggestions about REMs. Some of the thing Dr. Gottlieb have mentioned today are things that we've been thinking about also for a while, this idea of transition during the third party and creating more of arm's length relationship between the people administering the REMs and the branded company, and do that upfront. So several [INAUDIBLE], the biosimilar can obtain material and obtain access to the REM itself.

On citizen petition, at the end of the day, it's a very good thing to have a scientific dialogue between the innovators and the companies in the field with the FDA. The point is you want to limit that abuse of that system. The most obvious thing to do is to just increase the fee that people are required to participate in that citizen petition and the citizen petition, and essentially have-- and staff the group that does this using some sort of a user fee. And in terms of delay decision maker, one suggestion I received from multiple folks in the generic industry is essentially to make the first draft of the requirements to make a generic as part of the NDA process.

So essentially, since the FDA knowledge of the drug is maximized at the time of approval, that is the right time to put the first draft guidance out, which will give the generics a good idea of what they need to do earlier. And then the [INAUDIBLE] situation after multiple submission right, only then does the FDA begin to understand what the requirements are. And now this is almost a separate discussion. We focus a lot about competition and the price at the drug manufacturer level. However, the big question is what happens to the patient at the pharmacy when he comes to get his drug.

So if the price is essentially paid by a large organization, which has knowledge of the prices, like a PBM or an insurance, the net price to the ultimate buyer is very, very cheap, OK? On the other hand-- and then comes the second block, which is, if a patient is in a deductible window, and he shows up, and has to pay officially full price, typically, the PBM will have some sort of a guardrail, which we'd agreed with the pharmacy, he would not charge my client more than x. On the other hand, if you come and make a cash payment for the entire cost of the drug, there's nobody protecting you, and this is where prices are the worst.

We've seen that with EpiPen. That was one of the big issues, the group that pays the maximum price. But it happens with generic drugs as well. And this is probably the group who needs protection a lot more than the large insurance companies that have the negotiation power than anybody else. And I will thank you for your time, and I appreciate, and happy to answer questions.

[APPLAUSE]

SUZANNE MUNCK: Thank you, Ronny. Now I'd like to introduce Mike Carrier.

MICHAEL CARRIER: Thank you. My name is Michael Carrier I teach at Rutgers Law School, and I'd like to thank Chairman Olhausen, and Commissioner Gottlieb for their leadership on this issue. I'd like to thank Suzanne and Maarika for putting together this panel. I'll be talking about high prices and no excuses, six anti-competitive games. And so I think that as chairman Olhausen said, the Hatch Waxman Act, brands, patents, and innovation have gotten a ton of attention. Generic competition and post-patent market entry has not. I've comprehensively studied this issue as co-author of the leading treatise on IP and Antitrust Law, author of 100 articles on IPN Antitrust Law, author of Amicus Curiae Briefs on Behalf of Professors, and someone cited frequently on these issues.

We hear a lot about brand companies increasing drug prices because of their important patents and the crucial role that they play for innovation. Sometimes that's right, but many times it's not right. Many times the prices rise because there are weak patents. Sometimes the prices rise even when there are no patents. And so it's worth thinking about the brand companies incentive to prolong their monopoly profits through many aspects of the regulatory system, FDA exclusivity, the time it takes to reformulate to generics, the citizen petition process, distribution restrictions. All of these can delay generic entry, when there are weak patents, when there are no patents, and they prevent consumers from getting affordable medications.

When we talk about off-patent competition, it's also worth keeping in mind that that off period of patent competition comes much later than it used to in the past. In the past, there used to be more frequent competition quickly. Now long after the active ingredient patent has expired, we're still subject to many generations of patents. A couple of examples in the small molecule setting, we have the Lipitor blockbuster drug. We have patents expiring in 2010 and mid-2011. But there is a settlement with generics that says that the generics don't need to enter until after that period. Why? Because the brand company went out and got several patents that were less important that expired in 2016.

And then as several panelists have talked about, the biosimilar industry will present many of these issues writ large. And so for example, for one example, you look at [INAUDIBLE] composition of matter patent that expired in 2016. Rest assured, there will be no competition for a long period of time. For the next two decades, 100 patents will be enforced preventing biosimilars from entering the market. In terms of the games that brand companies play, the first is pay for delay settlements. The FTC has been on the front line on pay for delay longer than anyone. And we see that after the Supreme Court said that this could violate antitrust law, that perhaps it's making a difference.

Over the last three years, the number of potential pay for delay settlements fell from 40 to 14, showing that when courts and enforcers apply antitrust scrutiny, that the parties settle in other ways. The number of settlements has actually increased from 160 to 170 recently. But the number involving payment, the most concerning kind, when the brand pays the generic to stay off the market, have decreased. We also see that the number of patents involved in pay for delay are really not the active ingredient. There are a couple of exceptions. But by and large, this is dealing with patents after the active ingredient patent has expired, involving things like method of use, formulation, particle size, and time release.

You look at a couple of examples, the active ingredient expired decades ago. But still, you have the brand company paying the generic to delay entry because we have newer generations of patents. The second game that is played is product hopping. Now, sometimes brand companies switch from one version of a drug to another, and there is no competitive concern at all. There is no generic entry that's about to happen, and the brand company actually wants to put out a better product. And that's completely fine. But sometimes the only reason that the brand company makes this switch is to harm the generic.

And so when you think about the role of state substitution laws, the Hatch Waxman Act, which were undercut by these product changes, you think about the timing, the brand company wants to switch the market to the reformulated version before the generic of the original gets on the market. And you think about all of the hurdles, even apart from patents that it takes for the generic to reformulate its product, to get FDA approval each time, to deal with state substitution laws. And we see that this can delay entry, in terms of the litigated cases. In Prilosec, Suboxone, and Namenda we've got an extra 13 or 14 years just from switching to the new version of patent.

And even if there is no patent, the generics still is hamstrung in reaching the market. So for example, you look at the Dorex case, which treats acne. You have multiple product tops. The capsule goes to the tablet, then it goes to a higher dosed tablet, then it goes to a lower dose tablet with a single score-- the score is the line that you can cut the pill-- and then finally, it goes to a dual score. And each time that you add a score line, you have to have the generic start over all from scratch. And they have to reformulate their product, get FDA approval, and this is another reason why we have delayed competition.

Game three involves citizen petitions. In theory, citizen petitions are crucial to raise legitimate safety concerns with the FDA. In practice, they are not really used that way. I've done a couple of empirical studies of all citizen petitions in the past 15 years, and my most recent one found that the FDA denied 92% of petitions that brand companies filed with the FDA. That figure rose

to 98%. 49 out of 50 petitions were denied when the petition was filed at the last minute, within six months of the expiration of a patent or FDA exclusivity period.

And you can see examples, for example, Beyer's petition on the IUD marina, which came one day before patent expiration. You're saying that Bayer really discovered this one day before patent expiration? Very unlikely. Then you think about Allergan with Restasis, it's gotten a lot of attention. Even yesterday, there was a hearing on the hill on the transfer to a Native American tribe to avoid the patent review process. But even with the district court striking down these patents in a 135-page opinion, we still don't have entry because we have citizen petitions. Now Allergan is on its third petition. They all say the same thing. FDA, you can't approve the generics because they do it in-vitro in the lab we. Really need to in-vivo.

They say the same thing every time, and they tweak it just a little bit so that the FDA has to spend months and months dealing with this. In the meantime, we do not have generic competition. Game four involves REMs restrictions. Commissioner Gottlieb talked about the harm when you have risk evaluation mitigation strategies, which are designed to bring risky drugs to the market that are really being used to delay generic entry. In many cases, the brand companies deny samples to the generic. The generic is willing to pay the market price. The generic is even willing to offer an indemnification agreement. hey, brand company, you're worried about being on the hook? We're going to pay for your expenses.

The brand says thanks, but no thanks. The shared REMs setting is another one where the brand and the generic need to each work together. They each have their own REMs program. And we've seen like in the Suboxone case that this just leads to slow walking the process. And so Commissioner Gottlieb talked about a master file to deal with this. That would be great. But let's keep in mind that brand companies find every way to slow walk the process, even after the FDA does something. So for example, you look at the case of Actelion v. Apotex. Here, the brand said we'll give it to you if you get a letter from the FDA saying that this is safe. The generic gave the letter to the brand and the brand said thanks but no thanks. We still are not going to give it to you.

Game five is non-REMs restrictions. Even where there is not a safety concern, the brand company still can restrict its distribution system to delay generic entry. Pharma bro Martin Shkreli is the poster child for this. We talked a lot about the 5000% price increase on Daraprim. What we didn't talk about is the distribution restriction where it used to be all across the country, then was limited to one place, Walgreen's specialty pharmacy. And the [INAUDIBLE] official said, yeah, we're doing this to avoid generic competition.

It's not the only time this happened. You look at Shkreli's prior company. They did it on Chenodiol and Thiola, again, saying this is our way to keep generics off the market. Game six is one that has recently arisen in some antitrust complaints when insurers are forced to bundle products in order to get rebates. And so we see this with Allergan as well. Shire sues Allergan saying that Xiidra is a better product than Restasis. It doesn't have the side effects. It doesn't have to be taken with a steroid. But it only has 10% of the Medicare part D market because of these rebates.

And the same applies in the biologics industry, with Remicade and with the EpiPen as well. What to do? The moral of the story is to apply antitrust law. Have rigorous antitrust enforcement for all of this conduct. Again, pay for delay settlements. The FTC has been on the front line for decades. Product hopping, keep in mind there is some nuance here. The courts don't always get it right. Sometimes when there's a hard switch, courts recognize when you pull the old drug off the market. That's a bad thing because you're removing choice.

But it's not that simple that when you leave the new version on the market, a so-called soft switch, that it's automatically OK. These are complicated markets. And so it's not always the case that two is better than one when the brand company switches all of its marketing to the new best thing of the reformulated drug. REMs and non-REMs, I've talked about citizen petitions. There is a lot to be done. The FTC filed an excellent case in February of this year against Shire ViroPharma. And the FTC's leadership on that is crucial. The FDA can do several things on this. And I've offered some of them as proposals, and bundling, and rebates as well.

So in all of this, antitrust enforcement has a crucial role to play. Brand companies benefit from prolonging their period of monopoly profits. It's very complicated. We have complex regulatory regimes. But there is a crucial role for antitrust law to play. Thank you.

[APPLAUSE]

SUZANNE MUNCK: Well, thank you, Mike. I'd like to introduce Dr. Schondelmeyer.

STEPHEN SCHONDELMEYER: Good morning. I'm glad to join you today. We had an exciting entrance, as you all, if you were here on time realized. I must tell you, first, I'm a professor at the University of Minnesota. My area is pharmaceutical economics. I do have research projects with the Minnesota Department of Health Economics Division, where I'm studying issues and are all payer claims database. And secondly, I have projects with the AARP where I track drug prices in the marketplace. And I've done that for many, many years.

By way of giving an overview of what I plan to cover, to help us understand this marketplace, I contemplated the things that my colleagues on the panel might cover. And they've covered many of the things I expected. I may touch briefly on some of the same issues, although I've tried to deal with additional issues that are, if you will, in the weeds out there in the marketplace. I'll talk a little bit about demand, a little bit about supply, competition, and market power for generics, regulatory and legal influences on generics, price trends, and then finally, finding fixes for the future.

Now let's start with demand for generics. First of all, I want to make the point that generics are not a single market. We talk about in pharmaceuticals brand name market, generic market, specialty market. And in a sense, they're markets. But at the end of the day, no consumer buys every generic drug. They need the one that their doctor has prescribed. No consumer buys every brand name drug. They need the one that their doctor has prescribed. And same is true for specialty drugs.

So to a consumer, the market is one, or two, or three products. It's not every product, and it's not the weighted average market price that counts. It's how much is this product to me, and what's the cost impact? So really, this pharmaceutical market is a series of individual markets that are defined by therapeutic class and/or drug molecule, and/or dosage form, or even strength. So the reason product topping works is there are unique markets for each dosage form and strength. And you can switch from a tablet to a capsule, and the pharmacist can't substitute those for each other.

And this is a complex set of laws between federal FDA laws and between state pharmacy practice and medical practice acts that interplay to make this work and play out. Pace and demand for generics is market-specific. It's specific for a certain drug. And let me remind you, a way to illustrate that is if I'm a diabetic patient and I find out that my neighbor is using an anti-epileptic drug that costs less than my diabetic meds, I can't switch and start using the anti-epileptic meds. There is no cross price elasticity for the economists in the market between diabetic meds and epilepsy meds. Just isn't there.

Yet sometimes we analyze, quote, "the generic market" collectively with aggregate numbers. Now, I'm all for economics, econometrics, aggregate measures in the marketplace. But we have to remember that this market is very unique structurally, that these markets are unique to each individual and each drug, and the drug they need at the time to deal with their medical problem. Measures of market concentration then I think need to be focused at the level at which the consumer faces the choice, not aggregate generics, aggregate brand. Yes, we can look at those trends. I do those. I report that data. But I also report data at the individual product level. And I think that's critical. We need more of that.

And as I've already alluded to, economic substitution, and generic substitution are not identical concepts. There are some overlaps between the two. But there are some things about generic substitution and pharmaceuticals that make it very different than class economic substitution that economists usually assume and use. So we need to understand and take account of the difference. And it's already been pointed out that nine out of 10 prescriptions are filled with generic drugs. There is payer demand. Consumers want generics. Consumers trust, for the most part, generics. And consumers want lower cost generics.

But that concept has begun to erode. Consumer's trust in generics may be us moving back in the other direction for a variety of reasons. Let's look at some supply issues. There are fewer generic firms in the market. There has been consolidation within generic firms, brands buying generics, generics buying brands. Let me make another point. There really aren't just generic drug companies and brand name drug companies and specialty drug companies. Most drug companies are all of those. The companies you think of as generic companies have brand name products. The companies you think of as brand name drug companies have generic divisions and products.

And both of those have specialty products. So this marketplace isn't a matter of single industries. Most generic firms have a broad line of products. And also, that broad line is used to wield some market power. I'll give you a better deal on these three products if you buy more of this product. And they use-- economists would tell me it's not tying agreements. But they're bundling in

contracts is a form of tying agreements. Pay me more here, and I'll give you a better price over here. On average, who knows what price you really got and how it gets passed down the line.

Authorized generics also are not really generics. In some ways, they behave like generics, but they're not approved under ANDA. They don't have all-- they have some economic factors. They do bring some competition in terms of price, but not the full competition you would see with an economic independent decision maker that enters the market as a generic. So we need to understand and be careful with what we call generics. You. Remember what happened with EpiPen. And they declared that they were going to help the marketplace because their prices are so high. So now they're going to sell a generic.

Well, it really wasn't a generic. It was ANDA-approved authorized generic. And then they got in trouble with CMS about, OK, so this is generic. We should be getting rebates. How much are we getting on rebates, issues like that. PBMs also sometimes add price onto generics. I agree, it's not just what the manufacturer's price is that makes a difference in the market. It's what trickles down at the end of the day and who's lining their pockets along the way. And PBMs do add price on to generics, and not always, but at times. And often, they do this through their mail order pharmacy, through their specialty pharmacy, through their preferred networks.

I can show you data that I've examined by working with various employers and payers in the marketplace that shows they actually pay higher prices for generics through preferred pharmacies and preferred networks rather than lower prices, exactly the opposite of what you might assume if you assume normal economic principles. Next, competition in market power. We can't use a number of ANDAs in a market that are listed in the orange book as our only measure of number of competitors. I can show you generic categories where there are a number of ANDAs, but there are only one, or two, or three actual products you can buy on the marketplace.

I show you other categories where there are only five ANDAs, and there may be 12 different people marketing the drug. And so there's not a close correlation between number of ANDAs and number of people selling the product in the marketplace. And it goes in both ways. Only one or two ANDAs in a marketplace does deliver some degree of marketing power, even to a generic with no patents, with no exclusivity. But it creates what I sometimes call a functional monopoly, that if its going to take a competitor, one, two, three, four years to get in the marketplace, I can behave like a monopolist until they get in the marketplace.

And one part of that is the FDA's review time in getting products on the market. I applaud the announcements and the directions that Dr. Gottlieb's taken with FDA. I applaud the efforts to reduce the review times. But we need to be ever vigilant and keep that moving. API contracts, this is the active pharmaceutical ingredient. That's the raw chemical, the powder that you buy before you put it in a finished dosage form. And that industry largely is outside of the United States. And that industry is also very concentrated. And there are a lot of deals between if you don't give-- if you're selling a competing product to this generic company, then I won't use you to make my brand name product at a higher price.

And so we need to have examination of the behaviors going on in the API marketplace, and the contractual deals, and exclusionary behaviors that are taking place. You may remember the

Lorazepam case that FTC appropriately identified, and pursued, and settled back in the early 2000s. What's up with Atenolol today? Is that deja vu? I don't know. People at FTC will have to examine that. But I think there are concerns about a number of other products in the marketplace that look like they have some of the same characteristics of the Lorazepam case.

Some generics have faced over competition. As we've heard, the supply side has very concentrated and hospital buying groups, the retail buying groups concentrate and focus the generic market. And in some cases, they've driven the price so low that it's below a marginal cost to right at marginal cost and below reasonable return on investment to stay in the market. And we've had companies drop out. It's particularly true in this sterile injectables. And I think it's pushed the price so low that generic companies haven't been able to invest back in modernizing and appropriate equipment. And so even if they can still make it at that price, they're doing it by cutting corners.

They end up violating something that FDA doesn't like, appropriately about the quality and safety. And a plant gets shut down. And when you shut down one sterile injectable manufacturing plant, you're likely to have shortages in the market, at least for the short run, if not the long run. Some generics are just too small to be profitable in the first place, and we need to understand this. We need to look at incentives to encourage companies to enter this market. But let me caution us. Don't use the same incentives. If you're going to give them exclusivity or some kind of a unique market position, that won't solve the problem for a small market. If you don't have anybody in the market in the first place saying you can be the exclusive seller, it isn't a benefit. It still doesn't make it profitable to market that product.

FTC should evaluate shortages, particularly when a company-- we can look, when the FDA closed down a plant and there's some relationship to the shortage-- but sometimes the reasons given are business reasons. FTC should be evaluating shortages that list business reasons as the reason for the shortage and be looking at those APIs and other things in other companies in the marketplace, other agreements. Just a quick example, Verapamil is a product. And its price had been increasing as a generic over time, you notice here from 2005 to 2012.

Then there was a period of shortage. What happened to the price? Whoa, the price went up. And the other thing I'd point out is drug prices often tend to be very sticky. Once they go up, they don't come down very easy.

And that's been the case in Verapamil here. Regulatory and legal issues, yes, the review times at FDA have shortened. But those review times, we need to look carefully and make sure it's not just a shell game of shifting that time from FDA to the company. In other words, we won't accept that application for review. So it's not on FDA clock, it's on your clock. And so we need to look at the total time of generic ANDA approvals, both FDA time and generic firm time. And our real measure should be how much do we shorten the total time of both, not just FDA.

We can play games. And I'm not saying FDA is doing this. But one could play games and shorten FDA's time a lot, but increase the time that the company has to do to prepare for it. Yeah?

AUDIENCE: [INAUDIBLE] all the slides will be available after the program.

STEPHEN SCHONDELMEYER: I want to give one data slide on drug price trends. We've been hearing about-- and yes, the marketplace prices do go down. This is a cohort of drugs that entered the market between 1980 and 2003. But this is their prices from 2005 to 2015. Notice generics were at $0.71 per day of therapy, and they were bidding down to $0.48, just what you'd expect in a generic market. Then these are the top generic drugs in the marketplace. Then in 2011, notice they had a tick up of about 20% from $0.48 to $0.61. And A in 2013, and '14, it jumped to $1.26. Is this a competitive market? What's going on

There were 115 products in this market basket. A fourth of them had overnight increases of 100% or more for their products. Something is up in this marketplace. Again, we can examine it, look at it further. This isn't the normal generic market. This gets lost in averages, in an industry averages. We need to remember the market is individual for each patient and each drug. Thank you very much.

SUZANNE MUNCK: Thank you, Steve.

[APPLAUSE]

Steve, I think you closed on an important point of looking at individual markets and not necessarily drawing conclusions across the entire generic industry. We began this program really asking, are there enough incentives to enter markets where the branded drug is off patent. Do the market participants or policymakers have a role in providing these incentives? And I think that we heard really three large buckets from our panelists this morning, that there are factors that affect market entry. You've got patient use, and skepticism, small population consolidation, shortages.

You have strategies that can reduce competition, either pay for delay, product hopping, citizen petitions, or REMs. And I'd like to use our discussion time to explore both of those issues starting first with the market entry factors. And Aaron or Ronny, you both presented-- Aaron, you presented Albendazole, and Ronny, you presented the Concerta example. I'm wondering if you think that those are good examples to talk about this issue, or if you have other points that you'd like to make after hearing the panelist's presentations.

AARON KESSELHEIM: Sorry. OK, it does work. OK, so yeah. So yeah. So Mean I think that's as good example as any. The Albendazole case is an example where it's a very niche market. And therefore, there was no generic entry. And that allowed a manufacturer, or a company that had as its business model the idea of cornering a niche market and raising the price to be able to come in and do that. And so as to the question of, well, what do we do to try to encourage entrants, well, first of all, it should happen that once the price rises, that other market entrants, other companies will then be incentivized to enter the market because they see a higher price.

But then there is still an inevitable delay that can come from companies wanting to-- needing to do the testing necessary to come onto the market. So we could try to enhance those, accelerate those processes, as we talked about, by trying to devote more resources to getting to

understanding the bioequivalence testing and getting it done as quickly as possible. Another alternative would be for the government to actually enter in to offer government purchasing contracts, to try to stabilize the market and provide a certain amount of guaranteed demand so that manufacturers would enter.

And we currently do that in the context of childhood vaccines, where the government offers to purchase, and therefore it can stabilize these niche markets. And that might be another option. But I do think that some of the various ideas that were discussed in the panel are good starting points.

SUZANNE MUNCK: Terrific. And Ronny, you talked about Concerta in terms of high discounts leading to preferences off brand. Is that something you'd like to explore a little bit more?

RONNY GAL: Sure. So this is the place where the markets of the generic, the generic market and the brand name market begin to overlap a little bit. And I pointed to a couple of examples of friction. So what happened with Concerta was that the authorized generic has the Medicaid price. And the Medicaid price on Concerta is basically $0 because they raised prices so many times over the years . And therefore, if you are a pharmacy operating somewhere where there are a lot of children, Concerta is used. A good proportion of the market is children-- half the children in the United States are on Medicaid.

You have to stock the brand or the authorized generic because one of your largest payers, the state Medicaid wants you to stock it. So are you going to stock to a scheduled drugs, or are you just going to standardize your volume on one of the standardized drugs? So that's just an example of economic inefficiency. I think about this a little bit of-- you'd have to solve two markets here to solve that one, the generics and the branch, which makes it a particularly hard situation.

SUZANNE MUNCK: Terrific. Thank you. Before we move on, I'd like to ask the rest of the group. Do others have suggestions on how to ease entry in these situations? I heard the one about government purchasing contracts and efficiency in FDA, which of course we're paying attention to. But I would love to hear if others have suggestions.

STEPHEN SCHONDELMEYER: Well, I think there's some things we should do, and maybe some things we shouldn't do. I applaud FDA for their unapproved drugs initiative, but the culture scene example wasn't a stellar move in terms of creating competition . We went from a product that costs $0.10 per tablet to one that costs $5, at total costs to the Medicare program over five years about $1.2 billion, nationwide probably about $3.7 to $4 billion increase in cost. We need to look for ways.

I agree. We need to clear out the unapproved drugs problem. But the way to do it isn't to give exclusivity to the products that come first and not the other competitors out of the market. Let's find a way to go from unapproved drug to generic competition rather than unapproved drug to exclusive brand name. So that's a case of something we shouldn't do. I think as your FDA is doing and Dr. Gottlieb described, shortening the review time at FDA is important. But keep an

eye on the manufacturer time also, because, again, you can play a game of just pushing the time out on their clock. And so I think that's important. Keep your eye on the net prize. And what really will create competition is getting those generics in the market faster, safely, and effectively.

AARON KESSELHEIM: What I wanted to also just put on your list, and to come back to the idea of temporary importation, in the case of the pyrimethamine drug, which was the classic, the pharma bro drug. And that's now the second time his name has come up. If his name comes up a third time, I think he appears on stage. So anyway, in that case, that company was able to raise the price because there were no other generic manufacturers in the market, but there were manufacturers that we're making the product and selling it in other countries, and temporarily allowing, developing a system where you could import to try to address the price increase while you're working through the usual FDA approval process would be useful.

And I think that basically that would just entail considering these high price increases as equivalent to a shortage because functionally for a lot of patients, they are.

CHIP DAVIS: We just had two things, to pick up on the comments and avoid trying to reference the pharma bro for a third time. But my second week on the job at the NGPHA was when that story broke. So I'd like to thank him for that. One thing to Professor Schondelmeyer's comments, I think we have to be mindful as well though about the benefits of the exclusivity provisions in the generic space particularly related to first to file, because actually, if you look at the performance, I'm just saying in terms of on across the board exclusivity provision, I think we need to be mindful of the fact that exclusivity provisions, very limited in time, obviously and understandably compared to brand counterparts, is still, if you look at the revenue cycle of any generic drug, there is a profound market-based incentive to allow them to have that first to file exclusivity.

I think on the issue that Dr. Kesselheim has brought up, in addition to seconding all the comments about the work that Dr. Gottlieb and the FDA are doing to enhance visibility on areas where there is a lack of competition, I think the disclosure of Daraprim-like products that the FDA made is an important step. The prioritizing of the first three is even more important step. But I think one of the things that the FDA is also doing that hasn't gotten as much focus right now is working on mutual recognition policies. And so I think with an announcement-- I guess it was last week about the first eight markets in the EU-- I think there'll be an opportunity there to actually accelerate the timeline within which generics and the GDUFA II mindset are expected to be approved, but making sure that we are sharing best practices with other developed markets that's going to go a long way towards enhancing that.

And the point that was made earlier that I would just reinforce is, with a lot of our members, the ability to file and oftentimes believe that you could be the second, third, or fourth generic into a market, which gets you now to that commoditzed pricing level looks very different when you file. And then either through historical moving of guidances at the agency or others, you wake up and realize by the time you're approved, you're the eighth or ninth. And so that has a fundamental irrecoverable impact on your business moving forward. And I think there are being steps taken to minimize that risk.

AARON KESSELHEIM: So I will just follow up on that by saying from the FDA perspective, the one thing I would say is to start early. So your best position negotiating with a branded [INAUDIBLE] company around is probably when you are still looking at their ANDA for approval. So if you have ANDA guidance as part of the ANDA process, if you build the REMs up front when you have the most leverage with a drug company, with the innovative company before the drug is approved, then you're going to solve half of those problems down the road.

SUZANNE MUNCK: And I think those suggestions, in particular, some of the last ones really speak to initial market entry. But what about the situations where there's older drugs And and we have the potential or real world shortages? We often see that those aren't resolved quickly by new market entrants, where there really should be a market opportunity. Any suggestions from the group?

RONNY GAL: So some of the things that I'm hearing from drug companies, a couple of issues that come up all the time is, look, I have to make three batches, large batches. I have to deal with a bunch of regulation. I have to do all my analysis before I can come to the market. So OK, how big those batches have to be? I have to think about two or three cycles of approval. Is there a way to work with them much closer for those shortage [INAUDIBLE] will be one approved cycle?

A lot of the things that the agency can do beyond this issue-- look, the drug has to be a good one-- is to think about the requirements that you have for a large market and think about how much that applies to a small market in terms of how you view it, how you do this analysis. And perhaps those small products where you could have much more likely to run into shortages, you have some of those tools available to you to waive some of those requirements when you know there's not enough competition.

STEPHEN SCHONDELMEYER: Another place where we have existing products that don't have effective generic competition is in specialized dosage forms. And one reason generics work well is the orange book, therapeutic equivalence, evaluation of immediate release, and even sustained released products. But when it comes to inhalers, dermatologics, ophthalmics, and other specialized doses forms, FDA doesn't have therapeutic equivalent standards, or even a way to establish an orange book rating for some of those products. That's a major inhibitor to generic entry and generic competition.

SUZANNE MUNCK: Great. Well, thank you. Chip, turning back to you, you talked a lot about shortages, which we've just addressed, and also consolidation. And so I wanted to ask you if you would like to expand on some of your proposals to address those issues or talk a little bit about what you think policymakers should be considering in addressing those issues.

CHIP DAVIS: Sure. So I think there's a-- on a couple of fronts, an overly simplistic economic model to have the robust competition that has been really the foundational success of the generic industry since the passage of Hacks Waxman. You need that robust competition on both sides of the negotiating table, right? So as you've seen the consolidation on one side, the simple economics are, ultimately, if one side has seen that level of consolidation, we have to mitigate the downside risk of seeing the other side in an effort to get the negotiating table back to a level par, taking the same sort of example.

So I think what we have to do is figure out what the right balance is of where there were synergies that made sense for buyers to consolidate to continue to drive prices lower in a competitive marketplace. That is, by definition, a positive development. I think where it was referenced previously though, is that when you get below the inherent economic value of a manufacturer to continue to market and manufacture the product, then arguably, you're in a scenario where you have too much of a good thing, if you will. So I think that's one area that needs a little bit more scrutiny if we want to make sure that we don't wake up and have three purchasing consortiums on one side of the table and only five or six large-m scale generic manufacturers on the other.

I also think one of the things that was talked about-- and this picks up on the discussion about really understanding the varying degrees of market dynamics that were raised. I was particularly struck-- and it was referenced by several speakers-- about the pending litigation in the biosimilar area around Remicade and Inflectra with-- pardon the expression, but this is a brand versus brand battle. This type of activity though is not new in the brand versus generic space. So I think it's getting a lot more attention in part because of the precedent setting about bundling of contracts.

So if you think you have too many markets now, if you have the ability to leverage a wide-scale portfolio to say I'm going to give you this level of rebate here, but additional rebates in other areas provided you keep that biosimilar from coming to the market, then arguably, if you're taking markets as therapeutic areas per se, then you're having disruptive forces that have nothing to do with the decision that a provider would have to make about what's the best available treatment.

And that includes taking price into account because you're putting in a whole host of other products that are wholly unrelated to the clinical workup of the patient. So I think that's something that as that practice-- there's been a couple of lawsuits filed already-- I think we should all probably expect to see more in that space. And I would suspect that that's something that's going to get more attention as we move forward as well.

SUZANNE MUNCK: Go ahead, Ronny.

RONNY GAL: If I can follow up on this point, so just as a heads up for the FTC, look, the three lawsuits have been filed on this issue of branded companies' negotiations with PBMs. Those who were decided, some in the next 24 months by district and an appeal court's decision, and will have a pretty entrenched legal statements being made. For the FTC to add value to that process, this is the time for you guys to put some fact based on the table so the judges who are not experts will know some of your work and how you think about it. I remember with Hutch Waxman, a couple of bad decision led to two decades of litigation to be undone. This is the time for you guys to act and put a view on this one and not wait.

MICHAEL CARRIER: And I completely agree with that. The law of exclusive dealing and rebates is muddied. It is oftentimes difficult for courts to apply. Frequently there are pro-competitive justifications to things like bundling and rebates, but in particular cases. Particularly in these markets, there is a potential for anti-competitive harm that courts don't always recognize. And so that's why the FTC's attention to this area is so important.

STEPHEN SCHONDELMEYER: A related topic, again, something FTC could look at, co-pay coupons have become a major problem an issue in the marketplace as well. And I serve as helping the University of Minnesota manage our drug benefit program. And we see prescriptions come through for high-cost brand name drugs instead of a generic because a patient was able to save $10 with a coupon. They thought they saved money. Actually, their premium will go up the next year because the experience rating and the cost of that brand name raise the total costs.

We've got to get out of this mentality of thinking that co-pay is the cost to the consumer. Premiums are an out-of-pocket cost also for somebody. And premiums count just as much, in fact more than co-pays. So we need to look at the reverse perverse incentives that co-pay coupons cause, particularly for generics versus brands in the marketplace. It's costing employers a lot of money because of those co-pay coupons. And it's driving patients away from generics and toward higher cost brands that FDA has told us are exact therapeutic equivalents.

SUZANNE MUNCK: And thank you, Stephen. And thank you for all the points with the FTC. I think you go to another issue that I wanted to address, which was many of you talked about issues with patient use or patient skepticism. Are there other steps that can be taken towards patient education in this space? And then once we discuss that, I'd like to move on to their strategies that can reduce competition.

STEPHEN SCHONDELMEYER: There is one. We've spent a few decades educating consumers about generic drugs, and that they're safe and effective. FDA's put out some great pieces describing that. But now that we have authorized generics, and now that we have a drug-like Concerta where the brand name discounts more than the authorized generic, payers are put in the place of having to tell the consumer, yeah, there is a generic, but we don't want you to use it this time. We want you to use the brand name because it's cheaper.

This confuses consumers. This creates skepticism and doubt, not just for that drug, but on the broader concept of generics in the marketplace. We need to look at the use of the term authorized generic, and maybe clarify that, because it isn't a generic like generics. And it doesn't have the same economic role in the marketplace as generics. And so we need to look at-- I think we're confusing consumers and making the issue worse again rather than better.

SUZANNE MUNCK: Thank you.

CHIP DAVIS: Yeah, I would add-- and I was intrigued by one of the slides that Dr. Kesselheim put up about some of the marketing materials. It's interesting, because if you look at the uptake, or in many instances, the lack thereof of biosimilars in the US market since BPCIA passed, there have been three for those that have not been as supportive as others about making sure there's robust uptake here in the US. There's been three main arguments around biosimilars. One is a quality-related concern. The other is that the FDA may have insufficient resources to appropriately regulate in the space. And the third is that they may not save payers in the US system and patients that much money.

Go back to 1984. It's the exact same three arguments that were used against generics. And so there's a piece of it that says, well, then again, over time, look at the traction that generics have

gotten and will ultimately get there. The problem is, as the science moves forward in advancing more and more targeted and specialty and personalized medicine, which by the way, is a great thing for all of us, the challenge of not getting the robust level of market uptake for biosimilars here in the US is going to be something that ultimately we will continue to lag behind Europe, and ultimately is the level of savings that we will never be able to recover that will be lost as a result of the lack of uptake.

We have seven that are approved in the United States as of today. Three are on the market. The other four tied up in litigation. All right, so we talked a lot about for the last several years in credit to the FDA through GDUFA II for the commitment to resolve the ANDA backlog. We're not looking at a risk of a biosimilar application backlog on biosimilars. We're looking at the risk of a litigation backlog on biosimilars, and that's not going to help the market.

SUZANNE MUNCK: Thank you. And, Mike, you talked a lot about strategies that you thought could be used to prevent competition outside of these market forces. I'd like to ask you a little bit more about that and what you think-- as we've talked about, the FTC has been, I think it's fair to say-- a leader in pay for delay and some of those other issues. And so what would you like to see policymakers focus on in this space?

MICHAEL CARRIER: So it is crucial for the FTC to continue its leadership on pay for delay. So the Supreme Court four years ago said this could violate antitrust law when a brand pays a generic to staff the market. But there are so many places that the brand companies are fighting these rulings on the application of the rule of reason, on causation, on the role of the patent. And any one of these could lead the entire antitrust framework to unravel. So it is crucial, as courts do not always get it right as the Third Circuit and Wellbutrin tried to relitigate activists, taking the position of the dissent, that the FTC beyond the front lines of each of these issues.

I think with REMs, we hear that the FDA is concerned with this. I know the FTC has weighed in with amicus briefs on it. But perhaps there is future room to coordinate with the FDA in the future. We hear brand companies saying, oh there are safety concerns and product liability concerns. That's why we're not giving to the generics. If the FDA is saying we have made as clear as we can that there are no safety concerns here, that argument doesn't work, perhaps that's worth pairing up together.

Product hopping is another area. Here, I think it's not just litigation, but maybe study and reports as well. So product hopping is an area where I have little confidence that the courts are going to get it right. Courts have recognized that a hard switch, in which it pulls the old drug from the market, could be bad because it reduces choice. But they have not recognized that a soft switch also could lead to anti-competitive harm. Even if you leave the old drug on the market, and you put billions of dollars into investing in marketing, and the new drug, and switching your whole prescription base to the new drug, courts are likely to say, as the Walgreens court did, oh, two is better than one, very simplistic, tough to fight against that.

So I've offered a no economic sense framework, which is very conservative in antitrust analysis, but some support from the FTC, showing that perhaps soft switches could also violate antitrust law are worth attention as well. And finally, 6B studies, 6B studies were used to great effect in

the generic space more than a decade ago. They were used with PAEs. And a lot of what we're talking about today, especially later on with PBMs, and rebates, and this whole [INAUDIBLE] process, is such that we don't really know what's going on. With a 6b power, the FTC has a unique ability to get information that we can't otherwise see. And if we think that there are anti-competitive rebates going on, but we don't know, the FTC can help put that on the table.

STEPHEN SCHONDELMEYER: Just a quick comment on that, the product topping issues, and many of the things that come before the courts. The penalties aren't strong enough to deter behavior either. I've been an expert on a number of these cases, and seeing the inside documents, memos. And there are a lot of equivalence of the Ford Pinto memo saying it may cost us to put the gas tank where it is. But we're going to leave it because it costs too much to change it. I've seen companies and people inside companies say this is probably against the law, probably antitrust. We may not get caught. Even if we do, the penalty is not that great. Let's go ahead. The penalties aren't great enough to deter the behavior even if the law is right.

AARON KESSELHEIM: I just also wanted to make the point that I think one of the reasons that the FTC has been such a leader in the pay for delay cases over the years is because the law provides them an opportunity to become aware of the settlements when they happen, and then to be able to act on the ones that they're evaluating. And I think that we need to make sure that that kind of reporting is something that becomes part of the market. And so among the pay for-- the similar kinds of pay for delay cases may be arising among biosimilar similar products and manufacturers.

And the same kinds of reporting needs to go on in those kinds of cases as well so that the FTC can continue to be a leader in this area. I would also point out that one of the things that we can try to do given the inefficiencies in the time and the fact that courts may sometimes get this wrong is to try to keep some of these cases out of the courts. And one of the ways that is available to do that is through this patent trial and appeals board that exists to be able to review brand name companies patents. And in many of these secondary patents that are used to extend market exclusivity and keep generics off the market, maybe once they're reviewed by this administrative body, not hold up and be able to facilitate entry.

And so when brand name companies list their patents with the orange book, we could talk about-- there might be a system where we could have that be formally reviewed by the Patent Trial and Appeals Board. And I would just point out that there is actually a case right now before the Supreme Court that that's reviewing the Patent Trial and Appeals Board, and may ultimately undermine its ability to continue to function. I think we need some with continued vibrancy in that kind of market, in that kind of examination of patents can help prevent a lot of these episodes.

CHIP DAVIS: Two brief things, one on patent settlements and then one on REMs. On patent settlements-- and I would really reaffirm the point that was made earlier, that there's been a significant reduction post activist in certain ways. I think the one thing to keep in mind, though, in terms of the issue, at least from the generic side of the importance of certainty and clarity, and knowing that a late date is not ideal to be able to go to market, but it's better than not ever having knowledge of whatever date you may actually ever be able to go. And with the increase in

certain anti-competitive practices, the uncertainty on the generic side is increasing in terms of whether you'll ever get to market, and if so, when.

And on REMs I think-- and REMs, like abuses, I think the one comment that's important to move forward-- and I applaud the commissioner for his comments earlier today on this-- is ultimately this was 10 years ago. And it was spelled out in statute that the use of REMs or use of REMs programs was not intended for anti-competitive behavior. There is no enforcement mechanism. And that's why we continue to see it. If you consider CMPs, if you consider average CMPs, it will not be a sufficient amount in and of itself to curb that type of behavior.

There are people including the likes of Senator Collins as the chair of the Aging Committee that have been talking publicly about tying future participation into government programs, like Medicare, as a potential hammer to get this type of behavior to stop. And I think if the shenanigans aren't ended, as we've heard earlier today, then I think it only increases the momentum of people looking at that type of thing to create a sufficient incentive to make sure that this type of behavior is not tolerated moving forward.

SUZANNE MUNCK: Terrific. Well, I think we have had a very robust discussion today on considerations that may preclude entry after relevant patents have expired. I'm looking forward to our next panel after the break, which is going to begin to discuss how these market issues can play out as you move along the chain to the consumer. We'll be looking at intermediaries. But before we do that, I'd like to thank our panel for the terrific discussion today, and also let everyone know that we'll take public comments on all of these issues through December 8. So if anyone here feels like they have something that they'd like to say more on this topic, or anyone on the audience, or anyone from the webcast, we encourage you to file public comment. So please join me in thanking everyone. It's been a terrific discussion.

[APPLAUSE]

Great. And we'll--