FEDERAL TRADE COMMISSION

FTC ROUNDTABLE ON FOLLOW-ON BIOLOGIC DRUGS: FRAMEWORK FOR COMPETITION AND CONTINUED INNOVATION

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FEDERAL TRADE COMMISSION

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WELCOMING REMARKS

MR. WROBLEWSKI: I would like to say good morning and welcome to the FTC's roundtable discussion on the competition dynamics of follow-on drug product competition. And I apologize for the long security lines, but hopefully we will stay on schedule.

My name is Michael Wroblewski, and I'm an attorney in the Bureau of Competition here at the FTC. Before we start, I'd like to go over a couple security and housekeeping details.

First, if you would please turn off or place in silent mode any cell phones, BlackBerries, or any other electronic devices.

Second, the restrooms are right outside the double doors to the left, and the cafeteria is upstairs on the seventh floor.

Third, in the unlikely event that the building alarms go off, please proceed calmly and quickly as instructed. If we must leave the building, take the stairway to the right and follow the FTC people to the Sculpture Garden, which is across the intersection of Constitution Avenue and Seventh Street. We need to assemble there.

And last, if you spot any suspicious activity, please alert me and/or the FTC security staff.

To open today's discussion, I'd like to introduce FTC Commissioner Pamela Jones Harbour. Over a year and a half ago, Commissioner Harbour suggested that the FTC engage in a principled and rigorous analysis of competition dynamics in the markets for follow-on biologic drugs. It's because of her leadership and interest in this issue that we've assembled here this morning.

Commissioner Harbour.

COMMISSIONER HARBOUR: Good morning, everyone. I am excited to see so many of you in the audience this early in the morning, and for those of you watching the webcast, I welcome you, also.

I'd like to thank Michael for his kind introduction, but don't let him fool you. He and his team, including Elizabeth Jex, Susan Drennon, and Chris Garmon, deserve the lion's share of the credit for today's workshop, and I am very grateful to them and to the rest of our talented FTC staff for all of their efforts in crafting this event.

But having said that, I will admit that I have played a role in getting us to this point, and I am very proud of that. In early 2007, I accepted an invitation

to speak at a conference on antitrust and intellectual property. I had addressed this same group several years in a row, and in the past, I had spoken about a number of pharma issues, including the Commission's exclusion payment cases. I had also spoken about cases in the computer industry. This time, I was hoping to debut a new and innovative topic; While brainstorming for ideas, I remembered that I had carefully read and outlined the FTC's first IP report from October of 2003, and I had noted that buried in a footnote somewhere the concept of generic biologics had caught my attention, and I made a mental note to return to this topic.

This led to a series of conversations between my office and FTC staff, and we began to explore the subject, and we identified some key competition questions that would need to be addressed if ever there might be an effective, abbreviated approval process for follow-on biologics. I knew I had hit upon an interesting topic, at least one that needed to be developed further. So, in June 2007, I gave a speech entitled, "The Competitive Implications of Generic Biologics."

More recently, this September, I spoke at the Biosimilars 2008 Conference, where I highlighted the FTC's recent submission to the Subcommittee on Health of

the House Committee on Energy and Commerce. As most of you know, the Chairman and ranking member of the Subcommittee had sent a letter and multiple pages of questions to a long list of organizations to solicit views on biosimilars and to inform the development of legislation. I was gratified that the FTC was included on that list.

In my first speech back in June 2007, I had urged the Commission to play an integral role in the dialogue on generic biologics, and when we received the subcommittee's letter, I viewed this outreach from the Hill as a signal that legislators had, indeed, heard the message loud and clear that the Commission had expertise to share and should be treated as an important stakeholder. Now, while some of you may disagree, I am convinced that this is a worthwhile expenditure of Commission resources and exactly the kind of work we should be doing to fulfill our mission to protect the interests of consumers.

As Michael correctly noted, from the beginning, I have advocated for a principled and rigorous analysis of competition dynamics. Our letter to the Subcommittee was the Commission's first formal attempt to provide preliminary thoughts. And looking at the agenda for this workshop, I agree that we now have taken another

great step down that path, and I am very pleased.

As an enforcement agency, we have targeted a great number of resources to the healthcare industry over the years. We review mergers, examine potentially anticompetitive practices, and examine unfair and deceptive advertising claims, just to provide a few examples. In all of these efforts, we recognize that the regulatory structure governing the healthcare industry can and does have a direct impact on how competition works or does not work.

Our goal today is to learn more about how competition is likely to develop in biologics markets, a critical and fast-growing sector of our economy. Once we begin to understand what competition might look like, our intent is to provide technical advice to policymakers who will be faced with different options to structure an abbreviated regulatory pathway for the approval of follow-on biologics. As legislators weigh these options, ideally, we can help them to evaluate the likely competitive effects of their choices.

On behalf of the Federal Trade Commission, we are tremendously grateful to all of the panelists who will contribute their time and their expertise today and to everyone whose written submissions will also add to our knowledge database. Thank you for being part of

this important project, and I hope you enjoy today's event.

(Applause.)

MR. WROBLEWSKI: Thank you.

Before we get going, I'd like to introduce our distinguished participants and panelists for this morning. I'm only going to give their names and their affiliations. More detailed biographical information is in the folders and on the FTC's website.

First, my comoderator for this morning's session is Elizabeth Jex, my colleague in the Bureau of Competition.

Starting on the right-hand side, your left-hand side of the room, we have Alexis Ahlstrom, Director of Avalere Health. To her left is Steve Brugger, Chief Operating Officer of Momenta Pharmaceuticals. Next is Ted Buckley, Director, Economic Policy, at the Biotechnology Industry Organization.

Coming around the corner is Dave Golding, Executive Vice President For Specialty Pharmacy Services at CVS Caremark. Henry Grabowski I'm sure is downstairs in the 50-person line, will be coming up shortly, Professor of Economics at Duke University.

To my left is Paul Heldman, Senior Health Policy Analyst for the Potomac Research Group. To his left is

John Lane, Vice President, Biologics, at Hospira.

Coming around the corner, Mateja Urlep, Head of Global Marketing and Pharmaceuticals for Sandoz International. Rounding out the panel this morning is Dr. Rachel Behrman, Director of the Office of Critical Path Programs, Office of Commissioner, at the U.S. Food and Drug Administration. Thank you all for joining us this morning.

We will have two presentations first to lay a factual foundation for today's discussion. First, we'll hear from FDA's Dr. Rachel Behrman, who will describe how biologic drugs differ from small molecule drugs. Following her will be Paul Heldman of the Potomac Research Group, who will provide an overview of existing competition with follow-on biologic drugs.

Dr. Behrman, you can start.

OPENING REMARKS:

"HOW DO BIOLOGIC DRUGS DIFFER

FROM SMALL DRUG MOLECULE DRUGS?"

DR. BEHRMAN: Thank you, and on behalf of the FDA, thank you for including us in this important meeting, and I would just like to say that I enjoyed the line downstairs, because the FDA always is accused or often is harangued for the pipeline problem or the bottleneck, and I know it's not just us.

So, I was asked to provide an overview of the science and perhaps a little bit of the regulatory paradigm having to do with follow-on biologics, and I put in the word "brief" because in 15 minutes, I obviously can't do that methodically, but I hope to spend most of my time on the foundational issues, the terminology, and some of the concepts, and that may help you in your deliberations, because I think we're not all speaking the same language, and if we're not all speaking the same language, we really will not get to where you want to be, which is have a content conversation.

And, Michael, you mentioned that I would be discussing a little bit the difference between small molecule drugs and biologics. So, right there is part of the problem, because what we really want to talk

about is the difference between drugs and biological products and then talk a little bit about how small molecules may differ from those that are larger and more complex. So, I am going to start with some basic definitions from the Food, Drug and Cosmetic Act.

Articles intended for the use in the diagnosis, cure, mitigation, treatment or prevention of disease in man or other animals; articles intended to affect the structure or function of the body of man or other animals. So, it doesn't have to do with the size or complexity. It's a product that, in fact, is approved under 505.

Then, a biological product is, as defined in Section 351 of the Public Health Service Act, is a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, and so forth. So, it's a very, very specific definition, and you'll notice there it doesn't say anything about coming from a living system, which is often the term that gets thrown around.

Penicillin, if you think about it, is a mold; that's a living system. Insulin and recombinant insulin, so insulin is produced by DNA, their bacteria have been DNA altered for this insulin; it's a living system. So, there are many hormones, there are many

proteins that, in fact, are regulated as drugs. So, when we think about biologics versus drugs, we're really talking about very specific definitions.

Some biologics are defined by their origin, like blood, and some by their use, such as a vaccine, but that is the definition, and I think it's important to keep that in mind, because it will help you think about which products currently have -- a term I will define in a moment -- abbreviated pathways available to them and which do not.

So, as I was mentioning, there's a very wide spectrum of biological products and products in general. Biological products can be thought of as cells, living tissues, vaccines, and so forth, and I think that's, again, a crucial point to keep in mind when thinking about potential economic, competitive implications, which will actually be right for some sort of follow-on process in the near term and which will not. And the bulk of the activity, we believe, will be in the protein world. So, sometimes you hear the term "follow-on proteins" kicked around.

And proteins, for the nonphysicians or nonscientists in the audience, are chains of amino acids, like peptide bonds. That's very, very simple, but they can range from very simple to extremely

complex, and when they're very complex, they are folded; they have things stuck on them; they can unfold again; and then they can aggregate. A lot can happen to a protein. So, it can go from something that I once did and could make in a laboratory to something that is extremely difficult to characterize. And as I said -- and I want to reiterate -- they can be regulated as biological products under the PHS Act or as drugs under the Food, Drug and Cosmetic Act.

And that is just a picture of what I said. There's a primary protein we can all draw, and then it increases in complexity. I'm fond of saying it's like a plate of spaghetti, and you really couldn't easily reproduce it.

Just to give you a sense of size, a statin, everyone is familiar with a statin, that's the size of a statin, a more complex protein. So, there's a huge difference in size and complexity and our ability currently to characterize them.

I'm sorry about this. This I got from a biochemist, who offered more slides, and you'll be pleased to know I declined them.

Okay. So, what is an abbreviated application, because that's really what's at the heart of -- I believe of the legislative battle, and Liz Dickinson, my

colleague and good friend from the Agency, is in the audience, so I'm very careful, surrounded by lawyers, on what I say. One that relies, to at least some extent, on the Agency's conclusions about the safety and effectiveness, that's in the case of a 505, or the safety, purity, and potency, in the case of the PHS, of an approved or unlicensed product. And as we all know, under the PHS Act, there is no explicit pathway. That's just a given. And that's where the legislative activity or interest might be.

And under the Food, Drug and Cosmetic Act, there are two pathways, and just to very briefly review them so it's clear, because the term "biogenerics" and so forth gets tossed around little, but there's 505(j), which is the generic pathway, all right, so that's within a confidence interval of 80 to 120 percent, we believe that those products are the same, the same active ingredient, the same route, same dosage form, in general, and expected to have the same safety and efficacy profile. So, to the extent that we understand it, they are the same. And so they are what I will define as "therapeutic equivalents," so they can be substituted in many jurisdictions.

Then there's 505(b)(2), which is, if you will, a similar pathway, and then in a 505(b)(2), the follow-on

product has depended, to some extent, on information that already existed about another product, about an innovative product, and additional information has been developed. And in general, those are not therapeutic equivalents.

So, pharmaceutical -- and, again, I think these terms are important, because they influence how we, at least at the Agency, think, and these are -- I'm using only terms that are -- that have regulatory meaning to us. I am not using any of the terms that float around that many of us use.

So, "pharmaceutical equivalents" are drug products in identical dosage forms that contain identical amounts of the identical drug ingredient, that deliver identical amounts of the identical active drug ingredient. So, in other words, they are the same, but to get to a therapeutic equivalent, to get to the point where it can be substituted at the pharmacy level, you have to demonstrate bioequivalence, and bioequivalence means essentially that you get the same amount of the active ingredient where it's supposed to be producing the effect that you want, and you get a therapeutic equivalent and you get an AA equivalent evaluation code. So, that's the framework, the (j) versus (b)(2) framework, which leads us to substitutable, which leads

us to an enormous amount of the savings that goes on in the drug world.

Two terms that I think are also important to define, "comparability," and we hear comparability tossed around a lot in terms of would a follow-on be comparable, but for the Agency, we have guidance promulgated in 1996 that talks about comparability, and in our world, that means a comparison by the manufacturer of the product following a change in manufacturing, that we believe they're comparable and, therefore, are close enough. They're not -- again, you can't assure -- we can't assure ourselves they're the same, but they're close enough. We believe they're comparable. And that's the -- that, we believe, is the meaning of comparability. That's how we use the term.

"Follow-on," which we all toss around, and I just thought -- and this is the only informal term I will define -- refers to products intended to be sufficiently similar to an approved product to permit the applicant and the agency to rely to some extent on that information and then add additional information that would be necessary to assure the safety and effectiveness or safety, purity, and potency of the product.

So, where does that leave us? Some things that

we think about when we -- and we thought about this a lot over the last few years, not surprisingly -- when we think about what these applications might look like, and I do want to emphasize that we know how to review applications. We get asked that a lot. Are you, the Agency, ready to review applications? This is something we know. Every application we now look at has some uncertainty associated with it. We learn how to balance that uncertainty.

But if we were to work through what we would need to know, we would first have to decide if the product was sufficiently similar to the licensed product to allow us to rely to some extent on existing information. That's a threshold, getting in the door. And then, as our colleagues in OCC remind us, do we have access? Do we have legal access to those data? And that's a big question.

Then, we go back to the science. That's the policy, and now going back to the science, what additional information would we need to support the claim of safe, pure, and potent, because again, we're talking about a licensure under the PHS Act.

And finally -- and this, I think, for those that are thinking about the economic potential benefits -- are there any data provided that would support the

safety and efficacy of -- and there I used in quotes -- "switching"? In other words, can one go back and forth between these compounds? And that's very tricky in the protein world and in the biologics world, in general, because these compounds have a much higher potential to create an immunogenic response that can diminish efficacy, that can also, obviously, reduce the safety. So, in our minds, that would be a separate data set, proof that, in fact, you could go back and forth. And we believe that unless there are data that one is safe going back and forth, the physician would have to make the decision about which product and whether, if ever, to, in fact, change that product.

So, just sort of summing up, first of all, just put on the table that we believe, with current science, current technology, in most cases, at this point in time, it will be impossible to establish, in the biological world, because of complexity, that the active ingredients are identical, as we do now in the (j) world. And in terms of the -- we get asked not infrequently about the potential impact on the Agency and what the reviews might look like and so forth and the time lines, how quickly could these molecules be brought out. We believe that the more complex the product is, the more difficult and time-consuming it is

to manufacture. So, that speaks to the time line for getting it out, and also perhaps speaks to the interest of how many companies -- and I'm surrounded by companies, actually -- how many companies are going to be lining up at the door to do this, and that's just that we think they're harder to make, and so there's more risk involved in trying to bring one out.

Then, as I say, concerns about immunogenicity will likely need to be addressed in any and every application. And then finally, what I said before, that the review of any application, be it drug, be it biological product, makes an assessment of what is in the best interest of the public given the available information. There will always be uncertainty. There is uncertainty about the simplest small molecule drugs. We have seen repeatedly, for example, in the antibiotic world. So, that assessment, that judgment, is not new to us.

And finally, I would like to leave you with a thought that some of us put into a paper we published as scientists a year or two ago in Nature Drug Discovery. We talked about historically what had happened, and as a physician, I would like to make the point that we are not just obviously talking about the economics and the legal ability to develop or not develop a product. We,

as a society, are facing -- and I made a joke about the line -- but we are facing a crisis in the availability of innovative medical products. And any resources we devote to developing information that already exists or researchers do not use to answer the pressing questions that face this society medically and in terms of development of medical products, and there's a huge ethical problem with exposing patients to studies that don't have to be conducted.

So, what we said was, "The Agency has a long-standing policy of permitting appropriate reliance on what is already known about a drug, thereby saving time and resources...and avoiding ethical concerns associated with unnecessary duplication of...human testing."

With that, I'll stop.

PANEL ONE:

LIKELY MARKET EFFECTS OF FOLLOW-ON BIOLOGIC (FOB) DRUG COMPETITION

MR. WROBLEWSKI: Thank you.

As Rachel's presentation made clear, there's a lot of uncertainty as to what various terms mean when we talk about follow-on biologic drugs. For the purposes of today's discussion and today's discussion only, we're defining three terms that we hope the panelists will use and that we'll ask people to be clear about when we're talking about these, and these don't necessarily tie exactly with what Rachel said, but it's looking at it from a different angle.

The term "biosimilar drug product," we're going to mean -- refers to a product that is comparable or highly similar to the referenced product. The term "biogeneric," on the other hand, refers to a drug that is therapeutically equivalent, interchangeable, and substitutable at the pharmacy or the point-of-use level with the referenced product. A follow-on biologic includes both biosimilar and biogeneric drug products. And we understand that the FDA has not defined the terms biosimilar, biogeneric, or interchangeability.

And with that terminology in mind, I am going to turn to Paul Heldman to provide an overview of biologic

drug markets.

MR. HELDMAN: Thank you, Michael, and thanks to Elizabeth and the agency for having me here. I am going to go to the podium to work off the nervous tension, and I'm just wondering where Dr. Behrman was when I was taking freshman biology. She makes it all so clear.

It's an honor to present today. I'm with a new group called Potomac Research after spending four years at Citigroup, where I was able to join my colleagues in doing a lot of research on the potential market for follow-on biologics, and while I benefited from that effort, what I'm talking about today is fresh and unrelated to the work that I did at Citi.

As you know, the market for biogenerics is in its infancy. The European Union from 2004 to 2006 created the legal framework and the guidances for an abbreviated pathway to win approval of a similar version of brand name biotech drugs, and today, E.U. country biosimilar approvals are limited to versions of erythropoiesis-stimulating agents, or ESAs, or EPO, as they are known, and human growth hormone.

In the U.S., Novartis, a Sandoz unit, is the only company to date to win FDA approval using abbreviated clinical data of a follow-on biotech drug using the 505(b)(2) pathway that Dr. Behrman mentioned.

In this case, a similar version of Genotropin made by Pfizer is what Sandoz used as the reference product, and it won marketing approval in May '06 and began selling it in the U.S. in January '07. The first prescriptions, based on IMS data, were in March of 2007.

My presentation has three goals: To use what data we have to date on the sales of follow-on products to suggest how the U.S. biotech market might be affected if Congress and President Obama enact follow-on biologics legislation into law; to highlight key differences between the market for traditional chemical medicines and the biologics market; and to discuss three areas that could act as impediments to rapid share gains for follow-on biologic drugs.

So, the short marketing history of Sandoz's Omnitrope shows some potential for follow-on versions of biotech drugs, and I think it's interesting to note there, early on, there's a spike in monthly prescriptions of the drug. The data is inconsistent, and it's been noted to me by stakeholders at companies that are dealing in this market that the IMS data is imperfect, but it looks to me, from what I've seen, that the greatest discounts in the marketplace were offered during that period where you see this large spike in sales before they dropped off a little bit.

So far, however, the market for follow-on biologics is limited, and for Sandoz's Omnitrope, it still has a very small market share. Some of that may be because the original version of Omnitrope had a delivery mechanism that was inferior to the branded competitors, and that's changed with the introduction of a pen liquid cartridge version of the drug, with FDA approvals at different doses in March and I think September of this year. And that improvement may show up later this year or in '09 in the sales numbers.

The limited market to date may also be associated with saturated market with more than half a dozen other products, and with that many choices, there might be some resistance to use of an alternative that can be categorized as highly similar to Genotropin but not substitutable, and this gets to what the FDA was just talking about as a potential impediment to growth of this market.

In addition, 15 to 18 percent of the market for human growth hormone is Medicaid for the poor, and I'm told that there may be some additional rebates to the states in those markets that might have enabled the innovator companies to maintain their market share, and that wouldn't necessarily show up in the data. So, that might allow them to stay on state-preferred drug lists

and maintain market share.

If you look at the wholesale acquisition cost -- and it's important to note that that's before any discounts in the marketplace or rebates -- you can see that the price of the branded human growth hormone products continued to rise even after the introduction of Omnitrope. As I said, the wholesale acquisition cost doesn't take into account discounts offered in the marketplace by manufacturers, and there might be some discounting going on in the market to hold on to market share, especially in Medicaid.

But I think this pricing trend, along with the market share data, shows the challenge of acceptance in the marketplace that makers of follow-on biologics will face, and until they convince regulators that their products should be considered interchangeable with the branded or reference product -- and the scientific challenges were just mentioned and I'm sure we will go into greater detail of that during the course of the morning and the afternoon.

Regardless, there is some success in the marketplace if you characterize success in terms of discounts. I would say that the discounts are significant, and yet they're significantly below the 80 percent discounts on drug prices that take place with

traditional small molecule drugs once they face competition from multiple generics. Here again, I think one of the problems is the question of substitutability of the product; however, with the caveat that these are early days in the market. So, it takes time for those kinds of discounts to evolve.

We find some of the same preliminary lessons with the ESAs in Europe. This slide is a little bit distorted in the sense that it shows market share for these products in the G7 European Union countries, when the biosimilars are only on the market in the E.U. countries of Germany and the UK. So, you see a very low market share there.

It's a little bit higher if you just take a look at Germany. There, you can see that the market penetration, based on about a year of biosimilar sales, is modest, but it's a little bit higher. It's probably about 10 percent market penetration if you look in terms of sales; if you look at biosimilars, it's all folded into the line for Binocrit -- I hope I'm pronouncing that correctly -- okay -- and actually, I've looked at some prescription dispense numbers as well, and you're talking about a 10 percent market share or a little bit above to date.

I think it's clear, even though you're talking

about smaller market shares than what you will get in the traditional drug market, that this is a competitive market, and the introduction of follow-on biologics was a contributor to that in the ESA market from what data I could gather. Amgen cut its price for its second generation ESA, Aranesp, in early 2008 to try to maintain market share, I assume, and first generation brand name makers of EPO reduced their prices about 15 percent, and biosimilars are sold at a 25 percent discount to the innovator product on top of that. So, I think those are significant discounts, especially when you consider the expense of biotech products.

This slide is meant to get to a key barrier to maintaining market share. I'm really just focusing on the second bullet, that until the science evolves sufficiently to satisfy regulators that a follow-on can be declared interchangeable with a branded product, the take-up for the lower cost product will be hindered. And we go back and we think about passage of the landmark 1984 Waxman-Hatch law as creating the regulatory framework for growth of the generic drug industry, but many states had laid the groundwork already, and there was, I think, 19 percent market penetration in the generic drug market.

States had passed laws allowing pharmacies to

substitute a generic for the branded version, and I think that was important for growth of the generic drug market, and I'm not sure that those laws would apply to follow-on biologics, especially because most drugs are delivered through a physician's office; most biotech drugs are still delivered through a physician's office or in a hospital setting.

So, another potential impediment that actually exists in the small molecule medicine market as well is the question of a second generation product being on the market and either being perceived as or actually being better than the first generation product and thus maintaining market share. Amgen still commands a premium price to first generation ESAs, according to Amgen, and based on the data that I've seen, it still has a premium in Germany, although it's narrower than the 15 to 30 percent in the European Union, and it remains a leader in sales, with less market share erosion in Germany than first generation ESAs.

Now, I would point out that even though second generation products, such as Aranesp, may allow the innovator to preserve market share, there's an interesting twist that I'd love to hear the scientists talk about in the follow-on biologics market, which is that it's conceivable that you could develop a follow-on

biologic that has a better side effect profile or is more effective than the first generation product or maybe even the second generation product. So, you could develop a product that was lower development cost and come up with a better product, potentially.

Now, the future of follow-on biologic products doesn't just depend on the science. It also depends on reimbursement and coverage policies by payers, especially the Medicare product. Almost two-thirds of biotech drugs are delivered through a doctor's office. Medicare actually spends about $10 billion a year on these drugs, and a physician's office spends another couple billion dollars a year for hospitals for delivery of these products in an outpatient setting and another couple billion dollars in a dialysis setting, and payment policies in this area are adopted by commercial insurers.

The current reimbursement formula under Medicare provides a financial incentive for physicians and hospitals, when using the drugs in an outpatient setting, to use the higher cost drugs, the higher cost drug in a category. That's because Medicare reimburses at the average sales price plus a 6 percent markup.

In addition, current law requires Medicare to give new single-source drugs that are not the same as

other products -- the definition of single-source -- on the market a separate payment code, and thus, a follow-on biologic that the FDA doesn't deem interchangeable would get a separate billing code, presumably, although interestingly, I think human growth hormone is an exception to that, and it would be interesting to see how Medicare interprets the law going forward.

So, if the follow-on, assuming that it has a separate payment code, is sold at a discount to the original brand name product, the physician actually would have a financial incentive to bill for the more expensive drug or, at the very least, less of an incentive to use the follow-on biologic.

It also remains to be seen how much authority Medicare will exercise and will be able to use to use the coverage process to steer patients towards a follow-on biologic. I think that that gets into issues of medical necessity, and I can envision the litigation that probably is going to come with that.

Actually, though, Congress has already taken some steps that will reduce the cost of biotech drugs to taxpayers, and that actually creates an incentive for the use of follow-on biologics. Congress, last summer, overrode President Bush's veto and passed Medicare

legislation that will set, beginning in 2011, a single bundled Medicare payment for dialysis care, which is actually a policy within the legislation that the Administration supported.

If a lower cost follow-on biologic comes on the market for Epogen, used in a nephrology setting, the dialysis provider will be incentivised, under the bundled payment system, to use the less expensive product. So, in that area, one of the highest cost products in the Medicare program, there's already a policy in place that would encourage the use of follow-on biologics.

And another policy change by the Administration might, as a result of any sort of downward pressure on Epogen reimbursement, drive down reimbursement for Procrit, the same drug licensed to a different company, in an oncology setting, because the reimbursement rate, the ASPs, are blended, and as a result, if the average sales price for Epogen goes down, so does the average reimbursement for both products under the Medicare system.

So, what do we know from our experience so far? There is a market with, I would argue, significant discounts for biosimilars, but several obstacles remain to their gaining the market share and driving down

prices to the level that we see in traditional small molecule drugs. Some of that can be overcome if the Federal Government and the states, but especially the Federal Government, in addition to creating an abbreviated pathway for approval of follow-on biologics, change reimbursement incentives and create a process for allowing biogeneric substitution.

And I recognize that there are safety arguments on the other side of this issue that I'm not going to pass judgment on, and I'm sure we'll hear about later. And to that point, it also requires scientific advances and evidence on the part of the biogeneric industry that these products are substitutable.

So, thank you very much.

(Applause.)

MR. WROBLEWSKI: Thank you, Paul.

You packed a lot into that presentation that we're going to explore in more detail throughout the day.

The objectives of this first panel are really two: One, to discuss current market experience with follow-on biologics; and second, to identify the differences in likely market effects caused by biosimilar entry compared to potential biogeneric entry.

The panels today are going to be moderated

discussions. The moderators will pose a question and ask a specific panelist to start off with an answer. If another participant would like to add to that discussion on the same point, please just turn your name card on its side, and we'll be sure to call on you if time permits.

The one other thing is, these microphones are always on. So, please, after you're finished, lift your microphone up.

And one last thing, many of the questions in this first panel will focus on eliciting information from the FOBs' -- follow-on biologics' -- viewpoint. The second panel this morning will focus more on the innovators' point of view.

So, with that background, the first issue that we would like to get a discussion about is following up on some of the things that Paul brought up in terms of the two markets that he examined, both the HGH market in the U.S. and Europe and the ESA market in Europe. And I'd like to ask Mateja and John, who are both competitors in those markets, to address two issues.

First, on what reference product data did you rely on to obtain your authorizations in those markets? And second, have you engaged in primary marketing of your product?

So, I'll let John or Mateja, whoever would like to go first.

MS. URLEP: Thank you very much, in the name of Sandoz, for inviting us here. We are happy to share our experience as a pioneer in this follow-on biosimilars arena.

What kind of data did we rely on? Well, actually, we did rely on the agencies, the FDA or the EMEA, to approve products which are safe, potent, and pure, but the data we generated ourselves on our product as well as on reference to show comparability and high similarity and to gain the approval on our products, which were shown to be as effective and safe and of the required quality. So, there were no data which we would rely on that would be accessible for us from the reference product. We created our own data set.

On the primary marketing, in U.S., we have one follow-on protein product on the market, which is Omnitrope, and we do not extensively advertise this product, whereas in the European Union, it is a different situation. We do primary marketing, and we do invest into, let's say, having a booth at professional meetings; calling on the physicians. So, we do have the calls and we do produce marketing materials and we do also advertise in the professional journals.

MR. WROBLEWSKI: Thank you.

John?

MR. LANE: Yes, thank you. I just want to make sure everyone knows who Hospira is. I know I have got a bio here, but many of you are probably not familiar with the company.

Hospira is a global healthcare company that has businesses in specialty pharmaceuticals and medication delivery devices. We're the worldwide letter in generic injectable drugs. We're also the only U.S. company that has launched biosimilar EPO in Europe.

So, having said that, a couple of things. Our reference product that we used to show comparability was Epoetin alfa. It was Eprex. We went through what the Agency would call an abbreviated pathway, where we had to run three Phase III pivotal trials: two on the renal side to demonstrate therapeutic equivalence; one on the oncology side to show safety. And then we had the individuals on the therapeutic equivalency side on the renal go through a full year for safety data as well. So, all in all, we tested roughly a thousand patients through our product.

The other comment regarding marketing, we are engaged, like our competitors, in very aggressive marketing, because the innovators, frankly, are very

aggressive in terms of combating messages against us. They are putting messages out there that we're not safe, not effective, inadequate pharmacovigilance, and we have had to combat that fairly aggressively.

And one of the ways we do that is we hold up data like this (indicating), which are manuscripts of two key, pivotal Phase III trials, which demonstrate that we are therapeutically equivalent, and data like this can do a lot to diminish a lot of the comments that are being spread around to clinicians, et cetera, about the potential inferiority of biosimilars.

If I could add just one other comment on the slide that Paul put up, I think it's important to note, in Germany, you mentioned that there was about a 10 percent market share on sales dollars. If you look in Germany, biosimilars, on a unit basis, have actually captured 23 percent of the first gen market, 23 percent through August, and if you also take into effect that Aranesp sales, prices come down 10-15 percent, and you equate that to the U.S. market, where you have got a $4 billion first gen EPO market and a $2 billion second gen Aranesp market, you would drive savings of well over a half a billion dollars. So, we have a different perspective in terms of how well biosimilars are doing and actually are very happy about the experience with

EPO.

MR. WROBLEWSKI: Let me ask one quick follow-up, John. What actual data did you rely on from the innovator product that you didn't have to do yourself --

MR. LANE: Well, I mean, from --

MR. WROBLEWSKI: -- in terms of clinical testing?

MR. LANE: -- specific data?

MR. WROBLEWSKI: Or in terms of just classification of the type of data.

MR. LANE: Basically, what they had us do --

MR. WROBLEWSKI: What didn't you have to do?

MR. LANE: What we didn't have to do? In other words, we didn't have to do Phase II results. We had to do Phase I; we had to do preclinical studies; and we had to do pivotal Phase III studies. Phase III is the biggest area where we didn't have to do work on.

MR. WROBLEWSKI: Is that similar?

MS. URLEP: It is exactly the same. That was the only data we didn't have to generate to show comparability, because with Phase I, we had showed the comparability already, so that the PK/PD data showed that we didn't have to go into dose-defining clinical trials, which is Phase II.

MR. WROBLEWSKI: Okay.

Rachel, you wanted to add something.

DR. BEHRMAN: I did. Thank you.

Omnitrope is a terrific example, because it's detailed in excruciating detail in a citizen's petition response, which is everything you ever want to know about 505(b)(2)s, and it's worth mentioning it's not the first follow-on protein approved by the FDA. It's the first follow-on human growth hormone. And replacement therapies, such as growth hormones, some things that we know a lot about, are different than things where we don't understand the mechanism as well.

But I think for Omnitrope, an important point is that while the clinical data were developed with a pediatric indication, the clinical data were not developed for the adult indication. The Agency relied on existing information. So, a big chunk of the approval was, in fact, not de novo data.

MR. WROBLEWSKI: Okay.

Steve, you wanted to add something, and I wanted to ask you, are these the type of things that you would be saving as well as you develop your follow-on products?

MR. BRUGGER: Yeah. Actually, my comment was, I just wanted to clarify, just for the completeness of the discussion, in Europe, EMEA does not have any real --

doesn't take any authority to determine interchangeability. So, I think Mateja and John could probably comment on how each country in Europe determines whether or not these products should be substituted, and if so, how.

I think the one challenge we have to keep in mind is that in the U.S., without an interchangeability status, the physicians will have to rely on these extensive data sets that Mateja and John described and their own personal experience, and I think as we look forward, that will be one of the issues in the U.S. that will initially blunt that market share, because physicians will have to rely on the product since it will be declared as not the same.

MR. WROBLEWSKI: Right. Thank you.

Professor Grabowski -- and thank you for joining us. We apologize for the line downstairs this morning.

DR. GRABOWSKI: I just wanted to ask John and Mateja to give some feel for the cost of doing these studies. That may be, you know, competitive kinds of information, but in sort of your small molecules, we're generally talking a few million dollars to kind of get on the market, and for an innovator, when you figure in probability of success and discovery and all, we're talking hundreds of millions, and some generics, some I

have heard the costs are in the $10 to $20 million, but, you know, I don't know if you could give us some feel for the barrier that might exist, if you want to characterize that way, or the cost to sort of doing these tests with a reference product.

MR. LANE: No, that's a fair question. Thanks, Professor.

With regard to our EPO product, we have a partner who actually did all the clinical work. So, we didn't do those trials. So, I can't comment on specific costs for that program.

But in a more general sense, I would say for the less complex proteins that we're looking at, you could expect anywhere between, maybe, $30 and $50 million, and for the more complex proteins, it's not inconceivable that you could approach $75 to $100 million if you have to do full development. And a lot of that's going to be driven by what are the requirements that the Agency puts in place, so...

MS. URLEP: Well, basically, the extent of the clinical trials for a similar biological additional product, as biosimilars are defined in the European Union, is defined by the guidelines, which are product- or class-specific, and, therefore, this was the guideline for the company, for the sponsor to do the

development work.

But based on the fact that the developments have started far prior to the first guidelines being accepted and published and enforced, I have to say that our experience was that we have even overdone and did a lot more than was finally requested and required. So, the challenge here was even higher for the pioneer, for the first one, to do more than finally the agency would require.

And if I may say, the European Agency has concluded -- and it's publicly available -- for both products, which are already approved from Sandoz's side, for Epoetin alfa as well as Somatropin, that the active ingredient, active substance, is the same as that for the reference. So, this is a conclusion of the EMEA.

MR. WROBLEWSKI: Thank you.

I'm going to change subjects just a little bit. Are the price discounts and the market share capture that Paul mentioned for the products that he examined, are they predictive of what the U.S. markets will look like?

And I can either turn to Professor Grabowski or, Alexis, if you would like to add in some thoughts as well.

DR. GRABOWSKI: I'll just make a brief comment.

I think you have to look at this as an evolutionary process in that initially, for the reasons that were mentioned earlier, there may be a slower uptake, but over time, given all the changes that we can expect in the healthcare system, wider coverage and all the cost savings are going to be a kind of key factor, and we are going to see evolutionary changes in the reimbursement system and otherwise. And so I would expect the uptake to kind of increase significantly as we gain experience.

You just have to look back even to small molecules. I studied that. In the first decade, there wasn't the kind of rapid substitution that occurs now, where an innovator can lose 90 percent of the market within a few months if it's a big molecule drug. The erosions were much slower in the eighties until people even got comfortable with A-B rated drugs that the FDA said were interchangeable. So, I think you have got to keep in mind the evolutionary characteristics of the market.

MR. WROBLEWSKI: Sure. Thank you.

MS. AHLSTROM: I think there are three major differences that I would talk about --

MR. WROBLEWSKI: If you can turn it towards you.

MS. AHLSTROM: There are three major differences

I would highlight relative to the small molecule market that Dr. Grabowski was talking about. I think first is that in the follow-on biologics or the biosimilars, you're going to have products that in the near term are not interchangeable, and so even though today people are used to substituting the lower cost product, I don't think that we will see that kind of uptake any time in the near future.

You know, Omnitrope is probably not the best example for us to look at when we think about, you know, uptake. It is entering a very crowded market. First year, like Paul said, it didn't have the same kind of mechanism of action or it had a different delivery mechanism than the products that it was competing against.

Omnitrope also has a really interesting background, because we looked at the formularies for Omnitrope and all the human growth hormones in the United States, and we found that Omnitrope, in its first year, was actually only covered about a quarter of the time. So, I think that there is an access issue right now for patients with Omnitrope. That may go away over time, but I think that while the plans and the PBMs immediately cover and immediately put in utilization management tools to get people to switch from the brand

to the generic, you know, on the small molecule side, they haven't been that immediate on the biologic side.

We've also looked at formularies for products that, you know, have multiple products within a class, like the rheumatoid arthritis and multiple sclerosis drugs, where clearly a plan or PBM could find a particular product that would be the lowest cost product for itself and for the consumer. And they are not really differentiating products. They're not picking a preferred biologic within a class and making other biologics in that class be less preferred. They're not really, at this time, driving share toward the cheapest biologic, and I think that's because the biologics are, you know, therapeutic alternatives to each other.

They're not saying everybody must go to one, like they're doing on the -- you know, like -- and even there's more therapeutic substitution, I think, on the small molecule side. There's one preferred statin, you know, Simvastatin; then there is everything else is, you know, third or fourth tier. And I think that's really because of the science, and I think the science will drive the biologics, you know, substitution -- or, sorry, uptake in the near term.

So, I don't really see, in the near term, any sense that we'll get towards, you know, the generic

substitution rate of 90 percent or whatever it is for some of the small molecule products.

MR. WROBLEWSKI: Thanks.

Rachel, did you want to add something?

DR. BEHRMAN: Yeah. In case I didn't make it clear in my remarks, I think that whether or not something can be substituted -- it's not a question of whether the company makes the effort to do it. It may not be possible, in contrast to a small molecule. So, we -- I think some of the discussion seems to me focusing a little bit on if the company made the effort, they might make it to substitution, and they may, in fact, never make it to the point where they are substituted.

MR. WROBLEWSKI: Right. Thank you.

John?

MR. LANE: Yeah, one other comment.

I guess Hospira believes that the opportunity in the U.S. could be certainly greater than what we're seeing with the EPO experience in Germany. If you think about it, Germany is kind of the proving ground. It's the first regulated market where we're starting to see this. There's a lot of trepidation among clinicians, and over time, clinicians are becoming more comfortable with biosimilars.

You know, a lot of these products aren't going to launch in the U.S. for several years. So, when they do launch, there's going to be a wealth of experience and data that we've garnered in Europe. And, again, if you think about Germany, in just about a year's time, the biosimilars -- two biosimilar molecules have captured 23 market share of the first gen, which is the product that they demonstrated biosimilarity to. That's significant.

So, Hospira feels that there's a much greater opportunity, given time, when these launch, there will be probably more competitors, and even in a market where substitution does not exist automatically, at least for the early years, there's a lot of savings that could be generated without that.

MR. WROBLEWSKI: Thank you.

Let me change -- and, Ted, I am actually going to address this question to you in terms of -- and it's probably a follow-on to what John just mentioned, is what are the factors that are going to affect the uptake or the market acceptance of biosimilars, other than what we've been talking about already, which has been the kind of interchangeability?

Are there patient population characteristics or other characteristics that would make this different

than -- that would affect the uptake?

DR. BUCKLEY: Well, first of all, just a couple of points.

There has been this question around therapeutic equivalence and interchangeability. In Europe, to date, 14 countries have ruled that these products are not interchangeable, and I think that that point needs to be made and brought out.

Second of all, really, it's going to be the decision of the physician and the patient as to whether or not a drug will be substituted for a therapy that they may already be on or a therapy that they may be considering taking.

In addition, you think about where health insurance was back in 1984 when Hatch-Waxman was passed. Formularies weren't very restrictive. Tiered formularies were almost unheard of. And so, the generic market, as Henry pointed out, evolved slowly. You know, fast-forward 24 years, you've got restrictive formularies that drive patient populations to certain preferred drugs; you've got tiered formularies, which also give patients incentives to take certain drugs; and so the health insurance market has also evolved to this new -- what's no longer a new landscape of generic drugs.

In the case of a biologic, you know, biologics are typically a -- you know, dose per dose are more expensive than most small molecules. If I were sitting in the insurer's shoes right now, I would be thinking, okay, my marginal benefit and the advantage of switching a person or steering a patient towards a biosimilar drug is potentially much greater than steering one patient towards a generic drug. So, how can I design an insurance mechanism that helps to encourage this sort of switching?

MR. WROBLEWSKI: Thank you.

Thanks, Dave. I was actually going to turn to you next for a comment, and what strategies do you anticipate using as a PBM and retail pharmacy?

MR. GOLDING: First of all, I represent the payer side, so we have a lot of clients and payers who are paying for these very expensive medications, and on the other side, I also run a network of specialty pharmacies that run an enormous amount of these primarily branded biologics through it, so I'm both the payer side, and then the back end, depending on how all the regulations come out, I will be the administrator, so to speak, of executing this very important issue for me and for the company.

But, the clients, I can tell you, certainly over

the past 18 months, have a pretty enormous amount of focus and I spent most of my time talking to them about this trend, which is two and a half to 3X what their overall trend is. So, we've got their attention, and they are asking me and asking us around the table and beyond what they can do.

So, we will see them get much more aggressive as it relates to what their temperament is going to be versus what it has been as it relates to taking some tactics, which I agree have been relatively modest in the past, and we, as the PBM, have experimented with some biologic, you know, tier two, tier three, but looking at a $25,000-a-year drug and a $50 difference between copays is just not -- the benefit is not going to do it.

So, unlike the small molecules where as soon as a generic comes out, it trips it to a tier one typically, that is what's driving all the activity, and all the switching overnight should interchangeability not be here in whole or in part, it will act, at least in my opinion, more like a preferred branded product. So, me as the pharmacy and us as a PBM will need to put a lot more tactics in place in order to motivate.

I believe what payers are going to be looking to do and are looking to do today is they are going to be

looking to pay for an outcome. So, they are not going to get so tied up in what the drug is or are they equivalent or are they similar. I don't think that's the way that they're starting to look at it. They're saying, what is the outcome that we're willing to pay for?

And many of them -- and this is a very personal preference from a health plan perspective -- will say, and we're not going to pay for convenience. So, I think that's where Omnitrope gets into a very interesting discussion, CVS Caremark is a very large dispenser of growth hormone, I believe some payers in the near term are going to say, if there's a short-stature individual, I am obligated and willing to pay for that growth, but not necessarily all the convenience and, therefore, the cost that some of these alternative products are premium-priced at today. And they're the payer, and I can understand that. So, we as a PBM and ultimately the advocate of the payer and dispenser will be looking to put that forth.

I also think you'll see some different tiering, depending on how we ultimately work through this, that may actually create bigger spreads within certain products. Maybe it's stepped therapy. You need to start here, and if this doesn't work clinically, we will

allow exception processes in order for you to submit those exceptions in order to get alternate products that clinically are comparable, theoretically, in the masses, although don't seem to work effectively for you as an individual.

MR. WROBLEWSKI: Okay, thank you.

Ted, you wanted to add something, and then, Alexis, we will turn to you.

DR. BUCKLEY: Sure. Just quickly, we seem to be dancing or making this assumption that -- and I want to state, we don't think interchangeability is anywhere in the near term possible based on Dr. Behrman's comments, based on what the E.U. countries have said, et cetera, but there seems to be this assumption that if it were possible, all of a sudden, one generates much more savings, and I'm not sure that that's actually a true assumption, because if one were rated as a perfect substitute, you don't have to go out to market. You can, in fact, just shadow-price the reference product, say, with a 10 percent discount, and, you know, how the innovator responds to that is unclear.

Maybe they keep the price or maybe they match the 10 percent discount and you wind up splitting the market and you wind up with about 10 percent savings in the market, versus what the CBO has modeled, where after

four years, you have 16 percent savings overall with a 40 percent market share or 40 percent price reduction and a 35 percent market share, because if you're not rated as interchangeable, you have to drop your price more to attract the market.

And so in order to do this -- and it really is not -- if you look even in the generic context, it's not so much the A-B rating that drops the price, but rather, the number of entrants to the generic marketplace. So, with typical generic drugs, within a year, you see eight entrants, a price discount of around 60 percent, and a market share gain of about 80 percent.

But if you look at a subsection of generic drugs, what we'll call more complex generic drugs, those that are prescribed by specialists, those that have a narrow therapeutic index, those that have a black box warning, you find, after a year, very few entrants, only three; price discount, instead of almost 60 percent, a price discount around 35 percent; market share, instead of 80 percent, market share around 58 percent.

And so you see that it's the number of entrants that seems to be driving this price competition, not necessarily this interchangeable rating. And so I think that's something to really keep in mind going forward.

MR. WROBLEWSKI: And do you anticipate the

number of entrants to be fewer?

DR. BUCKLEY: The number of entrants will certainly be fewer. There are technological know-how, they alluded to the price of the clinical trials to deliver this, the length of approval process, the likelihood of a successful application, you know, and you just go down the list, and you start to see that the number of players that can submit a successful application for this is much smaller.

MR. WROBLEWSKI: Okay.

Alexis?

MS. AHLSTROM: Thanks. One thing I would add to what Ted just said is that in addition to all the sort of barriers you might see in terms of the number of entrants, one of the things is the market share that the follow-on biologics will be going after, and I think there are some key products, like the ESA market, where you might see more entrants than products where the class itself does not have a lot of revenue, and so that a biosimilar would not be able to -- because of all of the costs of manufacturing and development and the potentially steeper regulatory approval process, that there would not be follow-on biologics in certain classes because they wouldn't be able to, you know, break even and make a profit.

MR. WROBLEWSKI: Okay. Thank you.

Steve, you wanted to add a point.

MR. BRUGGER: Yeah. I guess I take a slightly different position than Ted on the interchangeability status. I think if the FDA, at some point in the future -- and we certainly hope that's the case -- designates one of these biologics as interchangeable, I think that has a huge impact on the kind of uptake it would have, because it would take physicians somewhat out of the decision-making that they are certainly are in with biosimilars.

I guess I should comment a little bit on Momenta as a company, because we are somewhat atypical in this debate. We've developed an innovative analytical approach to these complex molecules, both in better understanding the product, but also a deeper understanding of the manufacturing process. We actually have two complex mixture of products, Lovenox and Copaxil, that we actually have 505(j) or ANDA applications currently under review, and the reason we are so passionate about the interchangeability language is, because that pathway was open to us for these two products, it actually allowed us to raise capital as a young company and invest in this.

So, I think we have to not lose sight of the

importance of that legislative language for interchangeability, not just for the market advantage, but the innovation that will come from other companies like ourselves.

MR. WROBLEWSKI: Thank you.

Mateja, and then, John, I'll turn to you.

MS. URLEP: I would also say to Steve that we do believe that interchangeability definitely would ensure that the full economic benefit and the patient access benefit for the follow-ones could be exercised, and I have to say that European countries did not take a position on interchangeability, but on substitution, and there are a few of the countries, and one of them being France, has only a temporary ban on substitution, for two years, and then they will assess this once again.

So, therefore, there is no resolution on interchangeability, but on the substitution on the pharmacy level, whereas there is some examples in Germany where they have encouraged -- the payers have encouraged pharmacists to interchange and switch products on the pharmacy level; also biologics. This is our experience from the market.

About the savings and about the discounts, where at the moment I have to say the same as John has said, we have to overcome the barriers that were imposed on us

by the originators saying that the follow-on biologics or biosimilars, as they are called in Europe, could be substandard and that there could be some potential safety issues and pharmacovigilance issues with them. We have to invest into primary marketing to overcome this with our data, which we created during the development programs. And I would say that with the different market access, the discounts could be higher.

MR. WROBLEWSKI: Okay, thank you.

John?

MR. LANE: Yeah. The only thing Hospira would add to this is, with regard to interchangeability, no longer would a company have to spend an excessive amount of money into a sales force, proprietary marketing campaign, et cetera, and they would be able to reduce their price potentially quite considerably and still maintain the same level of profitability for the business. So, I do think there's a significant impact there.

To talk upon with my colleague here in terms of France, we have seen some of the nephrology associations in France say they could consider viewing EPO as being interchangeability if they saw two to three years of experience on the market. So, I have a feeling, in a short period of time, you are going to start seeing some

of those activities take place.

The other thing I would make a comment on, when we did one of our trials to demonstrate the therapeutic equivalence for Retacrit, Hospira, working with our partner, Stada, did a crossover study where we had a run-in of the innovator product, Eprex. Both products were switched, so then they switched patients to the other product for a period of three months, switched them back to the original product, and then followed them up for a full year.

So, I'm not saying this may meet the FDA's standards of what it would take to prove interchangeability, but we have done studies in some form or fashion at Hospira and with our partners to show that the switching of products have shown no safety issues and have shown therapeutic equivalence. So, this kind of work can be done. We just leave it up to the FDA to tell us what their requirements will ultimately be.

MR. WROBLEWSKI: I am going to turn to Rachel, but she doesn't have to answer that question, though.

DR. BEHRMAN: Oh, good. No, I have a question, actually, because I know you have put it out. Is interchangeability being used as synonymous with substitutability in this conversation, because you made

a distinction I didn't quite understand. Do you see a --

MR. WROBLEWSKI: That's a good point, yeah.

DR. BEHRMAN: Do you see a distinction between the two?

MS. URLEP: Well, in Europe, we have substitutability. So, substitution is official term, where it means that products can be substituted on a pharmacy level, so at the level of dispensing, when they are dispensed. So, this is in the European Union.

DR. BEHRMAN: And what's, then, interchangeability?

MS. URLEP: Interchangeability means that the products can be interchanged for each other without any additional safety issues being accompanied with and that they both have the same therapeutic -- that they are therapeutically equivalent to each other.

DR. BEHRMAN: So, you are using them as synonymous, then. In other words, it's not simply the initial prescription where you feel they can be -- a physician can choose from one or the other, but rather, a patient is on one form of therapy and can go back and forth?

MS. URLEP: But that's the term used in Europe, not as it is used now here in the terms of

interchangeability claim, which would be given from the authority which does the approval.

DR. BEHRMAN: Okay. And I can answer the question about what we require, and we require what is necessary.

MR. WROBLEWSKI: Professor?

DR. GRABOWSKI: Just a point that several people have made that I think will influence -- will be a positive course for uptake which is that we are seeing what's happening in Europe and the experience in Europe, which will lead us in several molecules in several years. To the extent that it gains acceptance, then I think that will also speed the acceptance.

And a question for Rachel is, would the tests that are done to get into the E.U., could those be used at the FDA?

DR. BEHRMAN: You mean data that was generated abroad?

DR. GRABOWSKI: Yes.

DR. BEHRMAN: Well, we recently published a rule, 120, and what we say is that data that are generated abroad -- we flip it slightly. We say we will not consider it or we may not consider it if GMPs are not followed. If GMPs are followed, then obviously, we would consider all data that were generated, yes.

Can I just ask a question on the other thing? With all this discussion around EPO, no one has brought up pure red cell aplasia. I was just surprised.

MR. LANE: I wasn't going to bring it up.

MR. WROBLEWSKI: Let me ask one other question just in terms of -- what effect the uptake of biosimilars, and does the difference that many of these biologic drug products are dispensed at the inpatient setting, either doctor's offices or hospitals, as opposed to actually at -- you know, at a retail pharmacy, does that affect the potency of, say, a payer's strategy?

Dave, I'll turn to you, or anyone who has a comment.

MR. GOLDING: Yeah. I'm not sure. Even though I saw the 64 percent number up there, I don't know what the right number is. I don't think it's 64 percent in hospitals or physicians, but it's something fairly large.

I think there is still, today, outside of hospital and inpatient, a lot of these products going through, and I would estimate about 50 percent of them are going through a retail pharmacy, where unless there is very black and white interchangeability, the script, the way it's written, is going to be the script the way

it's filled, with the exception of any interventions through, you know, a PBM or logic within the benefit design.

A little bit different with the business that we work in. The other 50 percent, me and my competitors have within specialty pharmacies, where we are more apt to be able to take interventions independent of any other activity. So, we have wrapped ourselves around the model of which we would go out and we could intervene based upon a very refined strategy and primarily cost-benefit.

So, they can operate two different ways, but I think the interchangeability will be very important in that subset that goes through retail pharmacies, at least as it exists today; less of a factor, because it will act more like the preferred brand within my space, where I will basically make the call, talk to the physician, exchange clinical information, and in some cases, switch that script over with his or her permission.

MR. WROBLEWSKI: Okay, thank you.

Alexis, did you want to add something or was it --

MS. AHLSTROM: Oh, sure. I think David covered it pretty well. All I was going to say is that I think

you have two different strategies. On the outpatient side, where the formulary is well understood by the beneficiary, you would have one strategy in terms of tiering, copays, et cetera, and on the physician side or the inpatient side, it's really about the payer and the manufacturer in terms of pricing and how you set up your incentives for physicians who may make more money by dispensing a higher cost product.

And I think we're seeing, you know, some payers experiment with that by, for example, you know, incentivising a physician to use the lowest cost product and maybe even paying them more for using a lower cost product, but still netting some savings to the payer. And so I think we'll see more experimentation, but I think you have different strategies.

MR. WROBLEWSKI: And how does -- if -- for many of the drugs that are -- have a substantial Medicare population, how does the Medicare pricing regime affect -- or reimbursement scheme affect prices for biosimilars?

MS. AHLSTROM: Sure. You know, I think that question -- I think there's a lot of ambiguity around that question, because we haven't seen what CMS would do, and I wish there was somebody from CMS here on the panel to really maybe talk about what they think will

happen.

I think that -- remember, all products are not just Medicare Part B, and the price the Medicare Part B pays is the average sales price, which is made up of prices that the manufacturer gives across payers.

Second of all, products that have both a Part B and a Part D component will have a potentially different pricing level than if they were just Part B. You know, I think Paul brought up that under Part B, if a product has a separate BLA, it would be given a separate code in Medicare, and that follow-on biologic could price at a premium; it could price ---it could parity price; or it could price at a discount to the reference product with its own code. It doesn't matter whether it has the same code or a different code. It can still choose a different pricing level.

But I think, you know, I think there's a lot of ambiguity. I think sort of my perspective is that the first step should be, you know, the scientific regulatory process, and then, you know, I think the operationalization of the biosimilars will -- you know, should come later.

MR. WROBLEWSKI: Paul, you wanted to add something?

MR. HELDMAN: I would just add that regardless

of what is actually taking place among the commercial payers and the PBMs in the marketplace with incentives, that what drives legislation, especially in an environment with a rising federal budget deficit, is the potential for the legislation saving money.

So, if you change the incentives under the Medicare physician payment system and make it more attractive for physicians to use the lower cost product, that's going to generate more savings for the Congressional Budget Office, which is basically the chief umpire of determining the cost and savings of legislation. That's going to -- they're going to determine that follow-on biologics legislation saves more money, and then it becomes of greater interest to law-makers.

MR. WROBLEWSKI: Okay, thank you.

Dave, did you want to add something on this Medicare issue?

MR. GOLDING: Two things, just one clarification on adoption, it is the tail of the dog in many cases on my pharmacy operations side. We can't forget about these products are primarily injectables. So, part of what we need to factor in, as it relates to adoption, is every time a patient switches from product A or product B, even in today's world, they've got to be trained

differently and send nurses out differently, and it's just a barrier that I don't want to lose sight of, because it's not just about the product. It's a lot about the product, but there's a lot of ancillary services, training, and just, quite frankly, these individuals may have been on the product for a long time, and physicians are going to be less apt, regardless of any clinicals, just say I'm not going to mess with what is working.

So, I just wanted to make that point, because that will mute it to a certain extent and/or put burden on me to get out there, which I do and try to do.

Secondly, as it relates to the payers in general but CMS specifically, very important, because depending on what happens, that is either going to drive -- that is going to drive incentives or disincentives, and as an example, for those familiar with the IVIG CMS market, where you had similar products, all within a single J code, the pricing was different, both on WAC data, but then as a cost to the pharmacy.

So, it's just created all kinds of incentives and disincentives, where I was taking scripts written by a physician, of which I had no control on, and some of the times I was filling it below my cost and sometimes I was filling it above my cost. That has been corrected,

fortunately, and those J codes have been corrected in order to align them within those various products, but I think hemophilia is another one that's similar to the IVIG today, where similar products, not like simply price, is in a similar J code, and depending on how CMS weighs in here, that will either drive or prohibit adoption.

MR. WROBLEWSKI: Okay, thank you.

Let me change gears a little bit. In terms of -- one of the things that, Paul, you had raised in your presentation was that there are a number of next generation products in the two markets that you had looked at, and I just wanted to understand or have some comment on what had spurred the innovators to develop those second generation products.

I'll turn to -- really, Paul, you're smiling, so it sounds like you have something on the tip of your tongue, but I'll turn to anyone else who would like to answer.

MR. HELDMAN: Well, I don't want to go too far afield, but as memory serves -- and the key market here, we're talking about the ESAs, and --

MR. WROBLEWSKI: We can talk about the interferon alpha or the GCSFs if you want to, too, not just ESA.

MR. HELDMAN: Okay. Okay. But I guess what I would say is that in addition to whatever improvements were made as a result of bringing a second generation ESA onto the market, there's also a licensing agreement that Amgen --

MR. WROBLEWSKI: Sure.

MR. HELDMAN: -- entered into before it was a profitable, successful company, in which it licensed away the rights to the oncology market for Epogen to J&J. So, for that reason alone, the development and approval of Aranesp in the U.S. was important for them to get into that market.

MR. WROBLEWSKI: What about in the other markets? Maybe I'll turn to John or to Mateja.

MR. LANE: You know, Hospira believes, in the absence of anyone else answering this from the branded side, that a lot of this is just general life cycle management, and when you look at the second gen products that have launched, and if we take EPO, Neupogen, or even the interferons, the second gen products have launched anywhere between nine to eleven years after the first gen.

Obviously, they're offering an enhanced benefit, but they're also certainly switching patients from one product to the other, to a product that theoretically

has got longer patent protection. So, in many ways, it's an ability to maintain a monopoly position over a franchise. So, that's one perspective.

MR. WROBLEWSKI: Okay.

Mateja?

MS. URLEP: Well, we believe there are multiple factors, because the technology, the medicine, everything is improving, and, therefore, you know, the improvement in various sectors of science is bringing also improvements into the medicine, and we also believe that once the patents -- the legitimate patents have expired, that it should bring out competition, and competition will spur innovation to the companies to give more effort to bring new products, to bring value to the patients.

MR. WROBLEWSKI: Thank you.

Professor Grabowski, you --

DR. GRABOWSKI: Yeah, I just wanted to say, just in MS and rheumatoid arthritis and several of these areas, there are several therapeutic alternatives, and a first-in-class can't just sit back and say, well, I have a monopoly now. You have other competitors that are getting into that market. So, a lot of this innovation will be spurred by competition.

MR. WROBLEWSKI: Thank you.

Steve, you wanted to add a point?

MR. BRUGGER: Two quick points: We actually are also an innovator company, and because the pathway was open to us to try to tackle some complex NDAs, such as Lovenox and Copaxil, we have developed analytics to try to understand these products, and we have actually engineered novel drugs. We actually have one that's in Phase II clinical trials right now for acute coronary syndrome. So, just because a pathway was difficult to tackle, we innovated and actually are not only trying to make what I would call a biogeneric; we're also trying to make an innovator drug.

The other comment I would make, having spent almost 30 years on the branded side of the industry, I know there's been a lot of concern on the part of the branded side that if such a legislation were to open up, it would stifle innovation. I guess if I put myself in the branded industry right now, with absolutely no potential threat of a generic, I wonder what R&D decisions I will be making with my very precious dollars.

I think if -- and Aranesp and some of these other decisions, I think you can at least look at them on their own merit, but I think if legislation were there and there was really significant generic threat,

whether it was real or not -- because it may take some time. As we all know, these are challenging molecules. I would think that the R&D decisions that some of those branded companies would be making would be much more around innovative, novel advances in patient care, because that's how they're going to grow their market share.

MR. WROBLEWSKI: When you said a generic threat, did you mean in the way we've defined the terms, a biosimilar threat or a biogeneric threat? And would the impact be different?

MR. BRUGGER: I was referring more to the biogeneric threat, because I think the impact there would be much more substantial.

MR. WROBLEWSKI: I see. Okay. Okay.

Ted, you wanted to add something?

DR. BUCKLEY: Sure. Actually, I'm not sure that, as I've said before, that the biogeneric threat would necessarily be -- or that the biosimilar threat would be less than the biogeneric threat. I mean, it's all about -- from the innovator's perspective, it's all about the amount of market share that is gained by the next generation -- by the biosimilar product, because to the innovator, every percentage of market share that's lost is revenue lost, whether or not the price discount

is 10 percent or whether the price discount of the follow-on product is 30 percent. The effect of that 1 percent market share decline is the same to the innovator.

One question or one thing that I would like to point out is that if you look at the biopharmaceutical industry overall, in the past 20 years, I mean, there has been no pathway for a follow-on product, but yet, this has been one of the most innovative sectors around. We've got treatment for rheumatoid arthritis; we have got the erythropoiesis; we have got monoclonal antibodies that are treating forms of cancer that weren't treatable before. So, there has been a great deal of innovation in the innovator firms over the past 20 years.

As we're thinking through developing a follow-on pathway, it's important to make sure that the $1.2 billion, on average, that it takes to bring a product to market, that there's enough time to recoup those costs, because if I were sitting in an innovator's shoes -- you know, our association represents innovator companies, but I'm not an -- I'm not a member of an innovator company.

If I were sitting there and if the pathway was developed such that it introduced a great deal of

uncertainty to whether or not I could recoup my R&D costs, I would really consider whether or not I should even be in this business anymore.

MR. WROBLEWSKI: Sure, that's a fair point, and we are going to examine that in depth in our second hour.

John, you wanted to add a point?

MR. LANE: Just a couple of comments. I mean, Hospira does believe that competition certainly provides an incentive to innovation. I guess I would want to respond to the comment Ted made. You know, how much time is enough to recoup the innovations? If you look at Epogen, that product launched in 1989, and it's not expected to receive competition until, you know, well after 2012, maybe 2015. Neupogen launched in 1991, and we are not going to see competition until well after 2010. So --

MR. WROBLEWSKI: Sure. And those are fair points, and I think we are going to get into that in more detail.

MR. LANE: I understand, I understand, but there's a point to be made.

But you also made a comment about how biologics, the industry, has provided innovations, and absolutely they have. The pharmaceutical industry provided

tremendous innovations prior to Hatch-Waxman, but if you look at Hatch-Waxman and the effect that's had in terms of what Professor Kolikoff pointed out, you've seen an increase in the number of patent applications and approvals; an increase in the number of new molecular entity approvals.

So, you have had an increase in the number -- in the spending that R&D is -- as a percent of sales for these pharmaceutical companies. So, there's no reason to believe that biosimilars eventually can drive that same type of innovation or at least incentive to innovate even above and beyond where we're at today.

MR. WROBLEWSKI: Okay. Thank you.

I am going to turn the discussion and really try to cover two more points before we break at 10:30. The first one is trying to examine the factors that FOB entrants will evaluate when they consider when and what they should consider when making an investment to develop an FOB product.

I'd like to ask either Mateja, John, or Steve to comment on the most important factors that their companies considered as they were preparing their FOB applications.

I'm going to start with Steve since I'm looking your way first.

MR. BRUGGER: Well, I will probably take a slightly different stance than Mateja and John, because we are much, much smaller, and actually, I think we've talked a lot about biosimilars and clinical data and comparability, but what is very important to us to make continued investment in this field is a very clear path towards interchangeability, and what that does is allows companies like ours to innovate in the analytical space and not in the clinical trial space. These clinical trials are a very crude way to detect similarities or differences between these very complex molecules, and the way that we will truly understand these complex macro molecules in the future is by innovating in this analytical space.

And that's why it's so important to us that the legislation has that pathway so that we can make those investment decisions, because ultimately, we hope to minimize those clinical trials. We hope to better understand these molecules. We hope to have a better understanding of immunogenicity issues with these molecules, to shorten those development time lines, because for us, if it's a biosimilar game, and these are large, extensive, $40-$50 million dollar clinical programs, a company like ours are not going to invest in the space.

MR. WROBLEWSKI: Right. So, you're coming at it from much more of a biogeneric angle, as we have been talking about it this morning.

Mateja, did you want to add something?

MS. URLEP: Yes. Sandoz, one of the leading generic companies, namely, the second generic company in the world, is, of course, looking to future growth, and, therefore, the biologics actually do represent more than 50 percent of the new approvals in the U.S., the place to go in the future. So, we cannot say that biologics are not the part of the market, pharmaceutical market, that our company will not enter.

So, therefore, we are preparing to compete on the market the way it is and the way it will develop in the future, but, of course, the challenge is how to be sure what kind of the requirements are necessary to develop the product. Sandoz has a long-lasting, more than 25 years, experience in development and productions of biologics, as being one of the first companies in this arena, and we do supply a lot of originator companies with their products, because they're developed and produced at our premises.

So, therefore, we have a lot of experience gained over time, and with this experience, we are ready to enter the market, and depending on the market access,

we can offer various discounts.

MR. WROBLEWSKI: Thank you.

Let me turn to John, and then, Rachel, I'll turn to you. John, go ahead.

MR. LANE: Yeah. You know, based on Hospira's experience with Retacrit, we firmly believe there is a tremendous opportunity for biogenerics to exist.

Regarding some of the things we think are important as we consider entering, the additional molecules, which markets, et cetera, you know, there is a number of provisions I think that people are talking about and have different perspectives on: the length of market exclusivity; whether evergreening is actually going to be an issue we have to deal with, where we could develop a biosimilar to the first product and patients switch over to the second gen product, that's certainly concerning; whether there's going to be a patent resolution system in place where you can resolve these patents in a timely manner; and certainly interchangeability is critical.

The patients will not realize the ultimate benefit of the savings of these products will be just as safe and therapeutically equivalent if interchangeability at some point in time does not exist.

MR. WROBLEWSKI: And you are using

interchangeability, again, as biogeneric?

MR. LANE: As, yeah, full substitution; automatic substitution.

MR. WROBLEWSKI: Okay.

Rachel, you wanted to add something?

DR. BEHRMAN: I wanted to respond to something that Steve said, because I couldn't agree with you more that the real advances will come in the analytics and the ability to, to the best of our ability, realize how similar or different these products are and may minimize or shorten or decrease the extent to which certain types of clinical trials are necessary.

I'm not sure that it will ever get you interchangeability, substitutability, whichever word we're using for substitutability. Those are not typically large and expensive clinical trials, by the way, but, again, I'm not a biochemist, I don't know, but knowing what we do know about protein products and even the multiplexed molecules, I'm not sure in the foreseeable future it will get you to what you've defined as the biogeneric world.

MR. WROBLEWSKI: And are there any benefits to the innovator companies for having the analytics to determine what interchangeability is in terms of, say, batch stabilization?

DR. BEHRMAN: Well, that's why we came up with the comparability definition, in fact, huge, because when -- and pure red cell aplasia comes to mind. When innovators make changes to their manufacturing process and if they can't demonstrate to us and obviously to themselves that they are producing a similar enough or essentially the same but a similar enough compound, then they have a problem.

So, yes, I think there are tremendous advantages to the innovators, and the innovators will do some of the second generation work, as has been pointed out, if for nothing else, maybe for the good of humanity.

MR. WROBLEWSKI: Say that again. I didn't hear you.

DR. BEHRMAN: Well, in other words, there was some discussion I didn't chime on, why second generation work? why innovate? why improve? Well, at the Agency, we hope that's done for the good of the public health.

MR. WROBLEWSKI: Right. Okay. Thank you.

Steve, did you want to respond to --

MR. BRUGGER: Yes. So, Rachel, I didn't mean to suggest that we were going to tackle all these biologics and chemical characterization. I guess the issue for us is we've got to legislate something for 20 years from now, and I would like to think that someday that we will

get there, and I think people thought we wouldn't get there with Heparins, and I think a great example of the innovation going across both generic and innovative industries was the work that we actually contributed with FDA and Mateja and others on the Heparin contamination issue.

DR. BEHRMAN: Absolutely.

MR. BRUGGER: And it was because the investments were made on trying to study and analyze this complex Heparin mixture that we were able to better understand how to approach those and very quickly adapt to somewhat of a major crisis.

DR. BEHRMAN: That's right.

MR. BRUGGER: So, we can't lose sight of the fact that this is where the future is. It's not in clinical trials; it's not in comparability of clinical trials. The future has to be around analytics. It may be five, ten, it may be 20 years, but we have to at least strive for that.

MR. WROBLEWSKI: You know, we have been talking about biosimilars and biogenerics as new companies coming in. Do any of the panelists anticipate that current innovator companies will be using the biosimilar and/or biogeneric pathways if they are developed? Why not?

DR. GRABOWSKI: I think a lot of specialty companies, specialty pharma, are looking at this issue and see it as an opportunity. Perhaps some of the large pharma companies that aren't in the biologic space will see it as an opportunity. So, I think there could be lots of competition from different sources.

MR. HELDMAN: Small biotech companies as well.

MR. LANE: I was just going to say we've seen several big pharma firms make that statement, most notably, Pfizer has said they're evaluating that in their business model. So, it's not inconceivable, with these companies having an infrastructure already in place, that this would be part of the their model going forward.

MR. WROBLEWSKI: Okay, thank you.

I'd like to ask one other -- Steve, did you want to --

MR. BRUGGER: I just want to make one comment, that actually, getting to John's earlier point, the final language around exclusivity and the patent process will dictate to a large extent the kinds of companies that will get into this space. So, the smaller biotech companies will be constrained from getting in if there's additional barriers, because they won't be able to make those kinds of investments that obviously large

companies like Sandoz and Hospira could make.

MR. WROBLEWSKI: Let me ask one question, and, you know, one of the interesting things about this market that we've talked about is that it's worldwide, that -- you know, the drug products, and I am interested to know about how -- and, Rachel, we touched on this briefly, and if you could maybe start off in terms of the ability to rely on innovator data that is generated abroad or should the pathway that is here be limited to an FDA-approved product or could it be data that's from -- do you see what I'm --

DR. BEHRMAN: I know exactly what you're saying or I think I do.

I don't want to touch on whether we can -- what innovator data we can legally look at. I think that's a question for the lawyers and the legislators. But philosophically, I did try to say that we do not -- as in a public health agency -- want to see studies duplicated. We don't want to see resources wasted. We don't want to see patients subjected to trials that, in that sense, would not be ethical.

In terms of where it's generated, whether it's generated in Europe or here, the development of medical products is a global process. We routinely look at data generated overseas in support of NDAs and BLAs, and we

will continue to do so. In some cases, there are some complexities, particularly from the research, monitoring and clinical practice realm, protection of human subjects realm, those are additional challenges, but yes, we want to look at all data.

MR. WROBLEWSKI: Thank you.

Did anyone else want to add to that discussion about --

MS. URLEP: Basically, for us, it's a discussion about the reference product, where we see that various different jurisdictions, they say that we should use the reference product which is approved under that jurisdiction, and here, European Union wants to have a reference product being approved in the E.U., whereas the FDA would be on the side to have a reference product being approved in the U.S.

MR. WROBLEWSKI: And what's the impact of that? What's the impact?

MS. URLEP: The impact of that is even though the originator in most cases had developed one development program, but it is approved in different jurisdictions, and it is the fact of the same product, but in Europe, these are different products in different jurisdictions, and we would have to repeat some of the trials with the reference products from the

jurisdiction.

Canadian authorities tend to be, at the moment, a bit more open for their subsequent entry biologics, as they call them, where they say that the reference product may not be approved in Canada, but it has to be approved in another prominent jurisdiction, such as U.S. or the E.U.

MR. WROBLEWSKI: Okay, thank you.

We're about one minute until 10:30. Any final comments before we break and I instruct people to where coffee is upstairs on the seventh floor?

(No response.)

MR. WROBLEWSKI: Okay. We'll start back at 10:45. Coffee is on the seventh floor. If you do decide to go outside for any reason, please keep your name tag. You'll have to go through security again, but you won't have to sign those papers.

(A brief recess was taken.)

PANEL TWO:

LIKELY COMPETITIVE EFFECTS OF

REFERENCE PRODUCT REGULATORY EXCLUSIVITY

MR. WROBLEWSKI: It's time to get started on the second panel, this morning. In this panel, we're going to examine the likely competitive effects of reference product data exclusivity. My comoderator of this panel is my colleague, Chris Garmon, from the Bureau of Economics.

Joining us for this discussion, I'd like to introduce everyone. Even though I've introduced some of them before, some folks may have missed the earlier introductions.

Starting at my far right is Alexis Ahlstrom, Director of Avalere Health. To her left is Geoff Allan, President and CEO of Insmed. To his left is Audrey Phillips, Executive Director of Biopharmaceutical Public Policy and Advocacy at Johnson & Johnson.

Turning around the corner is Dave Golding, Executive Vice President for Specialty Pharmacy Services at CVS Caremark. Henry Grabowski, Professor at Duke University. Thank you for joining us.

DR. GRABOWSKI: Thank you.

MR. WROBLEWSKI: Paul Heldman is to my left, Senior Health Policy Analyst at Potomac Research Group.

Linda Horton, Partner at Hogan & Hartson, here in Washington. Mateja Urlep, Head of Global Marketing and Medical, Biopharmaceuticals, at Sandoz, International. And then at the very far end of the panel is Alex Brill, a Research Fellow at the American Enterprise Institute.

More detailed biographical information about each one of the participants is in the folders and on the FTC website.

Before we get started, someone came up to me at the break and made a really good point that I failed to mention earlier. The FTC is keeping the record open for another 30 days, until Monday, December 22nd, for any comments that you'd like to add. If there were certain things that we didn't cover in that first panel that you thought, geez, I wish they had discussed this point, we actually welcome your additional comments at that time.

Before we get started on the second panel, Linda Horton has agreed to provide a brief presentation on how the EMEA, their regulatory pathway for the approval of biologics and how that approach can inform the U.S. approach.

Linda?

MS. HORTON: Thank you.

First, a caveat. My views are my own, not those of my firm or any of our clients.

You've asked me to focus on the European experience with a particular emphasis on regulatory exclusivity periods there and also upon the interchangeability issue. I would like to note that there was a bit of a mixup in the photocopying of the slides, and what appears on the screen is different from what's in your folder, and I will refer you to the FTC website, which has a copy of the longer version of my presentation, which has slides from both of these. So, there will be some difference between what you have in your folder and what appears.

First of all, these are the topics that the FTC has asked me to cover, and when we talk about U.S. and Europe, there are some similarities in this class of products. Here in the U.S., we're quite accustomed to having our unitary FDA system. In Europe, we do have much more centralization of the decision-making on these type of products, and since 1975, all biotech products have been required to go through the EMEA process, and now, since the year 2004, effective late 2005, there has been a biosimilar pathway, at least when it's a biotech biosimilar, it must likewise go through the centralized EMEA process, which the European Commission actually issues the decision.

There's a great deal of harmonization between

the content of the review, the depth of the review, much harmonization through the International Conference on Harmonization, although the FDA and the European Medicines Agency took a somewhat different approach to comparability. As it may come up, Dr. Behrman's slides showed the FDA approach to comparability was more the evolution of one company's product, whereas the European Medicines Agency, back a few years, was willing to take the position that they would consider comparability among different firms. But if we talk about guidelines, the ICH is a good place to do it, because it includes a place at the table for industry.

Patent life, this has now been harmonized at an international level to 20 years. In both the U.S. and the E.U., there's a shared belief in both patents and also in regulatory exclusivities as ways to incent innovation and to give companies a chance to recoup for their investments.

Some cautionary notes: We're not looking in the mirror when we look across the Atlantic. Each of the 27 member states has its own healthcare system, makes its own decisions about reimbursement, pricing, and medicine substitutability.

There also are persistent national differences in patents, and as here, a lack of complete security

that a patent will hold up. There is the European Patent Office, but when you get a European patent, it's a bundle of national rights.

My next bullet point I started worrying about, because you do need to understand that all of these provisions in the legislation are subject to intellectual property, so that it's not saying that the regulatory decisions can override patents, but at the same time, the listings you'll find, say, on the European Medicines Agency website or the European Commission website will not include any information about patents. So, you don't have any kind of Orange Book patent listing system in Europe, nor do you have a system of Paragraph IV notices, nor do you have 180-day generic exclusivities in the E.U.

In general, the pharmaceutical regulators -- there is nothing -- at member state level, there could be some taking into account of patents, but there's nothing in the legislation that tries to link together or relate how the resolution of a patent might relate to the approval of a generic.

You need to understand, too, that the origin of the ten-year exclusivity period goes back 21 years, to 1987 legislation in Europe, which was its kind of Hatch-Waxman law. It was not designed particularly with

biologics in mind. Indeed, it was only four years ago, effective three years ago, that the bioapproval pathway, biosimilar pathway, came into existence in Europe.

And so I think I would give a cautionary note about just, you know, we already have issues about should we copy the Hatch-Waxman formulation for biologics in the U.S.? I likewise would give a caution about just looking at the European system and assuming automatically that's the way to go. I think there are studies by Professor Grabowski and others that provide more empirical data than these experience models suggest.

On the eight plus two plus one, you need to understand that this system will apply only to submissions that were made to the European regulatory authorities after late 2005, after November the 20th, 2005 in the case of applications going to the EMEA process; slightly different time frames for those going through the national agencies, which we don't talk much about in this presentation, because when we're talking about biotech biosimilars, it's EMEA.

And this is the short description of the system is eight plus two plus one, which means eight years data exclusivity dating from the European Commission authorization filable. Before that, generic decisions

are not even filable. Then, for two years, no generic applications can enter the marketplace. If, before the eighth anniversary of the original authorization, the reference product's marketing authorization holder manages to get a new indication approved that constitutes significant clinical benefit, then any competitors are shut off the market for an additional year, which would give a total of 11 years of time on the market for the innovator product. And, again, I'll emphasize that this system kicks in effective with applications that were submitted late 2005 or after.

So, what happened before that? Well, for the European Medicines Agency, it opened its doors on the 1st of January, 1995, with legislation making it ten years, period. Before that, there had been a few products that were approved, high-tech products, that likewise got ten years under the 1987 legislation I referenced. At member state level, there was disharmony. Member states were permitted to pick between six and ten years, and in my longer presentation, you can see which ones picked which, because this old system continues to be relevant now until, you know, 2011, 2012, you know, on into the future.

So, when we talk about the plus one year,

there's a very good European Commission guideline, but it won't really kick in until around 2016, 2017. There's also, in the European legislation, a number of stand-alone exclusivities that, you know, we don't have time to go into, but there's one I might mention, an independent plus one for a new indication of a well-established medicinal product.

There's also the chance for ten years or the normal eight plus two plus one, rather, for a new product that combines two older products. That's treated as a new product, according to the European Commission. You can get a year of exclusivity for effecting a switch of a product from prescription to OTC, and I think we're about to have the first example of that at E.U. level with a diet product, alli, from GSK. And then orphan exclusivity in Europe, it's ten years of marketing exclusivity, unlike data exclusivity, where you can test your way onto the market with your own data set.

With marketing exclusivity, if the product is very similar to the orphan product and also with reference to the indication that's being used, then the product can enjoy ten years of marketing exclusivity and can even be extended with the new pediatric legislation. So, it's a very complex system, as you can see, and so

there's a lot of nuance to it.

Concerning improvements, this I know is a big debate in the U.S., and there are some issues in Europe that are not 100 percent clear. What is clear is that when we're talking about products going through the centralized procedure, the legislative provision to reference is not Article 10.4 of the Community Code of Medicinal Products, but Article 14.11 in the EMEA regulation. They do have uniform time periods, but they are separate, stand-alone provisions.

I am not going to read through all that. You are perfectly capable of doing that.

You know, on the face of this provision looked at by itself, any product that goes through the process of the EMEA shall benefit from an eight-year period of data protection. Applicants wishing to market their own versions of high-tech biologics, you know, already on the market could, by submitting full applications, enjoy the benefits. If somebody goes the biosimilar route, the same thing will not be possible.

Okay. There is, however, in the Community Code of Medicinal Products a provision that does appear to apply both to centrally authorized products and to those approved at member state level called the global marketing authorization, and this has nothing to do with

the ICH common technical document or anything like that. It's just a legal construct that was intended to codify certain case law that we will touch on next, basically trying to wrap up into one authorization various kinds of changes that can be made.

There is a European Commission guidance stating that where the applications come from different marketing authorization holders, then those different applications are not treated as being under the same global marketing authorization. This was one of the issues. So, this -- oh, dear. I keep pushing the wrong -- okay.

When we look at this definition of global marketing authorization, it will become very important to know what is a medicinal product, because it's only when we're talking about the medicinal product that all these changes and so forth will be treated as wrapped up in one variation. If you have a product that's very different, such as one that's been glycosylated and offers a very different profile in terms of the clinical testing and preclinical testing, native and the CMD, the chemistry and manufacturing data, and complete studies are done, there's no reason why that should be treated as being under the same global marketing authorization holder as the earlier protein that is very different.

However, if you look at the EMEA website or the FDA website, for that matter, and all the kinds of changes and evolutions and variations and more minor changes, those types of things will be treated as part of the original global marketing authorization holder.

And why is this important? Well, it has to do with two things, really: One is whether the follow-on company is kind of locked into the oldest original product or whether they can copy not only traits of the original product but also follow-on traits; and also it has to do with whether there's a restart of the exclusivity period, whether ten or eight plus two plus one, depending on when it entered.

There was a case in 2004, which in your handouts, you have a summary of two cases, a generics case of 1998 and the Novartis-Sangstat case of 2004, that both are relevant to how this whole area is interpreted. It's not in what will go up on the screen, but there is a degree of uncertainty, and many lawyers believe that the European Court of Justice decided the Novartis-Sangstat case improperly, and there's a lot of confusion in this area about what exactly will be treated as part of the global marketing authorization.

Now, as I mentioned, it's too soon to have experience here. The European law-makers -- and this

came from basically the industry, it came from the European Commission, whereas from 1995 through 2004, there was no kind of extra exclusivity period for the second indication, the decision was made that this was very important to add on, and so this guidance takes a very broad view of the types of benefit that would justify getting the eleventh year, but it's all indication-related. You won't find anything in the guidance that has to do with product improvements, other than new indications.

Also, I would point out, Michael, that a number of the companies that made submissions to the FTC docket took the position that one year is not enough time, and, you know, I won't get into that, but that's...

I'll just say, too, that as in the United States, in Europe, oftentimes the patent life extends longer than any regulatory exclusivity period, particularly when you consider that it's not just the 20 years but also the supplementary protection certificate that in Europe will add on five years. So, the regulatory exclusivity period operates as a kind of secondary type of protection.

It's important in some cases where there are very long development and registration periods, such patent has expired or is nearing expiry at the time of

the product approval. There also are some areas where, at least in the past and in some member states, the patent protection has not been as robust as it perhaps should be, and so in terms of innovation and incentivization, the regulatory exclusivity periods have provided a degree of certainty that the patents have not. And there also have been some differences, too, in the patentability of new uses, and that's where this can become important.

Turning now to interchangeability, we have up there on the screen a quote from the EMEA Executive Director pointing out that the Agency is in no position to guarantee that a biosimilar is interchangeable. This relates, in part, to the type of data which have been submitted, which the biosimilar applicants were not really forced to submit data showing their products would be interchangeable. The EMEA takes the position that substitution is a national competency, and we'll talk in a minute about what the member state experience should be.

There's a couple of other -- you know, I think on this definitional thing, what I find useful to say is interchangeability is a matter of science and substitutability is a matter of law, and I think what doctors do is really something different. I think

that's practice of medicine.

Interchangeability is when FDA says we do not think that Omnitrope is interchangeable with other products, nor do we think the innovator products are interchangeable, nor do we think insulins are interchangeable. That's where the expert authority makes a pronouncement in an area that is intended to set a standard of care and guide the world or guide the country, and there have been other statements beyond what is on the screen in the couple years following, and I won't go through all that. It's in the longer presentation.

Substitutability is handled -- there's not any more slides on this, but in your handout, there is -- you have partial information about which member states have forbidden exclusivity, because you've got slide one, and there's a second slide that's posted. So, if you have your handouts -- I'm sorry for this -- there's also some new European pharmacovigilance guidance that advises the inclusion of brand-specific information in adverse event reports, which really means that it's going to be very difficult to get that information if there's not prescribing by brand name and dispensing by brand name, since the INN, the International Nonproprietary Names, do not differentiate among the

different manufacturers' products.

There also had been a letter to member states from senior European Commission official Georgette Lalis in mid-2007 cautioning member states that they should not assume that glycoproteins are all interchangeable one with another, and this related directly to the experience with Eprex just a few years ago.

So, in addition to the nine countries listed in your handout, The Netherlands, Norway, Slovakia, Slovenia, Spain, Sweden, and the U.K. all have legal provisions forbidding substitution generally of biotech medicines or some say injectable medicines, some biologicals, some say biosimilars, but that's 16 out of the 27 member states -- or 28, I guess, because Norway is not a member state, but a sister country. So, more than half.

MR. WROBLEWSKI: Linda, could I ask you to do the one final slide, and we'll start with the discussion?

MS. HORTON: That's it. Thank you.

MR. WROBLEWSKI: Thank you.

MS. HORTON: I hope I didn't overrun. It's a lot of material.

MR. WROBLEWSKI: No, thank you.

You know, the objectives of today's discussion

on this second panel this morning are to identify the purpose of a reference product data exclusivity period and to examine the likely competitive effects of various ways to structure a data exclusivity period. As with the morning panel, we were going to try to stick to using these terms to distinguish really what the market effect is.

I think, Dave, you had made the point that a biosimilar drug in some ways, from an economic point of view, acts as though it were another brand product in that class; a biogeneric would be the one that would be interchangeable that would have the same economic effect as a generic drug; and that a follow-on would really include both of those. Those were the terms we were looking at from an economic point of view.

First, we're going to run the panel the same way as we did with the first panel, in which we'll pose a question, address it to a particular participant, and then ask for any follow-up. And please just turn your card on the side if you'd like to be called on, and we'll try to do that if time permits.

And the one other thing is that these microphones are always on, so if you are not speaking, if you can just move it up so there won't be any chatter in the background.

I'd like to open up really the first question to the panel, and I'm going to turn to -- I'll turn to Audrey first. What is a data exclusivity period and what is its purpose?

MS. PHILLIPS: Well, I first would like to thank the FTC on behalf of Johnson & Johnson for inviting us to participate in this dialogue, very important and we're happy to be here.

In terms of a data exclusivity period, we talked about in the first panel a lot on the tail end of this and what is important, but I think for data exclusivity, what we want to do is talk about its purpose when investment decisions are made and remember what it is and what it isn't, because there are a lot of terms that we're talking about here, and I think this confusion in terms probably will continue to go on for a little while.

But we need to make sure that we understand that data exclusivity is about protecting the data. It's not about market exclusivity, and it's not about monopoly. It is about the data itself and a period of time where the Government cannot rely upon that data and, in essence, cannot tap into the investment of the innovator.

I think it's also important that we understand

that just like all other industries, when patents expire in this industry, competitors are free to come to market. They're free to invest in their own development program and come to market. It's no different in this industry than it is to other industries.

Data exclusivity actually facilitates competition, because what it does, it allows the Government, at some point in time, to be able to rely upon the innovator's data, to rely upon the innovator's investment, if you will, to bring a competitive product to market, and that's how investors look at it as well. When investors are making decisions in their products and in -- decisions along the way, whether it be in large companies or whether it be in small biotech companies, they're looking at the future, and they're looking at the point at which their investment might be used to generate competition. So, it's an important factor.

I think some of the things that we need to think about when we're thinking about what that needs to be is that legislation moving forward for biosimilars is going to change the status quo for investment decisions, very clearly. So, as we consider this moving forward, as we consider investment moving forward in biotech, we need to understand that the game has changed, the

considerations are changed, the valuations are changed, the downside risk has changed, the upside potential has changed for these investment decisions. So, it's important that we get it right.

MR. WROBLEWSKI: Thank you.

Dr. Grabowski, would you like to add anything?

DR. GRABOWSKI: Yes. I would just say that, echoing Linda's earlier point, that the data exclusivity will run with patents, and so it will be important, selectively, in selective cases, essentially either situations where there's very long regulatory periods, review periods, so there's very little effective patent time left, or situations, as you put it, where the patents may be more -- not as robust and subject to challenges.

So, it is a -- it's designed more -- some people would use the word insurance policy to investors who are thinking about the future, and this would start way back in the biologic industry in many cases with venture capital, private equity. Are we going to be able to, at the end of the day, be able to recover our R&D investments? I think looking at it from an innovator's standpoint, it's how will it affect returns on investment, and it's a complementary feature to the patent system. In many cases, the patent system may be

sufficient; in some cases, it may not be.

MR. WROBLEWSKI: Thank you.

You know, in the earlier panel, the work that Mateja indicated that she didn't have to do was -- or the testing that they didn't have to do were Phase II clinical trials. How do you quantify the investment that is being relied upon? Do you look at it only as what the follow-on biologic doesn't have to do? Is that the investment? Or do you look at something broader?

MS. PHILLIPS: The relied-upon allows the FDA to proceed and depend on abbreviated data. So, what is accomplished with the relied-upon is the abbreviated patent. So, the investment is decreased.

In most of the guidelines that I've seen going forward, the Phase III clinical trials are also abbreviated, and I think that's the basis for moving ahead. So, there clearly is some economies to be had on the part of the biosimilar competitors in their development program, and that's what this is about.

I'd like to clarify, if I will, and perhaps apologize before the fact. I'm using the term "biosimilar" in a way that probably doesn't conform to what you've said up there, but we internally, in all discussions, have defined it in a way that I've kind of gotten used to. So, I'm going to try to hold to there,

if I can, but it does relate specifically to the question that you've just asked, because for us, biosimilar means a path forward where in analytical quality analysis and preclinical studies you demonstrate that this new product, this biosimilar product, is as highly similar to the reference standard and the innovative product as possible. And because of that, you are granted an abbreviated clinical program moving forward, because you've established that high similarity.

That's why you do -- you are able and the FDA is able to say, okay, because you're so similar, we will allow that clinical program in Phase III to be somewhat abbreviated on a case-by-case basis, and there certainly is savings there as we move forward with all these products. There could be some exceptions to that with some products that came out first, but in terms of moving forward, that would be the consideration. So, there would be abbreviation there, and it is relied upon in that way.

It's also relied upon ultimately in how these play out in the marketplace. There clearly will be a few years after market entry where these biosimilars will need to prove themselves on safety terms and post-marketing pharmacovigilance to follow up, and if

all is well, eventually they will be able to, in many ways, piggy-back on the investment and the marketing costs, et cetera, moving forward of the innovator program.

We do not, however, see how a biosimilar product and the biosimilar path, as we've thought about it for many years, would and could be used for improved products. So, I'm a little confused as to why that's grouped together, but clearly, in answers to my questions, I'm talking about a highly similar product and certainly not one that would be improved.

MR. WROBLEWSKI: Thank you.

Before I change topics in terms of the purpose of the data exclusivity period or how you would go about recovering your investment, did anyone else have any additional comments before we then move on?

Linda, go ahead. I'm sorry, I didn't see your card.

MS. HORTON: One of the most fundamental types of changes enjoyed by biosimilar companies -- and this is one that's often overlooked -- is the fact that they know what the target of the product development program is. If you think about the original discovery of interferons back in the eighties, those were tried on all kinds of things before -- interferon beta, for

example, was focused on MS, and so the biosimilar company comes into the area knowing already what disease state that they're targeting, and that's a very significant saving, and we can't ignore the contribution of the innovative companies in discovering that path.

MR. WROBLEWSKI: Thank you.

I'm going to turn to the next question in terms of if we have a data exclusivity period, what's the optimal way to determine the length of that period? It's kind of an open-ended question.

I'm going to turn to Alex first, just because I know Professor Grabowski has some comments on that as well.

MR. BRILL: Thank you, Michael, and thank you to the FTC. I will open with a comment similar to Linda's, which is that my views are my own, and my employer doesn't have opinions about these issues. So, I'm speaking here for myself, and the work that I've done on this issue is my own and not that of my employer.

I guess I would open by saying that the importance -- the data exclusivity is absolutely an important issue and an important protection, and the question that I think is the relevant one is not whether or not -- is not the question of if, but the question of how, and there is a balancing act here, and this is a

question of -- it's a trade-off between setting policies to encourage innovation and setting policies to encourage competition, and both factors are important.

There are a couple of ways to think about this question of what is the appropriate duration. Professor Grabowski has done, I think, incredibly important work on this area setting forth a framework for how to think about this question. I don't want to take too much time to explain what he did. I want to give him the opportunity to explain what he did.

But the framework that Professor Grabowski has laid out is a framework that he refers to and that I refer to in my work as break-even analysis, which is asking the key question, which is the investment question, I think -- I agree this is about investment -- of recouping the costs, recouping the R&D costs and recouping the costs of the money that's used in that investment. So, recouping the cost of capital as well and a whole associated number of costs that go into the risky development of developing or bringing to market new drugs.

If there was sort of one point that I would want to stress this morning is that the question of break-even point and where that is on average for a portfolio, when we think in the aggregate, that is an

important question to answer, but the answer to that question is not the answer to what is the right duration for data exclusivity. And the reason that there's a difference between what the break-even point might be and what the right data exclusivity duration may be is for the very issue that was discussed in the last panel, which is that post data exclusivity, when competition begins to enter the market, the innovator drug is, by all expectations, expected to continue to have market share, and while prices may fall, it's no one's expectation that prices are going to collapse.

What this means is that in the period following the end of data exclusivity, the innovator drug will continue to have the opportunity to recoup their R&D costs, and that's the relationship between data exclusivity and the break-even point.

MR. WROBLEWSKI: Thank you.

Dr. Grabowski, would you like to add some comments?

DR. GRABOWSKI: Sure. I'm happy to see that Alex is accepting the general framework, and in my original Nature article, I pointed out that the innovator would keep a part of the market, and so, therefore, that was one factor, and then I pointed out other factors. But I welcome additions and further

sensitivity analysis, and I have been working on extending the model, and some new results I can report, that if you take the CBO assumptions that essentially we talked about earlier, the CBO assumptions that at least initially, in the period that they were scoring, they expect the biosimilars to take maybe 35 percent of the market, the innovators to keep 65 percent, and then the -- but the branded firms would compete on price, and price would decline 20 to 40 percent.

If you take those assumptions and enter them into my model, then you can frame the question, you know, what exclusivity periods are consistent with the break-even point? And when you do that, you don't get -- when you look at things like how long would it take to converge, if ever, and when we put in a seven-year or a ten-year exclusivity period and then combine that with the CBO assumptions, you don't get convergence within 50 years. You don't get break-even.

So, you know, this is one set of sensitivity analysis. We're doing others. You have to get into the 12- to 14-year periods before you start to see a break-even analysis that's consistent with an exclusivity period, and, you know, I welcome balanced sensitivity that will look at a lot of the parameters that would be at work here, and I'll be addressing some

that Alex has put forth in a new paper that just came out this week.

MR. WROBLEWSKI: Okay, thank you. Let me ask you a quick question about -- oh, go ahead.

MS. URLEP: I would just have a comment here, just to support what Alex has said. Our data, which would show previously that suggests that even one year after the market entry of a biosimilar in Europe, there was still considerable market share of the originator brands on the market. So, they still continue to recoup their development investment.

DR. GRABOWSKI: But it looks like it's moving even much faster than what the CBO -- I mean, the CBO I think is an intermediate position. We've had payers say it's going to be 60 percent or more within a very quick period. We've had other people say it's going to be 5 percent. I think the CBO is a reasonable first starting point.

MR. WROBLEWSKI: Geoff, you had a point you wanted to make?

DR. ALLAN: Yes.

First of all, I'd like to echo the remarks that Audrey and Linda made. Data exclusivity is critically important, because it does allow the FOB developer a very focused, targeted approach to the development of

the product. So, that's a given.

So, it boils down to what is the purpose of it? It's a return on investment. And if I look at our personal experience, I work for a small biotech company called Insmed. We wear both an innovator hat and we wear a biosimilar hat. We're developing an innovator product right now. We're in Phase II clinical trials, and if that -- we've worked out all of the return on investment that we would require for that product, we've looked at all of the costs of development of that product, and if I look at the data exclusivity that had been talked about, I would say very, very comfortably that the costs -- that the price it takes us to develop the product, we can certainly recoup all of our costs within five years of -- five years' data exclusivity.

So, I think the factors that come into play are the factors of how much does it cost to develop a drug in the first place? And it doesn't cost us $1.2 billion. What happens to the product when the period of data -- when the FOB developer comes into the marketplace? And as Alex pointed out, there's a lot of rapid drop-off of profits. And then there's the other issue I don't think anybody has talked about, is the ability of the innovator to evergreen the product and continue to build a franchise that brings out more and

more profit and revenue.

MR. WROBLEWSKI: Okay, thank you.

You make a good point in terms of recouping the investment. What should be included in that -- from a conceptual point of view, what should be included in the amount to be recouped? Obviously it's all the clinical trials and those types of things, but should sales and marketing, should research for post-approval of new indications be included in that -- you know, the number from Dr. Grabowski's paper is 1.2 million -- billion -- million -- billion?

DR. GRABOWSKI: Billion.

MR. WROBLEWSKI: Seven hundred billion, whatever.

(Laughter.)

MR. WROBLEWSKI: 1.2 billion.

From a conceptual point of view, what should be included in that to be recouped? It's the investment, but what piece of that investment? I'd like comment on that. Anyone can start. If Alex wants to start? Audrey? Geoff?

DR. ALLAN: Well, as the CEO of a company, I'd like to see it all come back. So, I think you've got to -- if you choose to develop a certain product, you want to be able to obviously recoup all of the R&D

expenses, all of the market and sales expenses, all of the -- you know, all of the expenses of running the company. You want to be able to recoup that in an adequate period of time.

DR. GRABOWSKI: You have to do a cash flow analysis, right?

DR. ALLAN: Absolutely.

DR. GRABOWSKI: And would you include in that the probability of success and risk adjustment and all of those? So, you can't do it on a single product that just says, well, this has a high probability of success, so -- you have to -- you have to look at a universe of products and risk-adjust for probability of success, for discovery research, for a whole -- you know, the whole process.

And it's true that one company may be able to develop a product for much less than 1.2 billion. There are other cases where it could be more, and that -- what DeMassi and I have tried to do is look at it from, you know, what's the probability of success; what's the time; what's the opportunity cost of capital; what's the actual outlays that you make. All of those come into a kind of rate of return analysis.

MR. WROBLEWSKI: Audrey, you wanted to make a point?

MS. PHILLIPS: I will leave to the economists, which I am very much not, the discussion as to exactly what goes in a return on investment on the economic side, but I do think there's an important component of that that we haven't talked about yet, and it relates to what we spoke about earlier in this panel where you asked me what are the biosimilar companies getting that's abbreviated. There's one important piece that they don't experience and doesn't go into their analyses, and that's the risk.

The risk has been accepted by the innovator early on, and the biosimilar company doesn't have to integrate that risk into their own thinking. So, when we think about what data exclusivity and what the purposes are, a significant purpose -- we think the key purpose -- is to decrease the downside risk in moving forward.

I know you're going to have a panel where you're talking about patents, and we're not going to get into that here, but just to mention that patent circumvention is a significant risk moving forward. It's a new risk. I said before that the landscape on investment decisions is changing. The status quo is what it is today. It's changed a little bit in the last month, as well as it has for all of our pocketbooks, but it is what it is

today.

We're introducing two things, two differences, for investment decisions moving forward: One is a decrease in the value, because there will be more competition on the market in the future in biosimilars, and that is something that's inherent in a biosimilar path forward, and it's one that's appropriate and makes sense and is necessary. But there is also another downside risk that's being figured into investment decisions, and that's the potential risk of patent circumvention moving forward. So, as we talk about return on investment, let's not forget that that risk at the investment decision across, as Henry has reminded us, across portfolios, to be able to also use the successes to pay for the failures, is critically important for us to keep in mind.

MR. WROBLEWSKI: Sure.

Alex?

MR. BRILL: Sure. I just wanted to -- I think to extend a little bit of what your question was. Your question was what are the costs that need to be recouped, and just to give a sense of the framework that Henry and I are working from, there's sort of two sides to the ledger in this analysis. There is the cost that is sunk up front for the development of a portfolio

product, and that -- the portfolio notion is key, because this is not just a cost of succeeding, but it includes the cost of your attempts that fail, and that is, in part, driving what makes this number $1.2 billion.

And then the other side is how are we paying off those fixed, sunk costs? And obviously it's from the sale of the drug, but what we also know is that when we're selling the drug, we can't take all of those revenues and apply them to offset our initial costs. Some of those costs -- some portion of our revenue -- of the revenue from the sales of these products go to the production of those products, and I think that that's sort of a critical estimate in any analysis, and it's one of the points that Henry and I differ on. It's one of the few points that we differ on, is what -- how we split the share of the revenues to allocate to the pay-back of the investment costs.

And you can run a sensitivity analysis on the work that I've done using a historical average of this contribution margin, and you can plug in a couple different costs of capital, and you can still see that a portfolio is likely to break even with a period of exclusivity that could be seven and considerably shorter than some of the other estimates.

MR. WROBLEWSKI: Thank you.

MR. HELDMAN: I guess I would just ask, since the whole point of -- key point of biosimilars is -- and follow-on biologics is to bring down cost, is how does -- have you done any work -- has anybody done any work that takes a look at how each year of additional exclusivity affects the price of the innovator product when it comes on the market and how do you factor price into your -- back into your analysis?

DR. GRABOWSKI: What is the question? I didn't --

MR. HELDMAN: I'm wondering, if you shorten the -- if people are discussing different lengths of data exclusivity, I'm wondering whether you think that the product will be priced differently if the data exclusivity period is seven years versus if it's ten years and how much each -- how much of a difference each year makes.

DR. GRABOWSKI: Well, I think the key driver of prices will be if you're in a market where there's competition or anticipated competition; What is the price that will be set among other therapeutic alternatives? So, I don't see the length of the expected life being the first factor. It may have some influence, but price is going to be driven by your

interaction with payers and other competitors, and that's, I think that's the first order of business.

MR. WROBLEWSKI: Let me change gears here for just a quick second --

DR. GRABOWSKI: Just to respond to Alex, you know, he indicates that you can get with reasonable contribution margins and cost of capital, but I would point out a few points that I will elaborate on in a paper, but he's drawing his contribution margin from the six most or six of the most successful biologic firms. So, it's important that you also include firms earlier in the life cycle. He's using Amgen, Genentech, Biogen to get these margins, which we will take a closer look at.

Also, his cost of capital is very much focused on the larger, established firms and doesn't really account for all of even private equity firms that have to go to the capital markets for venture capital and who have cost of capital. You know, I've been with companies that have had to do that, and you're talking about giving up significant equity and cost of capital in excess of 20 percent.

So, I think that without getting into the numbers, but there will be an exchange, and I think a balanced look at that will not support a seven-year

exclusivity period.

MR. WROBLEWSKI: Chris and the FTC developed, anticipating this discussion, if you'll look at the graph, we tried to borrow from the model that was there. If you have cumulative cash flows on the left-hand.

MR. GARMON: Net present value.

MR. WROBLEWSKI: -- net present value on the vertical axis and along the horizontal axis is time. The line is the investment, you know, as you start at the beginning of the investment period or the research and development. As you go along the line just losing, going down, investing more and more. Then, the point zero is basically when you have gotten marketing approval. And then that's where you start recouping because you're now marketing the product, and that line is, we're going to say, without competition.

Okay, so now, if there is branded competition, if it's maybe a more crowded therapeutic class or had more competitors, the line looking at it from the point of view of the innovator, that would be kind of the curve. If you had, let's say at that point, FOB entry at some point after approval, a biosimilar FOB comes in, similar to the terminology that we had used before, that's the way the curve would be. And if a biogeneric FOB came in, that's the way the curve would look.

Would that be a fair summary of the discussion in terms of if we looked at it from a break-even point of view, assuming the investment is -- you know, we had discussion of what's in that investment, but would that graph be a fair conceptual representation?

DR. GRABOWSKI: I don't know about fairness. I'm an economist.

MR. WROBLEWSKI: Efficient. Efficient.

DR. GRABOWSKI: You know, I think over time, you are going to get some convergence of those curves. As we talked earlier, there's the science and there's the reimbursement agencies, and as they get comfortable with biosimilars, that curve will shift maybe closer to what you label as a biogeneric.

I think it's fair to say if you had interchangeability, which we don't have and we don't know when we'll have it, the curve would be a little lower. I would agree with that.

MR. WROBLEWSKI: Okay.

DR. GRABOWSKI: Initially, anyway.

MR. WROBLEWSKI: Okay, thanks.

Geoff, did you have a point you wanted to raise? Then I'm going to change topics.

DR. ALLAN: Well, maybe I'm not understanding the graph, but that would strike me as it's telling me

that the innovator product never becomes cash flow positive.

MR. WROBLEWSKI: No. You become cash flow positive right when you cross the dotted horizontal line.

DR. ALLAN: Right.

MR. WROBLEWSKI: Cumulative, because that's a cumulative cash flow. You would be getting all of -- that would be the point that -- assuming an appropriate --

DR. ALLAN: Sorry. The FOB entry comes in before the product itself has become cash flow positive.

MR. WROBLEWSKI: In this example, that's exactly right. In this example, yes, that would be entry comes before it's cash flow positive.

DR. ALLAN: The only point I would make regarding that is if you looked at every biologic that's been generating sales in the last few years, the cumulative revenue of every major biologic exceeds $5 billion or more after the first five years of sales.

MR. WROBLEWSKI: Right. That's all included in the kind of the V.

MR. GARMON: Again, this is cash flow, not just revenue. This is profit.

DR. GRABOWSKI: But it's not discounted cash

flow.

MR. GARMON: This is discounted. I wasn't trying to make any specific assumptions about anything. It's just are the shapes of the curves correct.

DR. GRABOWSKI: So, these are not just dollar lines.

MR. GARMON: This is just the same kind of curves that are in your paper and in Alex's papers.

DR. GRABOWSKI: Okay, just you haven't used the word "discount."

MR. WROBLEWSKI: It is discounted.

MR. GARMON: It is net present value, and something I would also like to ask, is the correct way of -- let's see if I can get the -- is the correct way -- the correct data exclusivity period one in which the curve would essentially become asymptotic? If we could all agree on the assumptions and find the data exclusivity period that would make it so that this cumulative net present value becomes asymptotic to zero, is that the correct criteria for figuring out the data exclusivity period?

MS. URLEP: Asymptotic?

MR. BRILL: Touching the zero line but not going over.

MR. GARMON: Just approaching it over time just

to get right there so that you just break even.

DR. GRABOWSKI: Well, you know, as I mentioned, and I have some slides that can be part of the record, but when we look at seven- and ten-year exclusivity periods with the CBO assumptions, we never get convergence for 50 years. You know, maybe if we went out to 100 years, we might touch the line, but, you know, I don't think we are going to base laws on, you know, what happens after 50 years.

MR. WROBLEWSKI: Okay, thanks.

Let's change gears for one quick second, and it's really raising -- following up on a point that Rachel had made earlier this morning.

If we use this model or a recoupment model as the -- as one way to gauge the length of a data exclusivity period, does this model provide for an optimal amount of incentive for new innovation or does it reward inefficient innovation because it recoups all investment? I think she had mentioned there was a crisis in new innovative medicines. So, I wonder, is this type of model -- is this the right way to go or do we have any comments on that point?

DR. GRABOWSKI: Well, I think you're looking at this as -- again, as a complement to the patent system, and we don't want innovative medicines to sit on the

shelf. You know, if you talk to research directors, as I do on an occasional basis, they say, you know, when we look at a new molecule, we want to look at unmet medical needs; we want to look at, you know, a period that we can recoup our investment, and so forth. And if we determine either that we can't get a patent on it or the patent's too short or the patent may be vulnerable, then we put that medicine on the shelf, and we go to something else.

And so we don't want a lot of medicines that could be innovative for patients to languish because of problems with the patent system or shortcomings, and, therefore, seen in that light, I think trying to do an exclusivity period that would allow these innovative incentives to operate, even in those cases where the company determines that there's issues with the expected life, I think this provides a framework for that.

MR. WROBLEWSKI: Okay, thank you.

Alex?

MR. BRILL: Yeah. If I understood the question correctly, I mean, I think the answer is yes, it is -- it's important to include, in the development, all of the costs of those who are successful, as well as those who are not, because it's not until we get to market that we -- and, in fact, oftentimes post market -- that

we can really measure those successes.

If I could also just add, on the question about asymptotic to the zero point, I would, if I put only the theoretical economist hat on, I think that that would be the right answer, that the goal would be to come to the point that's asymptotic to zero, but this comes -- however, that's not the approach that I took in my paper.

I took what I consider a more balanced approach, similar to what Professor Grabowski undertook, which is more along the lines of the maroon or purple line, which is the biosimilar FOBs line, which is allowing for there to be profits in excess of break-even. And this comes to this balancing point question, and it's my view that it is important to encourage innovation. There's uncertainties in the model, and that this extra cushion, which is the -- in some sense, it's cream on top, but it may be important to the investors.

And as Henry just mentioned, one of the criteria in the investment decision is not just will we break even, but the question is also when, and the paper and the results that I released earlier this week, under those specifications, a seven-year data exclusivity period has a fairly modest impact on the point at which break-even occurs, and that may be important to

investors, not just that they get their money back, but the duration. If that's a critical factor, then you wouldn't want to just be asymptotic to zero, but sort of from a pure cash flow analysis, it would be.

MR. WROBLEWSKI: Did you want to add something? Your thing's up.

Okay --

DR. GRABOWSKI: Oh, sorry.

MR. WROBLEWSKI: Okay, that's an old one.

If we're using -- are there other policies that could be used to encourage R&D, such as, you know, tax credits for investments rather than a data exclusivity period, and would that be more inefficient or more efficient than using a recoupment model?

DR. GRABOWSKI: Well, I think tax credits are always useful in things like the Orphan Drug Act has played a role, but also the market exclusivity was even more critical to many companies than the Orphan Drug Act. You know, I think the issue with tax credits, everyone is besieging Congress for tax credits, and -- you know, chemo prevention drugs and much broader than pharmaceuticals. So, when you do tax credits, you get into further CBO scoring. You know, I think it's a welcome incentive, but then you're competing with, you know, food stamps and everything that's in the budget.

MR. WROBLEWSKI: Okay, thank you.

Alex?

MR. BRILL: The politics are certainly something it's important to consider, but it's, in my view, no question that the Tax Code is interacting with this process here, and not just are credits a way to offset some of the cost that's trying to be recouped, but I think more importantly and more broadly, the Tax Code imposes a tax on capital which raises that cost.

I don't want to go too far afield into the world of tax, but the structure, including the very concept of a corporate income tax, is affecting the cost of capital, and that is affecting the decision processes for the investments, and that's -- that is part of what will be affecting the -- you know, the decision to innovate.

MR. WROBLEWSKI: Thank you.

You know, in Linda's presentation, she talked about how the European approach has been an eight plus two plus one, and the plus two was for -- plus one was for additional indications -- yeah, I think --

MS. HORTON: Do you want me to explain again?

MR. WROBLEWSKI: No, I was just verifying that plus one was for additional indications. What type of incentive is necessary if we do a data exclusivity

period in the U.S.? How do you determine what that plus should be? How much time? Do you look at the R&D expenditures for post-approval R&D and then kind of try to figure out what that is and then try to put a year to it, so to speak, and then add that on? How's the best way to go about doing that?

DR. GRABOWSKI: I think all of the bills that are -- say a plus one or two or three years in some bills for products that the FDA just deems as clinically significant. So, there will be a novelty test, first of all, on the indication.

Then, I think you -- it's fair to say that some -- some investment or some reward for the additional investment is appropriate for clinically significant new indications, and a biologic that's particularly rich with this -- you know, you go down one pathway, and then you discover it affects all kinds of other indications. Jack Calfey at AEI has discussed that process, and there's just a very rich kind of pathway for new indications in oncology and several other things. And I think the investment decision would weigh in to try to pick that one, but also the novelty will weigh into it, as well.

MR. WROBLEWSKI: Okay, thank you.

Linda, did you want to add something?

MS. HORTON: Yeah. I just wanted to say that this appears to be a somewhat difficult area of policy-making. If you look at the submissions to your docket, very few companies kind of gave you a number on this, and I suspect it will end up being a large issue in the coming debate, but I just wanted to say, you know, again, you know, coming from the FDA background, that -- where I worked for a long time, the FDA views the -- each new indication as being a new, distinct new drug or biologic, as the case may be.

It's true that the data package for -- the part of the data package dealing with chemistry and manufacturing and some of the basic safety is referred to -- you know, the company's referring to its own earlier data set when it comes along with a new indication, but there's a lot of clinical data that must be generated by the innovator company to support each new indication, and this needs to be recognized.

Now, this has developed into somewhat of a problem in the European system, because although the overall umbrella guidelines issued by the European Medicines Agency in late 2005 said that there would need to be studies done in each indication to support new indications, in fact, what has happened in each of the three tranches of biosimilar approvals that have come

along is that the biosimilar companies have gotten all the indications, even though they may have done studies just in one disease, and this may be unique to those proteins that were being considered, that these were among the older and, at least in some cases, better characterized proteins. But I think this will come to be an important issue.

We have several different viewpoints on the U.S. side on this issue. The letter from Secretary Levitt of June last year says FDA believes that each indication will need to have -- be supported by its own clinical studies. Biosimilar applicants cannot assume, as a matter of science, that their product qualifies for each indication the pioneer has qualified for without doing studies.

We also have some bills in Congress that try to legislate the science in this area, which also doesn't seem to be the way to go, and I think probably this is an area where maybe, you know, whether it's your docket or the Congress, I think, you know, there's need for more thought going into this, because I would just caution that we're dealing with a statute that's 106 years old, and we're dealing with an economic and scientific environment in which companies have entered this field on the belief that anybody else coming along

was going to likewise produce a full data set of their own.

So, we're kind of -- this chart, there's a very small piece there, you know, so I think this is an area where we want to tread lightly, because this has been an area of great innovation, and we don't want to disincentivise research.

MR. WROBLEWSKI: Thank you.

I am going to turn to Mateja and then Audrey, and then I will have one last question as a segue for our afternoon panelists.

MS. URLEP: Thank you.

Well, the Novartis group of companies, which Sandoz is member, we do support fully that innovation has to be incentivised. Therefore, our position is that a model on exclusivity should be taken into consideration, but on the other hand, as well, we should allow for competition when the time comes, when the patents, which are legitimate patents, expire and exclusivity is over.

And just to mention, for the European Medicines Agency, the biosimilar sponsor could argue for all of the indications where we could, as a matter of science, prove and justify that mechanism of action if each of the other indications is just the same, and, therefore,

the repetition of unnecessary trials in humans would not be necessary to be done.

MR. WROBLEWSKI: Thank you.

Audrey?

MS. PHILLIPS: I can't comment on the math. I get the impression that you want to do a mathematical kind of formula --

MR. WROBLEWSKI: I think what we were trying just to do is make sure we understood conceptually what was going on. We think that the -- kind of a model like this is informative, but there are certainly many other policy things that you have to balance. This is just one way, and there seemed to be some disagreement, so we were trying to provide some clarity around that, but that's only just one take.

MS. PHILLIPS: I can't help you with the numbers, because I really don't know what that would be or whether there really is a mathematical formula, but I will say that medicine has changed over the last ten to 15 years. Discovery and development has changed. So, if you look at products today that are coming to the market, you'll see that they are often used for a broad range of different diseases, and that wasn't true in the past or it's true to a greater degree now. So, with whatever formula you use and wherever you end up, you

need to be mindful that there needs to be that time period to invest in those new indications.

We tend to think of new indications as kind of a product improvement, but for a patient who is finally treated with rheumatoid arthritis, it doesn't matter that that's a product that had been used before only for serious GI diseases. That is just as important.

So, the -- and as you're looking at more varied indications over time, getting back again to investment, it is more expensive and more risky to go into other therapeutic fields to investigate those new indications than the one that you started in. So, there is this additional investment consideration and risk, on top of all these things, that you try to figure in. So, in the end, there needs to be that incentive, but I can't help you with the numbers on that one.

MR. WROBLEWSKI: One last -- Alex?

MR. BRILL: Just very quickly.

Like Audrey, I can't help you with the numbers on this question either, but I would just stress that there is a -- I believe a very large interaction effect between how much exclusivity is granted for a secondary indication and how much initial exclusivity is granted, that there's an important trade-off here, so that it is important, and Jack Calfey's work is important in this

area, as are Audrey's comments. These other indications are important to the market, but the more protection that's provided for those, that's a trade-off against the necessary amount of data exclusivity on the original approval.

MR. WROBLEWSKI: Okay. Thank you.

We're going to take a break. This afternoon's panels are looking at kind of the nexus between patent protection and data exclusivity and innovation. We're going to start back at 1:00.

We have a cafeteria on the seventh floor. I've hopefully prepared them better than I prepared the security office this morning for the additional people that we have in the building this morning. If you do go outside, please keep your badges. That will maybe quicken coming back in. And we'll start back at 1:00. Thank you all very much, very much.

(Whereupon, at 12:03 p.m., a lunch recess was taken.)

AFTERNOON SESSION

(1:00 p.m.)

PANEL THREE:

BIOTECHNOLOGY PATENT ISSUES

MS. DRENNON: I'm not following the first rule of moderating. I think we have enough seats for the afternoon, but if anyone wants to come and sit in the panelists' part, that is just to make sure that at the breaks we have room for everyone, so I think we're good. I think we may still have someone in the overflow room. Overflow people, if you want to come down, we have room for you. I feel like I'm calling to the greater powers, good.

So this is the afternoon session of our workshop today. I'm just going to run over the matters. Please turn off your cell phones because as we all know, that's kind of distracting sometimes. Security issues, talk to any of us. Bathrooms, I assume that every one knows where they are. If you're new and need some help, grab Elizabeth Jex. She's sitting right in the front raising her hand, and she will help you out. I will help you out. We'll all help you out, excellent. Okay.

My name is Suzanne Drennon, and I am an attorney with the Federal Trade Commission's Bureau of Competition, Office of Policy and Coordination.

Welcome to today's roundtable discussion on biotechnology patent issues. With me today is my boss, so no pressure, my co-moderator, as we're calling her today, is Suzanne Michel. She is the Assistant Director of Policy with the Federal Trade Commission's Bureau of Competition Office of Policy and Coordination.

And before we begin our roundtable today, I would like to introduce our distinguished and expert participants for this afternoon session. I'm only going to give their names and affiliations, but their full bios are in your packets so you have those as well.

We have Ken Dow. Ken is the assistant patent counsel for Johnson & Johnson. Next to him, we keep the Kens together, we have Ken Goldman. He is the vice president of intellectual property strategies for Novartis International AG. Ester Kepplinger is sitting next to me now. You are the director of patent operations at Wilson Sonsini.

Jeff Kushan is a partner with Sidley & Austin. Bruce Leicher is the senior vice president and general counsel for Momenta Pharmaceuticals. David Manspeizer is the vice president for intellectual property and the associate general counsel for Wyeth.

Doug Norman is general counsel, patent counsel for Eli Lilly & Company. Naomi Pearce is IP director

and counsel for Hospira, and Rochelle Seide is senior counsel for Schwegman Lundberg.

So thank you all for joining us today, and we will be comoderating, but Suzanne is going to lead with the questions.

MS. MICHEL: Thank you. Thank you, and thank you for inviting me to moderate, which she really did not have to do.

The objective for this afternoon's session is to examine the differences between biotech and small molecule patents. To do that, we've put the objectives up on the slide there for you. We are going to consider both the differences between the biotech and small molecule patents, but also consider the relationships between the biotech patents and data exclusivity periods.

During this session, we're going to discuss four questions. I'll lay them out first, and then we will go through them one at a time.

First, are patents and patent portfolios claiming biologic drug products different from patents claiming small molecule drug patents, small molecules, and if so how?

In a second but related issue we will consider the susceptibility of biotech patents to infringement

and validity challenges. For instance, what are the issues that are being litigated in biotech patents and how do they differ from other industries?

Third, we'll talk about how an innovator's biotechnology patents preclude competition from either biosimilar follow-on biologic or a biogeneric follow-on biologic.

Finally, do the existing patent protection rights including patent term restoration help cover the investment in follow-on biologics and the relied upon data?

Well, let's start first with the first question. Like this morning, this afternoon's panels will be moderated discussions. I will pose a question, and if anyone would like to address that question, please just turn your name tent on its end, and we'll call on you to speak.

For the next 15 minutes, let's talk about the facts surrounding biologic and small molecule patents. How are the patent portfolios claiming biologic drug products different from the patent portfolios that claim small molecules? Jeff, would you like to start with that?

MR. KUSHAN: Sure. I'm going to start, and I'm sure we're going to have a lot of contributions because

the patent estates are always complicated.

I guess you can look at a biotech patent estate as implicating a few different types of patents. You will have a number of patents that derive from the initial discovery of a sequence. This will be a polypeptide sequence coating an interest, a protein of interest.

Around that you will see complimentary inventions of the nucleic acids and sequencing codes and post cells that have been transformed to produce that, things that are made against that such as a monoclonal antibody that have been produced against the protein.

This is an array I guess, the way I look at it is as kind of an initial wave of related technologies off of a first discovery. As you look at the development of the technology over time, you see additional portfolios of patents.

Some patents come into play because they are kind of generic techniques that are used to make proteins. Those can be more or less independent of the sequence that you're working with, but they're more platform technologies that have been license generally that cover many different approaches of making the protein.

You will see techniques for developing

specialized versions or improved versions of a protein, so, for example, if you have an initial wave of effort that produces a monoclonal antibody, effort will go on toward optimizing that monoclonal antibody, binding properties, profile and characteristics.

You will see an array of process technologies that evolve around making these proteins, in particular the specific one that may be from a candidate for a drug product.

Then there are an array of other technologies that are developed as you're moving forward. You find out typically the thing that drives you to do their initial research isn't the mechanism and the cell that you're trying to exploit or influence. As you do more research, you will find how to exploit that to treat different things so you can find additional applications of treatment methods and things of that nature.

Then as you're moving closer to the market, you will see some analogous technologies or analogous patenting strategies around -- compared to the small molecule drugs where you're trying to make an optimized formulation and how to deliver the drug as a viable product.

If I had to look at that and contrast it to the small molecule area, typically you will find an active

molecule, and then you will do some research to find out what a reasonable group of related compounds are to that that you can then base a patent on. There's a lot of processing technology in the small molecule space as well, but in terms of how that connects into the overall regulatory process is less important relative to the biologics.

Biologics obviously have a very important element of how they're made tied to what the basis of approval is. In the small molecule space, you will see less dependence on how the particular molecule is made. Often it's important but it doesn't form part of the approval conditions for the product.

Analogous to the biologics area, you will also see in the small molecule patents space new applications. Once you figure out what the molecule is doing in the body, you can see how to exploit that to treat new indications, new diseases, but I guess if I had to kind of distill it down, in that initial wave of activity around the biologic, you will see a few different reflections of the inventive activity.

You will see the nucleic acid sequence, the protein, the whole cell that makes it, things that are derived making the protein at the initial outset, whereas kind of the core innovative element in the NDA

space would be the molecule and what its biologic properties might be.

MS. MICHEL: So if I wanted to draw an analogy, core patents and small molecules are I think of as the active ingredient patent, the core molecule then for a biotech drug would be the protein?

MR. KUSHAN: Yes and no. So if you find the protein that is a receptor on a cell, sometimes that might be the thing you want to give people as a therapeutic, but many times it's not, so a lot of times you're going to want to make something that blocks whatever normally binds that receptor in the cell or mimics what should be binding to that receptor in the cell.

So your therapeutic might become the thing that is made that modulates a behavior that the receptor is involved in. So it's not necessarily the thing that you first find that becomes the agent. I guess in the early days, the kind of low hanging fruit in the biotech area was the hormones and the things that you find in your bloodstream. Take those proteins, and you make them using biologics techniques. Now you're doing it on different approaches.

MS. MICHEL: Great, we have an invention.

MR. KUSHAN: I'm turning off my mike.

MS. MICHEL: Well, let's start with Naomi then, and we're trying to also draw out -- that was extremely helpful to layout that background, I think, and we're also trying to draw out to understand better how patents operate differently in protecting biotech products from small molecule products, so whatever you can contribute to that, we would very much appreciate.

MS. PEARCE: Thanks very much, Suzanne. Hospira is happy to be involved in this discussion today. Hospira, as you've always heard this morning, a specialist injectable pharmaceutical company, which is the first U.S. based company that has launched Retacrit, Albaicin (phonetic) into Europe.

We structure our IP group so that a person who is responsible for a product clears the product on a global basis. I'm the IP director for biopharmaceuticals, and so I'm personally responsible for ensuring that each biopharmaceutical product that Hospira has an interest in is cleared global, and so I am as qualified to speak to the position in the U.S. as I am in Europe and Australia and Canada and Asia, et cetera. So thanks for the opportunity for being part of this discussion today.

So firstly, I agree with Jeff's summary about the complexity of the patent landscape, and I think we

sort of saw a nice slide this morning from Rachel setting out the differences in structure between a small molecule and a biopharmaceutical molecule. I think it's great. It's great to at least be able to pictorially see they look nothing alike, and there are complexities involved in the biopharmaceutical space that do not equate -- that there is no equivalent in the small molecule space. I think we'll all agree to that.

I also agree which Jeff's summary of the importance of process patents in the biopharmaceutical summary although I think my take on it is slightly different.

Certainly I agree that the process patent has elevated importance, and it will continue to have elevated importance in litigation space moving forward, but the reason is mostly due to the immaturity of the biopharmaceutical industry compared to the pharmaceutical industry. Hospira of course has a presence in both of those.

In the small molecule space, a process patent is generally circumventable because the industry is mature enough to have created a number of ways to circumvent such a patent. However, the biopharmaceutical industry globally is immature, and there may not be another commercially appropriate way to circumvent a process

patent.

I am not saying it's impossible to circumvent, but I am saying it's quite difficult, so compared to the small molecule space where it is unlikely or in most cases a process patent would not be a market entry barrier, in the biopharmaceutical space, it may very well be.

MS. MICHEL: Isn't that also because the process affects the product more when you're dealing with biologic molecules rather than small molecules?

MS. PEARCE: As a matter of theory, there may well be many ways to make a product that is identical, but as a matter of practice, because the industry is immature, industry has -- technology has not yet created those many ways in the biopharm space as compared to the pharmaceutical space. So that is the first main difference that I think we see.

The second main difference is a practical difference, and so in the small molecule space, it is extremely rare to see patent term adjustments. We see patent term extensions, which is of course a quid pro quo for regulatory delay, but we do not see patent term adjustments routinely, which is a quid pro quo for prosecution delay.

In the biopharmaceutical space, that is simply

not the case. We see patent extensions, but we also routinely see patent term adjustments, so if you look at -- if you take the top three selling small molecule injectable oncology drugs, there is no patent which has received a patent term adjustment for those three molecules.

If you take the equivalent top selling biopharmaceutical molecules in the oncology space, you will see an average between four -- somewhere between four and 15 patents which have received a patent term adjustment, and the period of that adjustment is on average just under one year, the maximum being just under four years. So it's a second important defense in this space.

The third important difference is the existence of submarine patents being fairly routine in Hospira's experience in the biopharmaceutical space.

Now, we all would agree that submarine patents being patents that are not published until grant. A theoretical risk, the small molecule products, as much as they are a theoretical risk for the biopharmaceutical products, but in Hospira's experience, every single biopharmaceutical product that we have looked at, there are submarine patents in effect.

Now, that may be because they have been granted

and because they have a 17 year period from grant because they'll get pre get filed, or it may well be because we found out information that there are pending submarine patents, so it's something that in practice really affects the biopharmaceutical space in a way that it does not affect the small molecule space. That's as a result of the complicated and complex prosecution history of a complicated and complex industry.

MS. MICHEL: All right. Thank you. David? I think we'll go around the table, just to warn you.

MR. MANSPEIZER: Well, there's a lot to choose from there. Let me start by saying that patents don't provide certainty, and that's something we'll get to later in this discussion about what kind of certainty is needed in order to encourage innovation and to properly balance competition and innovation, but biotech patents provide even less certainty than small molecule patents do.

One of the reasons they do, particularly when we're talking about potential biosimilar legislation, is we don't know what exactly the legal and regulatory schemes will permit in terms of adjustment to the product. When I say the product, I mean the innovator product, which is typically defined in our patents by its aminoacid sequence.

Now, if the biosimilar product has to have amino acid sequence identity to my product, then the patents that I own will likely be stronger from infringement standpoint, and I'm not talking validity.

At the same time, if I can change one amino acid, two amino acids, five amino acids, ten amino acids in this very large molecule and yet still be able to argue that I have an equivalent molecule or molecule that has biosimilar activity, then the patents that I own that cover my product are less likely, a lot less likely to be able to be enforced against the biosimilar product.

MS. MICHEL: You're suggesting that the scope of the claim is limited to the exact aminoacid sequence then aren't you?

MR. MANSPEIZER: I am suggesting that we don't see, as we see in small molecule claims -- and let's concentrate on the claim that covers the API. In a small molecule case, typically you will have a claim that covers the precise molecule. You will have a claim that covers a genus surrounding that molecule, and maybe a million compounds around that molecule.

When you try to do that in the biotech space, and there's people here more able to speak to that than I am, you run afoul of both the enablement and the

written description requirements of Section 112, and they render -- the Patent Office simply won't give you the claims of that scope.

The other thing that's very important to remember is, and somebody said it this morning, we're designing a system today that really is going to have very little impact on what happened already. That innovation has happened. Those patents have been filed. The research dollars have been invested. We've got to remember that the biggest impact of what we do, whether it's in the patent system or in the bid exclusivity, is on the future.

It's not on EPO and Enbrel and Remicade that the enormous impact is going to be. It's on the drugs that are bubbling up through small companies and large companies' labs today and the ones that haven't bubbled up yet. That's where the major impact of this legislation is going to be.

MS. MICHEL: Thank you. Rochelle, and also everyone else, I am trying to understand better this issue of the scope of the claims and how it will impact the infringement analysis, and in particular, I don't mean to limit your comments, so please add more to what I'm saying here, but I am trying to understand to what extent claims are limited to only the sequence claimed

or to what extent they might also cover protein that has ten different amino acids because it's not clear to me that the claim would exclude those minor differences.

MS. SEIDE: I'll be happy to explain that to you. I've been practicing in this area for almost 23 years, and the kinds of claims I could get now on a biologic are vastly different from what I could have done in the mid '80s to early '90s in regard to the scope of the claims.

And, I mean, probably patents that we've all sitting around this table obtained for clients in those days may be rendered invalid now if they get litigated. If they're still in existence they would probably be rendered invalid.

The reason, and when I was talking to Suzanne about this awhile back, there seemed to have been a perception that patents on biotech products were weaker, and that's not really the right term. They're not weaker. They're narrower, and again to reiterate what they have said, that you almost get what you have exemplified.

If you file a patent application now, and you are sort of forced to, in some cases, filing very early, and you may not have 25 examples of what you're trying to claim to get a genus claim. You have one. Maybe

along the way you get two or three.

You've been forced into it by decisions of the Court of Appeals For the Federal Circuit and the Patent and Trademark Office taking those decisions and making things narrower and narrower to what's allowed and then what you can actually litigate at a later time.

You're sort of forced into getting a claim that's almost what we would call a snapshot claim. It's a picture claim. You've identified a protein or an antibody, and it has a particular activity or a particular sequence or you've characterized it. You've humanized it. You've done a variety of things to it, and you set that up, and you've exemplified it in your application, and you get a patent out of it.

You only get a patent on pretty much what you've exemplified because the court considers this very unpredictable technology. They consider chemistry unpredictable technology, but biotech is really unpredictable.

MS. MICHEL: I think you're referring to the 112 enablement.

MS. SEIDE: I'm referring both to 112 enablement and 112 written description, both of which are at play.

MS. DRENNON: One of the questions I have with respect to the narrowness point you're making is: How

does the narrowness of the patent effect the strength of the patent?

MS. SEIDE: It's not the -- the narrowness of it is exactly what David said. If you have and all you get is a claim to a particular protein with a particular sequence, let's just exemplify with a protein, and say the biosimilar comes along, and it has an amino acid difference or two amino acid differences.

Back in the day, a few number of years ago, you might be able to litigate against a company that makes the biosimilar, and argue maybe not literal infringement but infringement under the Doctrine of Equivalence, which said it didn't have to be identical, but it had to have enough similarity to say being the same invention or a pretty similar invention, and the court had set out a test for it.

That has been severely curtailed over the last ten years by decisions of the Supreme Court and the Federal Circuit taking that to heart, saying that you cannot broaden out the scope of the patent at all to cover the equivalent.

So you're sort of hammered on both sides. You can't get the claim in the first place that's broad, and once you get the claim, you can't litigate it against something that's not absolutely identical.

MS. MICHEL: All right. And Doug?

MR. NORMAN: I'll try to be pretty quick. Thanks for inviting us here today. I look at small molecule drug patents, and actually if you think of small molecule, the chemical compound itself is something that always looks like chicken wire, so it's got a methyl on one end and maybe an ethyl on the other, but it's going to look like methyl ethyl chicken wire, and everybody that makes that molecule and puts it in a pill and tries to sell it is going to make methyl ethyl, and you're always going to be able to catch them for infringement.

If we look at biologic patents, we have to look at two different things. First of all, there are two types of biotechnologies that we're talking about. There are sort of the old biotechnology products, let's talk about human growth hormone, parathyroid hormone insulin, that look a lot like methyl ethyl chicken wire. They have a primary aminoacid sequence, and it looks the same way every time you make it.

And so you can get a patent on that, if you meet all the other requirements that you have under the patent law, and you can catch any infringer who is making insulin or human growth hormone or parathyroid hormone and you can always find that.

The more difficult aspect of all of this are from some of the larger sort of huge molecules that one would find, like a erythropoietin or human protein C, big blood proteins where you may know the primary aminoacid sequence, but when you go to manufacture that drug, you can never make it perfectly.

There's no way that any biotechnologist in the world can make that exactly how it's produced in the human body, so the front end of the molecule may be clipped off 40 percent of the time. The back end may be clipped off 5 percent of the time. You may have cross linkages that didn't quite work. You may have post translational modifications. You may have sugar molecules attached to it in different ways, all dependent upon the way you manufacture it, and that's how the FDA regulates those large molecules is by defining that manufacturing process.

We in the innovator industry, when we're trying to get life saving drugs on the market, have the time and the resources to figure out how to do that once, and we put together a cell line, and we put together a manufacturing process, and we put together a patent portfolio to try to protect the way we're going about doing it.

The weakness in the biotech patenting scheme

that we look at now is the fact that anyone, given the guidepost that we have laid out, we've already hacked away through the jungle, but many other people can follow along behind. They can walk through the trail we've made. They can ride a horse through the trail we've made. They can ride a mule or they can ride a motorcycle. They can find a dozen different ways to make the same sort of molecule that will not fall within the scope of the patent that we have made.

Therefore, that's why we look at trying to find some sort of data package exclusivity regime whereby we can have certainty when we're going to invest 1.4 billion dollars in the production of a molecule, we can protect that on something better than a break even aspect.

MS. MICHEL: What about the patent means that the follow-on product is not going to fall within the scope of that patent? Is it because the claim literally covers only exactly the aminoacid sequence cited, or is it something -- getting beyond the 112 issues, I'm trying to just get at the infringement analysis issue.

MR. NORMAN: Many times by the time you're on the market with your molecule, your initial primary patent has expired because it often takes that long, and so you're trying to product a claim around a molecule

that's posttranslationally modified or which has to be defined in some way by the way that it is manufactured.

And that is a major weakness in the current regime we have trying to rely upon any sort of patent is because we generally only expend the resources to get patent rights that cover the way we manufacture the molecule. We don't spend another several hundred million dollars trying to get patents on the way someone else may also try to make an equivalent product.

MS. MICHEL: Your non-infringement argument seems to focus more on the idea that different processes could be used to make biosimilar molecules.

MR. NORMAN: Sure.

MS. MICHEL: And your argument seems less dependent on the fact that a protein patent would not cover an amino acid sequence that was essentially ten amino acids different, not cover a protein that was simply ten amino acids different.

MR. NORMAN: Right. That would be another infringement analysis.

MS. MICHEL: Thank you. Let's go to Ester.

MS. KEPPLINGER: Well, I spent the bulk of my career at the Patent and Trademark Office, and as Rochelle said, I'm sure if I look at the patents that I granted or Jeff when he was there, they are now being

attacked or litigated under a different set of criteria than when we examined them.

At the time we examined some of those old biotech applications, the current written description requirement did not exist as the way the Fed Circuit has applied it. An enablement requirement was there, but that too has changed over the years.

So some of the old patents that were examined and that were granted in the old days and are now being litigated were broader patents, so they are much more vulnerable in the litigation because of the Federal Circuit decisions that have come out in the meantime.

MS. MICHEL: Ester, a quick questions about that. Most patents include a range of claims from broad to narrow. Is it necessarily all the claims that are susceptible to a 112 attack or just the more broad claims in a patent?

MS. KEPPLINGER: Well, it varies but, yes, there are typically a range of patents, but the way the Patent Office now is applying the written description requirements, it is very difficult to get much scope at all around what you show.

And they recently -- the Patent Office recently put out new written description guidelines, so you're caught between -- if you have a sequence of certain

number of amino acids and you try to get a percent identity or something that says, I'm claiming everything that's with 85 percent like this, they're saying that that would meet written description, but what they don't say is it won't meet enablement.

Then if you put the function, you say this particular protein and, oh, by the way it does this particular function, then they're saying that you have not -- you probably will not have met written description because you have not identified enough of the molecules that are within that genus that actually have that function.

So it is very difficult to get any kind of scope. Additionally, one other point I wanted to make with respect to the PTA, the patent term adjustment. The patent term adjustment is, of course, for any delays during the prosecution of the application, and patent term adjustments are relatively recent, but they are becoming somewhat significant because of the backlog at the Patent and Trademark Office, so there are a number of times that the office doesn't pick the case up at the time it should.

I would think that this would apply to both biotech and to the small molecule applications as they move forward. It just depends on how many applications

are there, how many examiners they have that are available to act on them.

MS. MICHEL: Follow-up one question there. I thought I did hear you say that a claim to a protein is going to have some breadth beyond the exact aminoacid sequence decided there.

MS. KEPPLINGER: Well, it depends. Obviously that's everybody's objective, to get some kind of scope, but it's not easy to get.

MS. MICHEL: It's not easy to get in terms of getting the Patent Office to grant?

MS. KEPPLINGER: Yes. As I say, in the old days you could get scope. We gave out patents with scope, but the way the Fed Circuit has been moving, they are not -- well, I think you did. They were not -- they are not permitting you much scope without significant additional showings of other exact compounds that will work.

MS. MICHEL: I understand, and I don't mean to belabor this point. A lot of the 112 cases out there like the Carnegie Mellon case from last month was about -- you've made a showing in E. Coli, are you then going to get the rights. It's like a whole other -- and I'm trying to understand the importance of that doctrine to other types of claims, and Jeff actually wants to say

something. Sorry to skip you, Bruce.

MR. KUSHAN: I'll be very brief. I just want to make sure you understand it's not that simple.

MS. MICHEL: Okay, thank you.

MR. KUSHAN: Because when you look at a claim scope question, you have to look at the scientific context of the molecule, so sometimes you can have these three domains of a protein in any protein and it will do the same thing, and in other protein, you can make one change to one residue, and it doesn't do like the one, so don't disassociate the scientific foundation of the discussion from the legal foundation.

A lot of the claim scope turns on the nature of the class of proteins you're dealing with.

MS. MICHEL: All right. I skipped Bruce, and I apologize. So let's go to Bruce.

MS. KEPPLINGER: If I can just say one thing. One of the things that the Patent Office is looking for is just that, structure function relationship.

MS. MICHEL: Thanks.

MR. LEICHER: I may be coming at this from probably a different perspective, which is -- and I'll take it back to what Jeff was saying at the beginning. If you look at small molecules, a particular small molecule may, as I think David was saying, in some ways

have a stronger opportunity for protection over the validity, but a small molecule hits on a target, and there are many, many other molecules that may hit on the same target.

So that they don't really provide the breath in that respect of protection that you often have in the biotechnology area. If you look at -- and I think we're all doing the economic analyses this morning based on what's going to happen in the next ten years, but then we're switching the patent analysis to what's going to happen 30 years from now, and I'm not sure that's necessarily -- it may be mixing apples and originals.

If you look at the existing set of -- I'll cite a few examples of products that are out there today and the types of claims they have, I'm not going to opine as to whether they're valid, invalid or whatever. If you look at something like Avinex, it claims on its face that it's not limited to specific sequences, and those patents are out there.

If you look at Rotoxin, it's something that covers on its face any antibody that binds to a particular receptor, so what you're doing and what historically was done in biotech is you look for a way, and it's what Jeff described, of patenting as much of the patentable invention that covers as much of the

biology as possible so that you can give yourself the greatest protection as possible.

And from my perspective, what that means is it's actually much broader protection for biotechnology patents. That doesn't mean there's uncertainty, but there's broader protection, and if you look at the track record of what's happened in the marketplace, which I think is what's important, you have products like EPO that were patented back in 1984 that are still keeping competition out today in the U.S.

MS. SEIDE: That's a unique situation, EPO. That's a pre GATT case, and I think the whole issue -- we're not going to have a lot of GATT like or I mean EPO like or maybe Neupogen like cases going forward because we're going to --

MR. LEICHER: No, I recognize the GATT issue there.

MS. SEIDE: That's a different issue.

MR. LEICHER: The point being that if there are all these patents out there today, there's no mechanism absent some change in adopting a pathway for people to challenge them early.

One of the reasons there's data exclusivity in Europe that goes eight plus two plus one is there's opportunity under the Europe system to deal with patents

that are uncertain, and so let me just make one last point, which is one of the compromises that was struck in 1984 with Hatch-Waxman was to trade-off the patent term extension for some of the advantages of being able to challenge patents early and some certainty with the patent system.

Biologics got the benefit, and we all did in the biotech industry, of those patent term extensions. We got the quid without the quo, and that seems like there's a need for remedy here.

MS. MICHEL: And before I move to Ken, another topic in this area, and don't feel that you have to address this just because I'm raising it now, but we've talked a lot about the 112 issues, the enablement and written description requirement issues.

If anyone was able to address what that meant for obviousness and other issues of validity, I think that would be interesting in that I think there's at least an argument that if you have a very narrow patent in a unpredictable art, you therefore have a patent that is not very susceptible to an obviousness challenge.

Another topic, so if anyone could address that, that would be interesting. I'm going to move on --

MS. SEIDE: I can address -- I think I can address that.

MS. MICHEL: Let me go to Ken.

MS. SEIDE: Go ahead.

MS. MICHEL: Unless in a somewhat different issue, but I think it's been encompassed in some of the points we've been discussing is trying to understand why the narrowness of biotech patents creates an infringement problem for follow-on biologics, which you think would be molecules that would have very similar structure and identical function.

So I understand the 112 problem in biotech. I need more input on to why it's an issue for follow-on biologics.

MR. GOLDMAN: I think you're absolutely right. I don't believe -- I think it's an issue for patent law, not an issue for follow-on biologics. Clearly what we've seen from everyone on this panel is that the biotech patent law is a complex and difficult area to understand, and everyone has their own viewpoint.

I certainly would agree with Rochelle and Ester and would agree that patents have been narrowed, the scope of biotech patent claims have been narrowed in the past ten years very much more than what we saw in the '80s and '90s.

I also, since we're back on this side of the table, would also agree with Jeffrey that biotech

patents in another sense are far more broad since they cover what may be a receptor that the patent might encompass claims for antagonists to treat diseases that are caused by over-activity, and they might also treat diseases that are with agonists that are caused by suppression of that receptor.

They might cover diagnostics, research tools, manufacturing platforms, and there's so many different areas that one -- that can be covered by one patent as well as I think Jeffrey mentioned another others, that there's an incredible array of rights that are available and out of one single invention, so it's a very complex issue.

I'm not sure that a regime that's going to deal with follow-on biologics, which are highly similar under the comparability standards as put forth by the FDA in 1996 and the ICH guidelines is the right place to address those kinds of issues.

I also wanted to address one thing that Bruce just said which is about the patent term extension. I believe that the patent term extension was a quid pro quo, and the quo was the 271(E)(1) research use exemption. So there was a quid and a quo there I think. It's not the Paragraph IV certification stuff that was the quo.

So I know we're running late, and I'll try -- there's a couple points I wanted to say. I agree with Naomi that one of the most important things that need to be done in any sort of development of a product, whether it be follow-on or innovator, is to have these freedom of operation studies done, and they're very complex and they're very difficult, and it's very important for a company like Hospira.

I've been a patent attorney for 20 years, 16 years in-house. I can't remember a single project that I worked on that didn't have that type of analysis, even for the innovator; in other words, the detailed freedom of operation, and there's always going to be risks associated with products, whether they be innovative products or follow-on biologics, so I don't think that that issue is particular to follow-on biologics.

So all of this I think points towards nothing particular about follow-on biologics, you know, changes the patents, requires a change in the patent scheme as part of the legislation.

MS. MICHEL: Thank you. And Ken Dow?

MR. DOW: I just have a couple things to add to what's been said. I've been working on biologics for the past ten years at Centocor, trying to obtain patents on biologics in this area, and I do agree that I think

that over the past ten years, it's become more difficult over time to satisfy the written description and enablement requirements and get the kinds of breadth of claims that we were able to get years ago, and there's a lot of reasons for that.

I think a lot has to do with the change in the law and the guidance that we've gotten from the Federal Circuit, and the other thing, the other reason for that is because in the small molecule area when you have a target or you have an initial pharmaco for it, it's easy to crank out a lot of compounds around that that can support a broad genous.

It's not that easy with large molecules to make so many variance, and we're starting to be able to do a little bit of that, but it's much more difficult to make the kinds of variance that would give -- that would support a broader claim and would support that written description and enablement requirement.

To be sure, we will go in there, and in our first instance we will try to get as broad a claims as we can. We'll put functional claims limitations in there. We'll try to get homology claims. We will do all that, but we get beaten back in the Patent Office, and in the process of cutting back our claims, we then surrender any kinds of Doctrine of Equivalence that we

might want to get in the courts because of recent cases, prosecution history estoppel.

So when you combine that with a similarity standard for biosimilars, it seems to me you're opening the door for design-arounds that make it very difficult for us to predict whether the patents are going to prevent competition.

MS. PEARCE: I would like to make a couple of comments to that, if I may. Firstly, I would just like to address a comment that Doug has made.

In my experience, in Hospira's experience, it is simply not correct that by the time a biopharmaceutical reaches the market, that its sequence patent has expired. If you take again the top three selling bio oncology products that were referred to earlier in this panel, the time between the sequence patent's earliest priority date and sale in the U.S. is seven years, seven years and five years.

MR. NORMAN: All pre GATT.

MS. PEARCE: Simply not correct.

MR. NORMAN: All pre GATT.

MS. PEARCE: But that's the difference between launch and priority date. It's not the difference between patent expiry or grant, priority date earliest invention of the sequence itself.

The second point I would like to make is that I agree with Bruce that it's simply not correct to say that these patents, especially -- if we're talking about an EPO sequence patent, which has been referred to a number of times in the panel today, of course there are small the biopharmaceutical patents, products, full sequence information that's patented out there.

For the large monoclonal antibiotics, it's simply not correct to suggest that there is a full sequence. What is generally patented in this space is CDRs, and the CDR is approximately 12 percent of the light chain of the molecule or 7 to 9 percent of the heavy chain of the molecule.

It's simply not correct to say that that full sequence is what is getting granted here, and when I look at obtaining clearance in this space, you are looking at the CDRs, and it covers any other part of the molecule. Any point in mutation that I would like to make outside of that will still infringe that.

I think it's important to say that a minor and immaterial sequence change is very likely to expose a follow-on biologic to an infringement risk, if it is material, then it's going to be patentable of course.

MS. MICHEL: And we'll go to David, and in discussing this very interesting conversation, and we

can go a little past two I've been told, I will throw another point out there, so please say whatever you were going to say, and if you can respond, that's great too.

It sounds like some of this debate is really turning on a question of how similar does a follow-on biologic have to be that even if we all agreed about the scope of the patents and to some extent whether or not those patents are of sufficient protection is going to turn on how different, and we've been using the word similar -- but how similar or different can the follow-on biologic be? What is going to be the ability of that follow-on product to go outside the scope of that claim.

That's something that we haven't addressed, if anyone has a thought on that, in order to talk about how well existing patent rights cover the investment in the innovative product. Maybe it's unanswerable.

MR. MANSPEIZER: Well, I don't think that any of us have that expertise, but perhaps if our FDA representatives are still here, maybe we can ask them, but to get back to the crux of the matter is again: Do patents provide the necessary certainty that people need to make the enormous investments in R&D? Whether we're talking about $1.2B, $1.4B or $700B, God forbid, the point is that patents are by definition uncertain.

There is no certainty.

We see that in the small molecule space. We will see that in a biosimilar space, and I don't think that anybody would debate that, and whether you're on the innovator side or the biosimilar side, everybody's going to agree that patents are by definition uncertain.

Once you accept that, you have to realize that in order to allow this industry to continue to thrive, you need to strike an appropriate balance between competition and invasion, and I'm not just speaking about the competition between the innovator company and the biosimilar filer.

I'm talking about competition between innovator companies. I'm talking about the kind of innovation we see where -- with sufficient data exclusivity, as you see today in the biologics area but as you're seeing a lot less in the small molecule area where drugs, proteins are being used outside of their original therapeutic area or even we see it with a lot of the monoclonal antibiotics where originally this was a product that was approved for the treatment of breast cancer, and then there's studies on lungs cancer and renal cancer and brain cancer, and the public benefits in the end from those studies.

Nobody is saying that that should go on forever.

That's not an appropriate balance. We need to find what is the appropriate balance that will protect both sides and benefit the public, but benefit the public both by providing the proper incentive to innovate, and the benefit of low cost drugs.

MS. MICHEL: Thank you. It looks like we'll have time to go around the table one more time, and we'll try to pace ourselves to do that over about a ten-minute timeframe. Hopefully that's a doable thing. Rochelle?

MS. SEIDE: Well, I want to address a couple of the points that were made, one of which is: We talked earlier, and I want to say what David said, most of the litigation that has been in the biotech sphere has not been between an innovator and a generic. It's between innovator and innovator.

Doug and I were talking about way back when, and we mentioned there are eight growth hormones on the market. The growth hormone patents are among the most litigated biotech patents that ever came down the pike. I mean, they were subject to litigation for 15, 20 years almost. Same thing with EPO, it's a different situation but there are eight growth hormone products on the market. It's not precluded entry of -- ultimately entry of other competing products.

The other aspect that I want to address that Bruce mentioned about breadth of claim, yes, you can get lots of different, kinds of claims around a biotech invention. You can get a research tool.

Research tools, you know, I mean, they don't have -- I would say they don't have a lot of value. I mean, one person's product may be another person's tool depending on how you use it. Certainly there are a lot of targets that are druggable targets that are patented, either on the DNA side or on the protein side, and certainly innovator companies, I've come to clear a lot of them for innovator companies because there are patents that are held by universities or small companies, technology companies that have target patents, and they're looking to develop a small molecule that will interact with these targets.

That hasn't precluded that kind of research either because you're protected by the research exemption for a long period of time, until you're on the market, and you may even be protected until the patent expires to some extent, and the Supreme Court has put a pretty big crimp into the ability of say a company that has a druggable target to soothe a drug innovator looking at the target.

The same thing I think with the whole

implication of biomarkers. We've talked about it. That's going to be thrown into a tremendous disarray I think in the next few months. Certainly the Federal Circuit's issued a recent decision in Bilski that's going to have a tremendous amount of implication on biomarkers, so all those patents that are out there on biomarkers may be subject to invalidity challenges.

So I think again, the whole issue is we are in an area of great uncertainty as to what the value of your patent protection on anything is in the biotech sphere. It's really disconcerting for most of us who practice in this area.

MS. MICHEL: And, Doug?

MR. NORMAN: Sure, thanks. I would like to get back and touch on one thing that actually Bruce and Ken both mentioned a little earlier, and that's the question about patent term restoration as it relates to bioproducts or even small molecule products.

There's a limitations under the Patent Term Restoration Act that came to us in 1984 as part of the Hatch-Waxman Act that puts a five-year cap on the amount of restoration that you can get once you obtain product approval.

So while it can be all the way up to 14 years, it is capped at five years. Therefore, if you only have

one or two or three years left on your key patent, whichever key patent that is covering your product, then you're only allowed to add a maximum of three or five years beyond that, giving you a total of maybe a whopping eight years of patent protection if you can get that far.

Now, a few things have happened since 1984, once of the most important of which was the United States signed on to trips, giving us a 20 year patent term from the date we file it rather than the 17 year term from the date it issued, and Naomi quite properly pointed out, there are patents issuing probably tomorrow that are probably pre GATT that will have 17 years of life.

Probably 95 percent of everything that people in this room are going to be dealing with from now on are going to be post GATT filings, and they're going to be 20 years.

Now, if it's 20 years from the date you file it and you try to launch a biotech product, I can tell you now it's going to take you 10 to 12 years based upon experiences that we have seen and things that we've heard in the industry, and therefore putting a five year cap of patent restoration on top of that doesn't get you up to the 14 years you otherwise were hoping that you were going to be entitled to under the Patent Term

Restoration Act.

Add on to that the difficulty it is to get things through the FDA nowadays. We can see that the number of new products being launched is declining rapidly from year to year, and add upon that then the inability to even try to carry out any clinical trials on something as important as preventative medicines because the length of time of the clinical trials need to be sometimes eight, nine, ten, twelve years, if you're working in the preventative medicine area.

We are literally leaving innovation behind us because no one can get the proper rewards for it, and therefore, an important thing, important aspect of anything moving forward in new legislation would be to remove that five-year cap so that we can still attempt to get a 14 year reasonable patent life based upon patent term restoration.

MS. MICHEL: Well, one question about that, and I may be wrong, so please correct me. I thought it was possible to choose the patent to be extended, and that if you had a later expiring patent, you would choose to extend that one rather than the one with only three years life.

MR. NORMAN: Well, you're right. You're absolutely right. You can choose to extend one patent,

although you really want to extend the one that's most important that's going to protect your market. Often you have some of these follow-on patents, which others here refer to as evergreening patents, that might be something, a formulation, a new delivery aspect, a slow delivery, a fast delivery formulation, and someone that can practice another aspect of your product placement and not perhaps infringe that patent, and therefore extending that one would protect that product line itself but may not protect your entire franchise.

MS. PEARCE: But it is correct, Doug, to say that in practice, people file a number of applications for patent term extension, and then choose the patent they would prefer for that extension to apply to and withdraw the others.

MR. NORMAN: At some point you have to make the final decision, yes.

MS. MICHEL: Let's see. Let's go to Bruce because I think he had his tent up earlier and then to Ester and Jeff.

MR. LEICHER: I actually just have a very brief comment which is that maybe to David's surprise, we may actually agree with him more than he realizes, in that on the point you raised earlier about similarity, one of the reasons that we support the legislative possibility

of biogenerics is because there isn't going to be the patent uncertainty associated with patent protection if you're actually able to demonstrate essentially that you have a copy.

MS. MICHEL: Okay, thank you. Ester?

MS. KEPPLINGER: Just a couple things. With respect to pre GATT cases, when I left the PTO in 2005, there were maybe a couple hundred, I'm not certain of the number, buy that's been almost four years, so it's diminishing, so there aren't that many pre GATT cases that could raise that question.

The second thing, just very briefly, about 103. You asked the question if you get a narrow claim, isn't that going to be a stronger cases against the validity challenge for obviousness? And certainly the less scope that you have, the fewer references that might be out there, they would not -- maybe not be able to find some little point within that scope that is vulnerable.

However, if the reference is there, it's there to make it obvious, and the Supreme Court with KSR, while it really didn't change the law so much, it re-emphasized some old case law. It certainly changed the way the Patent Office has been applying 103 and potentially the way the Fifth Circuit will. So it is becoming more difficult to get patents for obviousness

as well.

MS. MICHEL: Let me ask: The extent to which 112 is such a big issue in biotech is, I understand it, fairly grounded in the Federal Circuit calling biotechnology an unpredictable art, and to some extent doesn't that unpredictability then also help defend them against an obviousness case?

MS. KEPPLINGER: Yes, it can, but they'll take a piece of prior art and say A shows this and B shows this, and it would have been obvious, and the standards for the two are not necessarily exactly the same.

MS. MICHEL: Thank you. Jeff?

MR. KUSHAN: Listening to the discussions, I think one thing that would be good to do is pull back a little bit and really try to understand why people think differently about biologics relative to small molecules, and I've been thinking a lot about this over the last couple of years.

I think if you look at -- kind of when you're making the decisions to put money into your development as an animator, if you're in the small molecule space you know there's a lot of uncertainty about your patent estate, but one thing you pretty much know is that if you've got a patent on the molecule that's going through clinical development and you get that patent issued and

then you're drug gets approved, you know where your competition is going to come at is going to be at another molecule that's identical to that.

So your chaos of prediction of where you're going to be in the future is somewhat narrower in scope than it might be in the biologics area, primarily because in the complimentary decision making point, in the biologics development, you don't know whether the patent estate you're going to have necessarily would hit the exact molecule that a biogeneric or a follow-on producer is going to select.

I think the other part of this equation that's hard to grasp on to is that the scheme is actually enabling the follow-on producers to have a lot more latitude to navigate around the patent estate than the complimentary innovator or generics would have relative to the NDA holder.

So it's not just a one way perspective. It's the other perspective of looking at that patent that was cut through the jungle that Doug described earlier that they know how they get around a lot more readily the patent estate than the NDA holder and the end filer might be in that kind of a debate.

I think the other thing that we always talk about is hard, and we get paid as patent lawyers way too

much money to do our crystal ball function of figuring out where your patent estate is and how strong it is relative to your products. One thing we can't do, we tend to come in and say, all right, 30 percent chance you're going to win or lose your patent case. It really has nothing to do with facts, so let's take that variable and put it away upfront.

Second, we talk about the claim scope variables. Certainly the trend has been for the PTO to crimp down around the sequence that is the reference point of the early examination, and that does give you some instincts about at least mathematically whether you're going to have infringement by a certain number of substitution of amino acids in a protein sequence.

The thing that is kind of a killer variable that we're not talking about is the other thing it makes it impossible to predict where you're going to come out, and that's this wonderful doctrine called Inequitable Conduct because every single patent case that we're involved in, where were on the offensive side of fighting, we have to fight this unknowable risk of Inequitable Conduct.

So when you're sitting there 12 years out from launch of a product, and you're advising a company, Well, so how is this patent going to look to protect us

from a follow-on producer, I feel bad taking their money because it's just like there's this variable, there's that variable and there's so many variables that affect fundamentally your ability to say this patent estate is going to be worth anything that it's almost comical to have the discussion.

So let me say, that's a bit of an overstatement, but I want to make sure people appreciate that the patent calculus is one that is so difficult to predict that you need another thing out there to tell the innovators, yeah, you should do this, but you should do this in a long-term multiple indication focus development effort, and that's where if I had to still down the difference between the NDA and the biologics area, I know at least where I stand with copies of a molecule in the NDA's base, and that does reduce some degree of the uncertainty of coverage I might have.

MS. MICHEL: Do you have any comments on how the jury system plays into that degree of unpredictability?

MR. KUSHAN: Well, in the Hatch-Waxman cases, the juries tend not to be there.

MS. MICHEL: Well, they're not.

MR. KUSHAN: So we get enough uncertainty just I think -- a very big variable is in the Inequitable Conduct area.

MS. MICHEL: But on the biotech side.

MR. KUSHAN: Well, again if you're going to come up with an environment where you're going to be fighting about the patents before there's an actual infringement, you're probably not going to see a jury in that case as well, the reason we don't have damages in the patent cases and Hatch-Waxman. We'll see the same model I assume in the pre launch scenario in the biologics area.

MS. MICHEL: Yeah. Okay. Ken Goldman?

MR. GOLDMAN: I will try and make this quick. I think I want to make four quick points and hopefully answer your last question about whether biotech patents can preclude competition from biosimilars and biogenerics, and then also, ultimately we can get to your last objective, and I'll see if I can get that all in four points.

Starting with David, I think you're correct. In terms of the question about biosimilars and biogenerics, the FDA -- we need the FDA up here to tell us what the correct standards are going to be, but the FDA is clearly the right entity to be deciding which products will fall under the laws and to promote the consistent regulatory standards that would be required to implement such a scheme.

We believe that Novartis -- the Novartis group

of companies, if you haven't heard already includes also Sandoz, believes that comparability is the best standard as set forth by the FDA in 1996 and which is the standard used for manufacturing pre and post manufacturing changes for innovative products.

Now, given that that would be the standard, whether a patent that you get will ultimately prevent design-arounds is obviously not a sure thing. It might depend on the day of the week, the patent examiner that you have, what the most recent Federal Circuit case says, any number of possible outcomes, although we do believe that aggressive and intelligent patent prosecution should give you a broad enough patent, but again it's not entire clear.

Therefore, it's clear that the patent system alone is not going to satisfy the risk that innovators face of not getting a return on their investment. Therefore Novartis believes that the biotech patent should not be coupled with this scheme because it's never going to give you -- as we concede, it's never going to give you the assurance that you need to recoup your investment, but rather the data, some type of data exclusivity at least as good as the one that's currently in force in Europe today would go a long way towards providing that type of assurance, and reduce that risk.

MS. MICHEL: Thank you. And we'll give Ken Dow the last word, but I'll also just say, as Michael said at the earlier panel, the record remains open and we certainly welcome more comments, if there's anything that we weren't able to get to that you would like to comment on. Thank you.

MR. DOW: Well, obviously I would agree that the period of data exclusivity is absolutely critical here because of the unpredictability that we're going to run into.

Just a couple small points that when we were talking about the patent term extensions, there is one other limitation in there that in that the extension only applies to the approved use, so that's -- first approved use, so you would have to factor that in, if you were going to make that system over into biologics.

The other thing is when we were talking about the difference between biotech patents and small molecule patents, in my experience for biologics, the implications of third-party patents is much greater in the biotech area, and the so-called royalty stacking that we have in this area is something that the biosimilar may or may not have to deal with. Maybe those patents will be expired by the time they get to the market or they may have to deal with them

themselves, so good luck.

MS. MICHEL: With that, we'll conclude this panel and take a shortened break, a five-minute break. Thanks very much.

(Applause.)

(A brief recess was taken.)

PANEL FOUR:

LIKELY COMPETITIVE EFFECTS OF

FOLLOW-ON BIOLOGIC REGULATORY INCENTIVES

MR. WROBLEWSKI: Good afternoon. Thanks for coming back. My name is Michael Wroblewski. For those who are just joining us this afternoon, I'm an attorney in the Bureau of Competition here at the FTC, and my comoderator is my colleague in the Bureau of Competition, Elizabeth Jex.

Joining us in this panel discussion this afternoon are going to be Geoff Allan, president and CEO of Insmed; Aaron Barkoff, partner at McDonnell, Boehnen, Hulbert & Berghoff; Marc Goshko, executive director of legal affairs for TEVA Pharmaceuticals North America; Dr. Steve Miller, senior vice president and chief medical officer of Express Scripts; Doug Norman, general patent counsel for Eli Lilly & Company; Bill Schultz, partner at Zuckerman Spaeder here in Washington; and Bryan Zielinski, assistant general counsel for intellectual property at Pfizer.

More detailed information about each participant is in the folders and on the FTC's website.

The objectives of this panel, there are really two of them. One is to identify the likely competitive effects of follow-on biologic regulatory incentives and

to examine how Hatch-Waxman experience informs this inquiry.

As we mentioned this morning, we're trying to use some definitions and some terms that we have defined with a biosimilar drug being a drug product that refers to one that is therapeutically equivalent, interchangeable and substitutable at the pharmacy point of use level, whereas a biogeneric drug is one that -- excuse me, that was a biogeneric drug. A biosimilar drug, I'll go to the top of the slide, is one that refers to one that is comparable to the reference product.

We're going to run the panel the same we did it this morning. I'll pose a question, ask a specific panelist to start off, but if another participant would like to join in, please just turn your name tag on its side, and we'll be able to turn to you, if time permits, and once of again, these microphones are always on, so once you've finished talking, if you can just flip the microphone up, there won't be any excess chatter in the background.

Why don't we just get right to kind of the main thrust of this particular panel: Is a marketing exclusivity period necessary to encourage competition or encourage companies to develop biosimilar and/or

biogeneric applications and to seek their approval at the FDA?

I'm going to turn either to Bill Schultz or to Geoff Allan maybe to start this conversation off.

MR. SCHULTZ: Sure, thank you, and thank all of you at FTC for doing this day's session. I think it's going to be very helpful. It's certainly been very interesting.

We haven't talked much about legislation, but we all know that's in the background, and the legislation that's been introduced on the hill, a number of the bills have an exclusivity period that's really very different from what's in Hatch-Waxman. The purpose of it is not to create an incentive to challenge patents that are weak.

The purpose of it is to create an incentive to develop interchangeable biologics, and I think from just this morning's session, you couldn't listen to that -- listen to the FDA speaker without thinking that there's going to be a lot of work for any company to do in order to persuade the FDA that a biologic is interchangeable. Maybe we ought to just go back and talk about -- just say what we're talking about here.

The legislation, as I see it anyway, it really talks about two different kinds of approvals for

biologics, almost two different steps. The first step would be you would get an approval for what you all have defined as a biosimilar; in other words, you showed that you're close enough to the innovative product that the agency is willing to let you show safety and effectiveness with less data than the innovator had to use.

The bills don't say what kind of data or how much, and that will be up to FDA, and I think everybody thinks that's going to vary from product to product, but that lets you get on the market and market your product.

It doesn't allow you to do what generic drugs can do today or generic chemical drugs or ANDAs can do, which is to sell their products as interchangeable where a pharmacist can actually make the substitution without a doctor's permission. You would have to have a separate doctor's prescription for that biosimilar product.

The second type of approval that you can get is in addition to showing that you're similar, you can show you're interchangeable, and the bills have definitions for that, but the basic idea is that you have to produce enough data, not only showing that the product is safe and effective, but to show that it will have the same clinical effect in an individual patient.

I think it's envisioned that FDA is going to be the one to figure out what that data package will be, but I think everybody's involved, and as FDA said today, would say that there's a lot of work to be done here. It's going to be a tremendous effort. It's probably going to be very expensive, and yet I think the payors would say it is very, very valuable in terms of the healthcare system because the interchangeable products are the greatest opportunity for healthcare savings.

So the idea of these bills, and some of them are six months and some of them are a year, they would say to the generic company that if you show that you are a biogeneric, you get for a period of time, six months or a year, to be the only one that can promote your product as interchangeable. You're the only one that's interchangeable.

Unlike Hatch-Waxman, it does not block other products from the market. During that period of time other products can be approved as biosimilar, they just will not be approved as biogeneric during the exclusivity period.

MR. WROBLEWSKI: So to make sure we understand, are you thinking that if it's a biogeneric, it is a subset of bio similarity, of the biosimilar drugs?

MR. SCHULTZ: Yes, yes, absolutely. Every

biogeneric would be biosimilar.

MR. WROBLEWSKI: Geoff or Marc, if you wanted to add to this discussion.

MR. ALLAN: Go ahead, Marc.

MR. GOSHKO: I've been working on the generic exclusivity on small molecule drugs for probably about ten years, and for the last five, probably the three words in the Medicare Modernization Act, the later of. We still haven't come to an agreement on what those mean, but to emphasize things that Bill said and things that were said this morning, we're sort of building for the future here with establishing some reward for the investment that will be necessary to develop methodology.

To move one thing over to the table is if legislation is going to be done, it doesn't need to be redone every time that science makes an advance, so we really want to have the legislation in a position that when the technology meets FDA's acceptance, that everything is in place to accommodate the idea of a biogeneric and to incentivise it.

MR. WROBLEWSKI: Geoff?

MR. ALLAN: I guess my comments are somewhat similar. As a company that's in the business of trying to develop these molecules, I think one thing is

becoming very clear. These are going to be expensive drugs for the FOB, and we obviously want our return on investment and incentives for developing them in the first place.

So if there's an exclusivity laid out there for interchangeability, and as William said, I don't think there's any clue whatsoever as to how we're going to get to interchangeability, but if there's an incentive provided for the first company that does get to interchangeability, is that an unfair incentive for other companies who are chasing that same designation.

So my concern would be if you are investing a huge amount of money into this program relatively speaking, do you want any further barriers out there to allow you to get your own return on investment?

MR. WROBLEWSKI: Let me ask you a quick question in terms of how an applicant who is trying to show that they're a biogeneric, if there is one biogeneric that has been shown to be interchangeable and a second one comes in, does that under this scheme -- does that second one who is claiming to be interchangeable have to show that it is interchangeable not only to the reference product but also to that first interchangeable that has been designated interchangeable so that the investment to show both of those, to show

interchangeability with two products rather than just one would be more? Is that what you're anticipating would happen?

MR. SCHULTZ: Well, I mean, I think that the bills anticipate that you would be showing you're interchangeable to the reference product, to the brand grant product. How that second piece plays out I think is at the moment really left to FDA.

In the small molecule world I think it's assumed if you're interchangeable to the reference product, all the generics are interchangeable.

MR. WROBLEWSKI: What would be a guidance?

MR. SCHULTZ: I think it's a scientific issue as to whether that's true or not. That hasn't really been addressed.

MR. WROBLEWSKI: Anyone else?

MR. ALLAN: Well, I think we heard this morning from FDA representation that interchangeability is going to be designated on the basis of some form of clinical trial activity, switching products back and forth.

If the interchangeability goes beyond the reference product, that's going to make the conduct of those clinical trials extremely complicated.

MR. SCHULTZ: One motivating factor, I think it's envisioned there will be a much smaller number of

actual products in many, many cases than there are in the small molecule world. I mean, I think most people would assume that you're not going to on the first day see eight products coming on the market like you sometimes do for small molecules, just because they're so expensive.

MR. WROBLEWSKI: But if you're looking at, what we heard this morning was that the number of competitors actually is where the savings comes to the consumer and where the price competition comes, so what incentive should we put in for the second or the third or the fourth interchangeable, or is one necessary at all for them to show that interchangeability so that you can go from the reference product to the first interchangeable to the second, back to the first, to the reference?

I mean, are we building in a disincentive for that to occur then by giving the 180 days or some period to the first interchangeable?

MR. SCHULTZ: Well, there's a lot to that question, but one thing is I think once you show -- once the first company shows it's interchangeable, then at least FDA knows how to do this, and the effort is much less after you have one, and thus I think the incentive is somewhat less necessary.

MR. WROBLEWSKI: Bryan, you would like to add a

point?

MR. ZIELINSKI: I guess I just don't understand why you need any incentive at all. I mean, we heard previously today that the market is going to be fundamentally different with fobs, and some people estimate -- well, many people estimate that you're going to have fewer entrants and as little as 10 to 30 percent price discount off brand, so it's not clear to me that simply developing FOB requires an incentive.

You don't need an incentive to challenge the patent. The patents will be challenged, given the time and expense that's going to go into developing that FOB, so certainly tied to any exclusivity to a patent challenge would be inappropriate.

But having any exclusivity would have to be justified. The market is going to be smaller. There's going to be less of a price discount. The market dynamic itself will be sufficient incentive, so they would have to do something more than merely try to go down the same path that the innovator took.

The innovator spent all the money, took all the risk, and so simply following that in and of itself should not be sufficient to entitle an FOB applicant to exclusivity.

MR. WROBLEWSKI: Doug, you wanted to add a point

to that?

MR. NORMAN: I would agree, and if we look at history, we would recognize that just from some of the slides we saw this morning, that there's plenty of competition available in the biologic market regardless of whether there's any incentive to anyone who is creating another compound going into that market.

Looking at human growth hormone alone, there's eight molecules currently on the marked. Genentech had I believe 19 patents in one lawsuit against some folks, and yet people ended up getting to the market. They ended up settling they ended up litigating. They ended up knocking some out, and that was branded competition at its finest, exactly what we ought to want to see.

I fail to recognize why someone following on after that trail has already been blazed should need any incentive other than the market in and of itself. The market provides plenty incentive for people to do what reasonable persons do every day.

MR. WROBLEWSKI: Thank you. Marc, you wanted to add something, and then I'll turn to Steve.

MR. GOSHKO: Yes. I wanted to first address the idea of the incentive to the first interchangeable product. I think if the actual exclusivity period is based on some reasonable parameters that it will be

sufficiently enticing to develop the technology, but not sufficiently inhibiting to subsequent applicants.

As Bill noted, that the subsequent applicants can be moved into their non interchangeable status and still offered for sale during the actual exclusivity period. If the concern is that the exclusivity period is for some of the small molecules, it has the potential to go on for large periods of time due to that infamous word parking, I think that legislatively those circumstances can address that.

MR. WROBLEWSKI: Thank you. Steve?

MR. MILLER: Just as a reminder, the environment in 2008 is much different than the environment was in 1984, so in 1984 with the original Hatch-Waxman, we had to create a generics industry. That industry is now established, both for small molecules and for biologics, and it's very vigorous, and it's actually looking forward to it this newer era.

So I think when you look at incentives, you have to look differently today than you did when you were originally constructing Hatch-Waxman. The 180 days should be something that is earned, not just given for being first in line at the FDA.

So there has to be a reason you're giving the 180 days, be it what Bill discussed, all the way to

fully substitutable molecules or some other reason. One of those other reasons actually may be just addressing products of market size.

So if you were to look at EPO for instance, EPO is such a large market, you probably won't need incentives to get companies to line up to challenge EPO. If you look at some of the other orphan drugs, however, you're probably going to need incentives there because there's just not going to be enough companies willing to take those on.

MR. WROBLEWSKI: That's a good point. Thank you. You know, you brought up Hatch-Waxman, and I would like to know what experiences have we gained from the use of the 180 day marketing exclusivity period that's relevant to the biologic market. I will turn to you first since you're laughing.

MR. NORMAN: Okay. What experience have we had? I think the official name is the drug price competition and Patent Term Restoration Act of 1984, which is really the patent litigators full employment act of 1984, because if we've learned anything in the past 24 years it's that the United States Patent and Trademark office is wholly incompetent to issue any valid patent to a pharmaceutical product in the United States because there is not a single drug product out there worth its

salt that doesn't have 10 or 11 or 12 or 15, or in some instances even more, folks making challenges to those simply because there is a bounty on intellectual property coming out of the Hatch-Waxman Act.

If we're going to design anything for biologics, we can design some sort of regulatory scheme to allow biologics on. We can design some sort of patent term restoration. We can design some sort of meaningful incentives back and forth, but we should not design a bounty on the intellectual property rights of innovators.

In particular, I would say we should also not set up a system whereby that bounty arises simply because someone has shown that they can actually design around a validly issue but narrow U.S. patent. We've seen that time in and time out in the Hatch-Waxman context where the first person to show up perhaps could not competently design around a patent owned by an innovator, and therefore were unable to get their drug approved and on the market arising from the litigation after the Hatch-Waxman case was filed.

A second generic then shows up who is quite properly designed around, and yet because of the questions over who is going to be entitled to that 180 day exclusivity, we saw litigation all through the last

century, all through -- well, sorry, all through the last decade, and we are now seeing it over the last couple years arising from whether or not the Supreme Court's decision in the MedImmune case gives some sort of declaratory judgment action arising from the filing of later ANDAs that in some way can take care of all the 180 day issues that my colleagues down at the other end of the table have had to deal with.

It's terribly difficult. It doesn't reward the kind of innovation that we would expect the marketplace would be willing to pay for, and therefore, we shouldn't have a system set up that does nothing more than place a bounty upon the innovation of others.

MR. WROBLEWSKI: Thank you. Bill?

MR. SCHULTZ: You know, we could have a very interesting debate on whether the Hatch-Waxman 180-day exclusivity is a good thing, and we could have a very interesting debate on whether that system ought to be applied to biologics, which you're tempting us, but I think it's quite interesting that none of the bills or proposals that are sort of on the table adopt anything like the Hatch-Waxman provision.

And to the extent we want to focus on really the exclusivity that is in that legislation, the only thing I want to point out is it's very, very different. It

doesn't depend on first to file. It doesn't depend on patents. It's much more like the Orphan Drug Act. It's the first one to get approval of interchangeability gets six months or a year, whatever is decided, of being the only one who gets approved as interchangeable.

Unlike the Orphan Drug Act, other products can still come on the product. There's been very little litigation over Orphan Drug Act approvals, and I think there's good reasons to think -- there may be other reasons to argue against this, but I don't think there's really good evidence that it's going to lead to a lot of litigation, which may be unfortunate for lawyers.

MR. WROBLEWSKI: Marc, did you want to add a point?

MR. GOSHKO: Yes, I think a good distinction between this market and the small molecule is that one mechanism that small molecule applicants have for escaping the 180 day exclusivity of others is either to file an ANDA suitability petition and move a dosage form or to file a 505(b)(2) application for an injectable product and try to set up an alternate an brand market.

Now, where there is a lot of true generics, that isn't a very viable course of action, but in this dynamic, the idea that people will always try to go after the similarity pathway first already creates the

potential patent challenges even before the true biogeneric gets there.

MR. WROBLEWSKI: Thank you. Following up on one of the things that the Commission has spent a lot of time on in the Hatch-Waxman context, has been looking at settlement agreements, so I ask everyone around the table: Would you oppose a restriction in the grant of or in the way this provision is written for getting some type of marketing exclusivity for the first biogeneric from selling that right to an innovator company or to negotiate a delay of the entry?

MR. MILLER: Representing the payor community, this is actually been quite problematic because it's become part of the management of the life cycle of the product, and so you're actually not adding innovation to the marketplace, but you're extending higher prices for a longer period of time.

I believe that when it was originally developed, that was not the intention, but that's become one of the uses, and I think that whatever we do going forward, we have to be cognizant of the fact that there will be people that will try to exploit the intentions of it, and so we have to look for these unintended consequences as we're developing the regulations.

Otherwise we'll get right back to the situation

where we are today, just extending the profitability during the terminal phase of a product without really benefiting the consumer.

MR. WROBLEWSKI: Any other follow-up or comments on that before I change? Marc?

MR. GOSHKO: Referring to legislation introduced earlier by Mr. Waxman, I think that he tries to account for various scenarios, which may mitigate, if not solve the problem of that type of a settlement issue.

MR. WROBLEWSKI: Thank you. One of the things that we tried to do this morning, and Linda Horton was very gracious in terms of giving us an overview of the European experience, and I wonder how the Europeans have examined this particular question in terms of whether there is or should be an incentive for the filing of follow-on applications.

And I'll turn to Aaron, if you would like to start off on that?

MR. BARKOFF: Sure. First, thanks for inviting me, and I should say my views are mine alone, not those of my law firm or my firm's clients.

So in Europe, not only have they not passed any kind of provision for market exclusivity for biosimilars, but there is no 180 day period or market exclusivity for any generic of any kind, including small

molecule.

My understanding is, it's not just Europe, it's Asia and the rest of the world that don't have any kind of generic market exclusivity period for any pharmaceutical. The U.S. is the only country in the world.

So getting back to your original question, is this kind of 180 day exclusivity period necessary? That tells me it's not necessary for biosimilar drugs to be developed and marketed.

It's a separate question to ask whether it's advisable to have a 180 day exclusivity period or some other kind of generic market exclusivity period. In other words, would we have more cost savings to consumers, more introductions of biosimilar products than we would without that kind of period, and that's a real difficult question to answer, but along the same line, it's not restricted to Europe.

Another argument in support of the notion that this kind of period isn't necessary is the fact that many, many generic companies don't make the 180 day period kind of a cornerstone of their business model. There are many generic companies who aren't necessarily interested in being the first to file a Paragraph IV certification, and in fact, they file ANDAs knowing that

they're the second or third or fourth filer, and in fact litigate that.

So they're not always riding the coattails of the first filer's patent litigation strategy. Maybe they think they have a better litigation strategy, and so that also tells me that the 180 day exclusivity period is not necessary.

MR. WROBLEWSKI: Thanks. Bryan?

MR. ZIELINSKI: I would agree with Aaron. I don't think it's needed, and I think that if you took anything from Europe, while the experience is somewhat limited, it certainly highlights that having some type of FOB exclusivity hasn't been needed to encourage companies like Sandoz to pursue biosimilars in that market. They are doing so, and I expect that they will probably continue to do so.

MR. WROBLEWSKI: Bill, go ahead.

MR. SCHULTZ: The only thing I would like to point out is Europe is obviously very different because it has price controls, and generic drugs are just much less of a factor is my understanding there in terms of drug delivery and so on, and I think that really plays into this question.

MR. WROBLEWSKI: That's a good point. Geoff?

MR. ALLAN: Yeah, I would just go back to what I

said at the outset. Some day there's going to be legislation to allow these drugs to be developed. Once that legislation is laid in place, companies are going to possibly line up. It's going to take them four to five years to develop these products and get them approved.

They've got to wait for patents to expire, which will be five or six years out. They've got to invest 50 to 100 million dollars, and depending on how well capitalized you are, that could be a major investment, and if there are any other barriers before you can bring your drug to the marketplace to get your return on investment, it's only going to be in my mind anti-competitive, so I would rather not see any exclusivity provision.

MR. WROBLEWSKI: Doug, go ahead.

MR. NORMAN: Sure, thanks. That was a nice point actually, and it brings up a view that Lilly has concerning incentives, certainty, the level of risk in what to us as innovators is a high risk, high reward marketplace and to folks who would be follow-on, what would be a lower risk and probably lower reward marketplace, but one which is meaningful nevertheless.

That is from the aspect of the innovator, we've had some roundtable discussions this morning about the

lack of certainty with patent estates in biotechnology. We've had some discussion about the appropriate length of time over which the data package should be protected, and I would say at Eli Lilly & Company, the one thing that we haven't projected to the world, and I doubt if a lot of people have projected to the world, is the difficulty that we end up having to -- the difficult decisions we end up having to make regarding where we're going to place our investments for an innovative product arising from the uncertainty that we face from the patent estate on the molecules or from the lack of data protection going forward.

And thus, unfortunately there are many opportunities that we turn down because we can't possibly hope to recoup the investment that we would need to make in a molecule, and therefore, one thing that we've discussed and we've talked about publicly is in exchange for the appropriate level of certainty of -- what do you call it, data exclusivity, marketing exclusivity, if we could get a date certain that was sufficient, and here let's just throw out 14 years because that's what people talked about this morning, we would be willing to enter into a decision that we would call a fork in the road, that a year or two post launch or three or four years post launch of a drug, we would

be willing at that point to choose either to live with the data package period or our patent estate, one or the other, and give up the rights to one or the other.

So that the follow-on industry could then know for sure what Lilly drug is going to be available for a follow-on, and they can make their appropriate decisions at the appropriate time and lower the risk in their part of the business, and in the meantime the public gets access to a Lilly product through a certain period of time that's a date set certain. Then follow-ons can come along quickly after that, and the market can adjust to the level of lower risk, even if it's a lower return.

MR. WROBLEWSKI: Is one of the effects of a choice or a fork in the road, as you describe it, is that the innovator will always take the longest period?

MR. NORMAN: Probably.

MR. SCHULTZ: Why not?

MR. NORMAN: Isn't that what we're supposed to do with our patents?

MR. SCHULTZ: Either that or answer to your stockholders.

MR. WROBLEWSKI: The one last question I want to raise, and this was something that, Steve, you brought up: If the marketing exclusivity provision were tied to the size of the market, so to the extent that, as you

indicated for orphan drugs, if there's no economic incentive to develop the interchangeability, what would be the likely effect of that, of tying it to the size of the market?

MR. MILLER: Well, I want to go back to one point that Doug made and then address that. Amazingly in Europe they have a shorter time of data exclusivity and price controls. To ask for both the longer time and a free market in the U.S. seems to be counter to what's been successful in Europe where they have brought these molecules to the market.

I do think, and my biggest concern is for our membership where it is an orphan drug, where it is the small markets -- interestingly the innovator companies are still bringing to the marketplace products for extremely small markets. If you saw The Wall Street Journal this week, we're talking about diseases where the markets worldwide are often a couple thousand patients.

So there must be some incentive out there obviously for that, but our biggest concern is when you have these small markets, is there a way to use tax credits or time of exclusivity or something that actually incents the companies to go after making those products for those smaller markets, and we believe that

that's where a lot of the energy should be.

MR. WROBLEWSKI: Marc, did you want to add something to that?

MR. GOSHKO: I just had a question, a clarification. Is it your suggestion that the larger the molecule, the more the potential need for the --

MR. WROBLEWSKI: No, opposite.

MR. GOSHKO: Okay.

MR. WROBLEWSKI: Bryan, did you want to add?

MR. ZIELINSKI: I wanted to say, you're positing that the smaller the market, you might want some sort of variable exclusivity.

MR. WROBLEWSKI: A variability or there would be an opportunity to have exclusivity.

MR. ZIELINSKI: I would only say that if you're going to have some sort of variable exclusivity, I think it runs counter to the more positive approach having something clear and predictable. I think it's better to have something clear and predictable. It's less subject to gaming. It's easier to make reasonable investment choices on that basis.

And I'm still not sure that it's needed because even with a small market, the products will probably be priced obviously much higher than a small molecule. You will probably have fewer biologic entrants and you will

probably have less price depreciation when the generic or biosimilar does enter the market.

So I think you need some empirical evidence to suggest that you would need some exclusivity, let alone a variable exclusivity.

MR. WROBLEWSKI: Thank you. Bill, and then I'll turn to you, Doug.

MR. SCHULTZ: If the purpose of exclusivity is to make sure there's a sufficient incentive for innovation to discover molecules, then there's some attraction to the idea of having the exclusivity vary on the -- depending on the profit of the product, and I guess the sales of the product is sort of a rough proxy for the profit, so I personally think it's a very attractive idea.

I would say that when it's been tried on the Hill, it's always run into problems. On the other hand it's sort of a new day, and it doesn't mean it would -- these ideas would have the same debate that they've had.

The other thing I want to say is I think it's very important to pay attention to the question of whether any exclusivity, at least beyond that that's in Hatch-Waxman, is justifiable, and I feel like we've jumped into --

MR. WROBLEWSKI: And this way, you've moved away

from the marketing exclusivity for a follow-on biologic to exclusivity for a --

MR. SCHULTZ: That's what I thought you were asking about. No, to what? I'm talking about marketing exclusivity for a follow-on biologic.

MR. WROBLEWSKI: Okay.

MR. SCHULTZ: I'm just saying it's important to ask the question of whether the patent system provides a sufficient incentive, or whether there's really a case that you need, this is somehow so different from the chemical market, that you need additional exclusivity. I feel that often we just jump passed that and we start saying, what does exclusivity mean without really taking a hard look at that question.

MR. WROBLEWSKI: Doug, did you have something you wanted to add?

MR. NORMAN: Bill covered it, okay.

MR. WROBLEWSKI: Amazingly we're back on schedule. Unless there are other final comments, Steve, if you have one.

MR. MILLER: Yeah. I have just one other, and that is if you do not coordinate the development of these products with Medicare payments, you're going to miss a great opportunity. If you allow these to share J Codes, you will actually get much greater uptake of the

follow-on biologics than if you don't.

So I think it's going to be crucial to coordinate this not just through what this bill does, but how it's applied to Medicare because if you force them to get separate J Codes, you are going to delay the adoption of these drugs, and you're going to delay the benefits to society, and I think it would be a tremendous opportunity that would be wasted.

MR. WROBLEWSKI: Okay. Thank you. We're going to take ten minutes, until about five after 3:00, and then we'll start the last panel of the day. Thank you.

(A brief recess was taken.)

PANEL FIVE:

PATENT DISPUTE RESOLUTION PROCESSES

MR. WROBLEWSKI: Why don't we go ahead and get started. My name again is Michael Wroblewski. I'm co-moderating this panel with my colleague Suzanne Drennon also in the Bureau of Competition.

The objective of this last panel is to discuss the need for and the likely competitive effects of different ways to structure a process to resolve patent disputes between innovator firms and FOB applicants, prior to FDA approval of the FOB product.

Participating in this discussion, and everyone's actually been introduced earlier today except for Hans Sauer from BIO, so welcome, Hans, and Christine Siwik of RMMS in Chicago. Thank you, Christine, for coming this way.

This panel is going to be a little bit different from the earlier panels. We are going to try to discuss many of the issues in the context of a hypothetical patent portfolio claiming the XYZ drug product developed and marketed by the sponsor company.

The use of this hypo will hopefully help us put some meat on the bones to illustrate the points that we want to make.

Rochelle Seide has been gracious enough to

actually volunteer to present the patent portfolio case study. Rochelle?

MS. SEIDE: Thank you, Michael. The patent portfolio was set up to show you in reality for those who aren't patent attorneys also that biotechnology products tend to suffer from a fairly complex patent portfolio, maybe a little bit more complex than you see, and maybe this is another way of showing the distinction between small molecule portfolios and biologics because there seem to be a lot more players here, so let's go forward.

What we've done is we've put together the XYZ, and I'll go into what the XYZ product is down the line, but there are a number of different tiers of patents that we'll talk about. There's the university drug target patents, the third-party technology patents, and I think Ken Dow talked about all of the royalty stacking, and in a lot of cases and this is where it comes from because the company is in-licensing a number of patents that are not their own, and they have to pay royalties on those patents if there is a drug that is developed.

Certainly there's the sponsor company's own patent, and then there's a little wrinkle perhaps in some cases in the biologics area. Some molecules, and

this may be going forward in the whole area of pharmacogenomics, that you might want to -- the patient population may be better defined by use of biomarkers, which population of patients may be better suited for treating with a particular drug.

The prime example is certainly Herceptin where the patient population of those women with breast cancer who have been shown to have the HER-2 marker by a bioassay, and the bioassay may be that of the company or may be of that a third-party.

All right. Let's talk about the tier 1, the drug target patents. We have to say the first group of patents, these are owned by a university, so the inventors are researchers who are perhaps doing basic research and find out certain things that of interest.

They find a particular target receptor on a cell line that may be of interest for developing something or they've identified something about this target that may be a receptor for a hormone or the like.

So you've got the early patents from the university. You have claims that are drawn to the target itself, the target receptor. Certainly again like everything else, you do the DNA in coding the receptor. You perhaps, if you're lucky, also get the cloned receptor protein.

Now, again any good patent attorney will also claim a monoclonal antibody that specifically reacts with the receptor and perhaps inhibits or enhances the activity, depending on what it's doing, and then you will also see generic, sort of generic therapeutic treatment of say cancer, in this case cancer, using agents which inhibit the receptor binding.

We've been fairly broad about this, and again some of the comments are you can get broad patent protection. Some of these may or may not be claims that you will be able to get in the future, but we will see, but for purposes of the hypothetical, these patents which are owned by the university are licensed exclusively to the sponsor company for field of use, say a treatment of cancer or a certain kind of cancer.

But the university itself will retain enforcement rights of the patent, and this is not an unusual situation. Universities also take grant back licenses so they can keep the rights themselves, even if they license to a sponsor company, so again here we have patent rights that are fairly complex. They are not all in the sponsor company. They are all over the place.

University has some of them. They may be field of use and they may license -- and the university may license to another sponsor company in a different field

of use, and that's not uncommon either.

So the second tier of patents that we'll talk about or that will be involved are what we call tier 2. These are technology platform patents. I think certain things like in the biotech area, certain patents like phage display for identifying certain molecules may be an example of technology platform patents, but these are owned by a third party. These are not owned by the sponsor.

We are going to use antibodies as our example, and the technology platform claims technology for making recombinant antibodies with reduced immunogenicity. These are kinds of antibodies which originally the whole monoclonal antibody technique was developed in mice. You give a mouse antibody to a human, they're going to make an immune response to it, so there are technologies for humanizing or making chimeric or humanized antibodies that reduces the immunogenicity of these molecules so they may be more therapeutically valuable.

These patents, the technologies are licensed non exclusively to a sponsor company, but if they are used and a product comes out of it, the sponsor company owes royalties to the technology platform company, and again the patents have also been licensed to a variety of other companies and are being used in several other

biologics.

So again the situation is fairly complex. You've got -- the sponsor has to in license certain technologies so they can may their own biologic.

Now, with the sponsor companies patents, which are on the next slide, sponsor company has additional development and receives patents that the claims are drawn to what we call a masked recombinant antibody with lower immunogenicity and better binding to and an inhibition of the receptor or Ligand interaction, and again these may be, as I said, humanized or chimerized or the like or may be fully human antibiotics.

There is at least in the beginning treatment showing that these antibodies can be used in treatment of testicular cancer and prostate cancer, and you get claims to that, and then you get some process patents on the way these antibodies are purified using -- from affinity purification in making the monoclonal antibody so this is the process patent for making the antibody.

Now, we have a separate tier that can be important, and we put in here what we call biomarker patent, and I put this in with the caveat that we don't know -- again there's a great uncertain as to whether biomarker patents will survive Federal Circuit and probably Supreme Court scrutiny because there was a case

up at the Supreme Court dealing with biomarkers which was dismissed for improvidently granted cert, but there were three justices that dissented from that denial saying we should look at these and saying these are all product in nature patents, and they shouldn't be granted in the first place.

So they have some questionable aspects to them right now too, but let's assume that there are some biomarker patents out there, and that claim biomarker assays for identifying lung cancer patients who would be best candidates for treatment with the mass antibodies, remember again this antibody may have multiple uses as we've told before.

These particular bioassay patents are owned by the sponsor company. There are others biomarker patents that may be that -- for identifying prostate cancer patients who would be the best candidates for treatment with the antibody, and these are owned by the third-party and licensed exclusively to the sponsor company.

Then there's another -- then there's another possibility, that the sponsor company out licenses its diagnostic reagent to various third parties, each of which holds enforcement rights, and these licenses generate a royalty stream to the sponsor company, so

maybe they license out their lung cancer biomarker case to other parties who may have other ways of looking -- using those patents maybe with other drugs.

Okay. Let's for the assumption of our hypothetical say, just to make it simple, these are all post GATT patents, so they will have a 20-year term, inclusive of any extension granted. We're trying to make it simple. They will have a 20 year term from the date of filing. The innovator receives FDA approval for the treatment of lung cancer using the recombinant mass antibody at some point in time.

At the time of the FDA approval, the university drug patents have seven years of patent life remaining. The technology platform patents have five years of patent life remaining. The company patents have 9 to 13 years of patent life remaining, and the biomarker patents have 12 years of patent life remaining. These are some arbitrary numbers that we can discuss.

Now, there's some other facts that we put in here to discuss and how they may effect what may occur in a realistic situation where you have follow-on biologics using these because, as I said, you have a very complex patent portfolio.

Say the sponsor company does additional clinical trials and development on other indications and then

receives FDA approval of therapeutic treatment of prostate cancer three years after the first approval, which was for lung cancer.

The approval implicates a method of use and formulation patents not included in the first indication, again receives FDA approval for testicular cancer six years after the first approval, and testicular cancer in this case was also given an orphan drug designation.

At eight years after approval, a black box warning was given related to long-term side effects, and around eight years, also the FDA -- there was FDA approval to require biomarker assay to identify patients for whom use of the mass antibody would provide greatest benefit eight years after approval. All of these latter things require a labeling change for the biologic.

So here's sort of a summary of what we have of all of these. So we have, as you can see, a whole spectrum of patents covering a sponsor company's XYZ product. You have certain patent claims to the drug target, owned by the university, licensed to the sponsor, terms exclusive and field of use.

I mean, this is just sort of a summary of what we have. We have a technology platform. We have monoclonal antibody treatment processes. We have

biomarkers, and then at the bottom we have sort of a timeline over say 13 years from the initial approval of the product for the first indication of sort of expiration dates of various things or occurrences of various things.

So this fact pattern sort of sets up I think the discussion that we'll have for the next hour and a half or the like in regard to how patent scenario may be factored into the proposed legislation.

MR. WROBLEWSKI: Thanks, Rochelle. Before we jump into the series of questions that we have regarding the hypothetical, I would just like to ask: Why is a regulatory pathway or why is a patent resolution pathway prior to the expiration of any data exclusivity period necessary?

Before we get into the intricacies of it, why is it necessary or not necessary? I'm going to start with Christine, since she's our newest panelist. Pull the microphone down.

MS. SIWIK: I think the answer is yes, it's necessary, but...

I think if we learn from Hatch-Waxman, it's critical that key patent disputes get resolved concurrently with FDA review so that the generic is in the best possible position to launch as soon as you get

the FDA approval done, but I think we've learned a lot of other things from Hatch-Waxman too.

So my answer is, yes, it's important to have a mechanism in the bill for resolving certain patent disputes concurrent with FDA review, but the big but is, if the system doesn't work, if whatever this patent mechanism is doesn't work, I guess work in the sense that it can delay the market launch.

The reason to do it is because it can expedite, but if a process isn't right, if it isn't narrowly tailored to address those key patent disputes what you will end up seeing is significant delays to launch, and if the process is too cumbersome and it takes too long, because in litigation, length connotes a lot of money, and as a person who litigates patents for a living, that's fine for me. That's great.

MR. SCHULTZ: Doesn't it depend which side you're on?

MS. SIWIK: Either side. It works out fine. It's what's great about the whole thing, right, Jeff, it's whatever side you're on? But the longer it takes, the longer it's going to delay generic market entry, and the longer it takes, the more expensive it is, and the expensive it is, the fewer companies are going to be willing to shoulder the costs.

We've heard people from the generic side today saying, 10 million, 25, 35, 40, 50 a hundred million to do the drug. You throw on 5, 10, 15, 20, million for the litigation costs or whatever it's going to turn out to be, and that's just from the generic side, and I think most of us familiar with the industry know that the brands tend to outspend the generics significantly in litigation.

So if it's too long and cumbersome and it doesn't really hit the key patents, it's going to delay, which doesn't do anybody any good and if it takes too long and it's not well tailored, it's going to be expensive, and it could be prohibitive for some companies.

MR. WROBLEWSKI: Thanks, Hans, please.

MR. SAUER: Well, one can only agree with the need of a pre-approval patent resolution mechanism. I guess the difference is one of degree. I guess the way you would look at it from the perspective of an innovator is from the perspective of business risk.

So what does it mean to have a regulatory scheme that routinely contemplates the approval and launch of products at a time before you even know what kind of remedy you're going to get for infringement of your patents if your patents are held to be infringed.

So, in other words, as we look at it, there are two kinds -- from a patent perspective, two kinds of uncertainty built into the systems that we're contemplating today. One is the patent circumvention question that has been described in previous panels. That's uncertainty relative to what we see in the small molecule drug structure today where patents and follow-on products, in that case generic products, are much better paired than they will be in the follow-on biologic space.

The other element of uncertainty is that even for patents that are infringed, if products are launched before patent resolution is complete, you would have no way of knowing what kind of remedy you're going to get. I think it's going to be misguided to believe that follow-on products will be pulled off the market if you win your patent resolution suit once they've been established in the market.

I think it's just as misguided to believe that they will always be permitted onto the market and left on the market under kind of a compulsory license, but the point is you don't know what a court is going to do in that kind of situation and what kind of equitable remedy they're going to craft.

If you contrast that to the Hatch-Waxman Act

when it was crafted in 1984, that had built into it a lot of provisions to mitigate business risk, so you had an infringement safe harbor. You have an artificial act of infringement, so you can litigate without having to incur damages. Products and patents are much better paired. You have a 30 month stay so you can get the litigation done hopefully before you have to launch or before you get that launch pressure.

And these provisions to mitigate business risk we believe are one of the reasons why the generic industry has grown quite well and why the act has fostered an industry that has grown to what it is today.

Compare that to the biologic schemes we are discussing. Small drug development I think is going to look like a much more safer and interesting business proposition than biologics development where you don't have the same approval standards for follow-on products or you have a patent circumvention question.

And then if you layer on top of that a system that routinely contemplates launches before patent resolution, you get a double uncertainty that will make small molecule drug development look like a safer business proposition, and I think from our industry perspective, biotech's perspective, that would be quite intolerable because if anything, we think biotech

tolerates less business risk than small molecule.

So that's I think something that should probably be avoided. The patent resolution process is going to be necessary to offset the other risks that are already built into the process.

MR. WROBLEWSKI: David, you wanted to add a point?

MR. MANSPEIZER: Thank you. Three key elements to an early resolution patent mechanism have to be certainty, fairness and full disclosure, but we can't look at the patent resolution mechanism in isolation. You have to look at it in the context of the overall package.

So as you heard me speak earlier, we believe it's very important to have a system that adequately accounts for the uncertainty that provides, that patent litigation provides, with adequate data exclusivity.

Married to adequate data exclusivity, a patent litigation system can certainly be crafted, given all that we've learned from Hatch-Waxman, on both sides that provides fairness to everyone, certainty to everyone, and is based on full disclosure.

MR. WROBLEWSKI: Thanks. Ken, you had raised your tent?

MR. GOLDMAN: Yes, sir. I guess the Novartis

group of companies, which includes Sandoz, has a somewhat different opinion. Launching as risk, the fear that has been raised by Christine, is the norm as we have been discussing all day in the biotech industry, not just in the follow-on industry but in the innovator industry, as well.

There's not a single product that hasn't come on market in which launching at risk hasn't been a key issue. And companies are -- all of us here have the ability to take that business risk into consideration and decide whether or not to launch at risk. So the need for an early resolution, early litigation because of the fear of launching at risk is not a serious one we contend.

Furthermore, linkage, that is creating an artifical act of infringement by the filing of a follow-on biologic as like an ANDA is really quite an exception and not the rule in the patent world. In the U.S., the generic small molecule industry is the only industry that has such a scheme, and that was a result of the state of the industry in 1984, and we don't believe is required with the state of the industry in 2008.

Even in Europe, the biologic industry, there's no linkage. There's no linkage. There's no artifical

act of infringement in the European scheme as well, so it's a real aberration.

Another fallacy I would like to address is that early litigation means early resolution. I don't think that that's necessarily the case. We heard Doug Norman talk just on the last panel about the litigation on the 180 day exclusivities, combined with the new declaratory judgment standard, in Genentech versus MedImmune, which has really caused all sorts of complex difficult questions that can extend litigation for many extra years.

And besides that, we also see in those cases that there's serial litigation. You litigate one patent followed by another patent, and that can really extend the litigation pre-approval. Post approval, there's no incentive for serial litigation. You would want to bring your best patents quickly to get the product off the market.

Novartis does believe in the notification period following the approval of an FOB of a 45 to 90-day statutory stay so that would allow a patentee a chance to bring certain remedies to the judicial system, potentially get a preliminary injunction if that were warranted under the circumstances.

I have a few other points, but I think that's

enough for the moment.

MR. WROBLEWSKI: Thank you. Thank you. Bruce, did you want to add to that?

MR. LEICHER: Sure, I'll take a minute. We share some of those points and maybe disagree on some of those points.

The notion of waiting until the end of a data exclusivity period to litigate works for very large capitalized companies, doesn't work for the smaller innovators that may be developing in the biotech business, maybe going into developing biogenerics or biosimilars because they can't take the risk or raise the capital to fight those battles at that stage, and so it creates a different set of players in the industry along those lines.

From our perspective, we think it's really important, as Christine was saying, that there be certainty, that there be a reasonable period before the end of the data exclusivity period to have an opportunity to clear out of the way the patents that don't belong being in the way.

There's a natural, and as I'm sure others are going to disagree on the panel with me, but there is sort of a Darwinian process. There are going to be people making judgment on whether to develop a product

based on whether the patents are strong, valid, real or whether they're not, and if you don't have a process for clearing the path of the patents that shouldn't have the claims they have, we're going to be holding up competition inappropriately.

And by waiting until the end of the data exclusivity period, we're creating a de facto extension of exclusivity, and that's really the way we see it.

People refer to Europe as sort of a justification for having a longer data exclusivity than Hatch-Waxman, but in Europe you have the freedom to challenge patents at any time, essentially throughout opposition proceedings, through nullity proceedings, and we don't have that without some kind of artifical act of infringement or other kind of statutory mechanism in the U.S.

So we think that there ought to be a process. We think there ought to be an appropriate period perhaps and trade-off the balances that Hans was describing in Hatch-Waxman.

MR. WROBLEWSKI: Thank you. What would the effect be of, if there wasn't a process, and that once the FDA approved a follow-on application, that the innovator and the new applicant then decided to kind of fight it out? And does it depend on how long the data

exclusivity period is then? Ken, did you want to start with that?

MR. DOW: I would agree that it takes a certain amount of business risk to -- acceptance of the business risk to launch any one of these drugs, normally both for the biosimilar and for the innovator, but I think that without some kind of linkage or some kind of method to resolve the patent situation before the data exclusivity expires, you are going to be left with a situation where the generic is going to have to make the decision whether they are going to launch at risk in the face of a patent lawsuit, and if they do decide to do that, the market at that point is distorted.

There is -- the price will drop, and it's impossible I think at that point to put the Genie back in the bottle and restore the market, if ultimately the patentee wins, and the ability for the patentee to go and get a preliminary injunction to stop that from happening I think is going to be much more difficult in the future given a lot of the court rulings around preliminary injunctions.

MR. WROBLEWSKI: But how does that square with the idea that what we heard in the one of the first panels this morning was that at least in the near term, I would say near term is 10 to 15 years, that there's to

be little price competition. Won't a court judgment of infringement for damages compensate any harm that would be done to the innovator?

MR. DOW: That hasn't been our experience in the generic industry so far. I don't -- it remains to be seen whether you could adequately compensate. I don't believe you could.

MR. WROBLEWSKI: Okay. Jeff, you wanted to add something?

MR. KUSHAN: Yeah, I think first I will subscribe to the kind of more popular view I guess of saying it's probably better to have the resolution system in place. I think there are a couple nuances that need to be appreciated.

When you're looking at a window for drug development and you're within the data exclusivity window or some window that might be triggered off of a patent that's going to extend out passed that, you're looking at making your investments on the clinical development and expanding your base, getting more indications approved, and I think the impact of getting money at the back end of some calculus that you don't really know how it's going to work is hard to really filter into your decision ten years, eight years earlier when you're doing commencement of those trials.

So again we're looking at kind of where we know the outcome is going to end based on the patent portfolios and the data exclusivity, the more certain we know that there will not be a better molecule on the market during those windows of time is the stuff that leads into the decision to do the early stage and make those investments.

So we need to keep remembering it's not just kind of the immediate price erosion. It's just kind of a narrower perspective than what we actually would look at on an investment decision on clinical work.

On the system I think the critical thing to appreciate is there's really two bundles of patents that have to be resolved. The patents that are essentially blocking anybody who might want to make a molecule and get it on the market, and then the second basket of patents are the ones that the follow-on producers have elected to use, which aren't necessary to use to get their product made.

And I think in either of those bundles we should have the right to resolve our patent conflicts over either types of those patents, whether it's the one that's kind of dominating the product market or the one that the follow-on producer has elected to use a particular technology we've developed and patented.

There's no reason why we shouldn't be able to resolve that fight in advance of them getting onto the market.

I think the critical and difficult part of the equation is how do you know which patents matter and which patents have to be litigated? And ultimately I look at it very simply. We have to litigate the patents that are going to be infringed by the follow-on producer. It doesn't have to be any more complicated than that.

There are some choices that are not yours to make as a follow-on producer. You're going to make a product that's going to key off the end product covered by a dominating molecule patent, and then there's an array of patented technologies you might employ to make your product, which you don't have to necessarily employ but end up infringing in various rights. Those patents should be resolved as to their status before we see them getting onto the market.

Finally, we do have a somewhat artificial need for this because of the 271(e) exemption. We can't litigate until they're on the market, and so unlike Europe, we don't really have a parallel where we can start -- we need our artificial act of infringement because we kind of artificially exempted conduct from infringing in that context.

MR. WROBLEWSKI: Let me two more comments over here, and then we'll start into the hypo. Rochelle, I think --

MS. SEIDE: No, I think Jeff made a lot of the points I made because it's not only the sponsor's patents that may be litigated here, again the technology platform patents are very important, that no one can get on the market to do, and so there has to be some way of resolving third-party patents as well if they're known.

And it would be better to do them early on rather than with an at launch risk because the follow-on applicant will still be susceptible, even if there's a resolution with the sponsor. There's sill a susceptibility of an at risk launch after that, so there has to be a way of resolving all of this whole bundle of patents.

MR. WROBLEWSKI: Christine, yes, go ahead.

MS. SIWIK: A few quick response points. To Ken's point about at risk launch or the launches, it's a brand versus brand launch. That risk -- that isn't really in my opinion an appropriate model. The brand is going to charge its brand price. The other brand is going to charge its brand price.

If there's a damages calculus to be done, the infringing brand has sold their product at a -- I don't

say this in a bad way, but at a brand monopoly price. They don't have competition.

A generic, by definition, we launch at a lower price, so by definition we don't make enough money on each sale to cover the brand's lost profits, so to say that every other industry does it and the brands do it to each other, to me that's not a relevant comparison because it just doesn't happen.

And again I say this kind of tongue in cheek, but not every generic has Novartis's checkbook to write a check at the run, and if we launch at risk and we owe $2 for every dollar we made, that's going to put some people out of business and not everybody has that money, and that means we delay.

I guess a little bit going back to Jeff's point, the idea that they want to litigate the patents that are going to block everyone, that everyone has to infringe, you just had a panel two hours ago where we just talked about the fact that we can design around basically everything, and as generics, that the patents are narrow, that it's going to be easier for us to design around.

So I don't know what this universe of patents that we are all going to have to infringe necessarily is anymore. Maybe there are, but I didn't hear them

discussed on the panel about meeting data exclusivity because patents aren't good enough, so I think that, and the other thing is it all comes down to who decides.

I mean, we get sued on Hatch-Waxman everyday because someone thinks we infringe, but we don't always lose so it's a question of who decides what patents we infringe as the generics, and there's just some tension here in some of the arguments.

MR. WROBLEWSKI: Thank you. I'm going to turn to Ken and then to Bill, and then we'll start on going through the hypothetical.

MR. GOLDMAN: Thanks. First of all, Christine, about the branders, I wasn't necessarily talking about brand versus brand. It could be patent, just any patentee. Like for example in the EPO case I believe the Amgen versus Chugai, that was not brand versus brand. That was just two patent holders and just one product that was getting ready to go on the market at the time.

And on the point of the size of the bank account or the checkbook, I mean, it surprises me that if you're worried about -- that the companies that are worried about not having enough money are the ones that are advocating jumping into expensive litigation 30 months early.

I would think you would want to avoid that, the litigation. If you file any -- with the system in which you create an artifical act of infringement, you may in fact be bringing on expensive litigation costs earlier when you might not want to do that.

So a couple of points when Ken was talking and I guess Christine about launching it at risk, and whether waiting for post approval, going on the market and then being sued would artificially extend patent terms, and of course that is not really the right model because if we were talking about launching when there are existing patents so we're not talking about extending any patent, any patent term longer than the patentee's entitled to.

And under the Novartis scheme in which you would be required to give the innovator 45 or 90 days notice and be on stand until they had a chance to litigate, if an injunction is granted, then of course there will be no market and price erosion, and there will be -- and there won't be any extension. It will be -- the patent term will just continue.

If there is not an injunction, then there may be some mark in price erosion, but I think that we have the Plavix case which demonstrates that no price erosion is not irrevocable, so it's not clear that that is the situation.

And in terms of creating an artificial act of infringement, I think Bruce made a good point, which is that that's not the only option here. We have the option of following the European system of post-grant opposition, and I believe that that has been on the table in Congress with bills for quite some time, and that may be the very appropriate way of solving that problem without couplings.

In fact, you could solve -- you could get certainty far earlier if you can challenge the validity of a patent as soon as it issues and not when you're having to wait until you file your abbreviated new drug.

Just one last thing, I think I wanted to emphasize I think what Doug was saying on the last panel which is why do we want to create bounties on valid patents by creating this incentive system, especially in a situation that we're talking about, we're going to talk about now, in which you have very broad patents that cover -- and large patent estates that cover many different things, many different applications and potentially putting them at risk on the basis of someone filing a drug application that hasn't even yet been proven to be able to market an approvable drug at the time of filing of the application.

That's the wrong time to put at risk an entire

portfolio with broad and far-reaching implications outside of the FOB.

MR. WROBLEWSKI: Thank you. Bill, did you have something you want to say, and we'll turn to Suzanne and start going through the questions for the hypothetical.

MR. SCHULTZ: Yes, and this is on the record, and in the last panel after the panel, Michael and I talked and I think there's a misunderstanding between him and me about what market -- what the question was, and what the answer was. I'm not going to go through it all, but I thought the record ought to reflect that.

MR. WROBLEWSKI: Sure.

MR. SCHULTZ: I want to make a very broad point. The basic trade in Hatch-Waxman was that the brand companies got patent extensions of up to five years, maximum of 14 years, and the generic companies got a streamlined system under which they could get generic drugs on the market, and the whole theory of it was that on the day the patents -- or it could be exclusivity but it's usually patent -- expire, the generics should be ready to go on the market.

And as part of that they set up a system so that you could challenge -- if there are patents that the generic wanted to challenge, the idea was to challenge them early, so those could be resolved, so again the day

the valid patent expires, the generic goes on the market.

Now, there can be a lot of discussion about whether that works or not, but that was the theory, and I think it's absolutely what we should be striving for here, but what it means is that, first of all, there shouldn't be an issue about the remedy because the patents -- the idea is to resolve the patents before the generic even goes on the market, so there shouldn't be an issue about the brevity. If you don't do it, you're giving the brand an extra monopoly, an extra period of time while litigation ends up extending the monopoly.

MR. WROBLEWSKI: Doesn't that all depend on the length of the data exclusivity period then?

MR. SCHULTZ: Well, that's the third thing I want to say, and I don't think what I say matters, the data exclusivity or not, matters. Even if you had no data exclusivity, you still need a system to resolve any patents in dispute early so that again on the day the valid patents expire, the generic can go to market.

MR. WROBLEWSKI: Okay. Thank you. I'm going to turn to Suzanne, and we'll start going through kind of the nuts and bolts of if you had a patent resolution system, what are some of the tension points and things that would make it workable or not workable, so Suzanne?

MS. DRENNON: Thanks, Michael. Now, we're going to assume there is a patent resolution process, so the earlier questions were focused on whether or not there should be one, and at the beginning of the panel, Rochelle outlined our patents covering sponsor companies XYZ product, so now we're going to begin to use the chart that's behind us.

In using this case study, I would like to walk through the potential market consequences of patent resolution procedures relatively chronologically, so beginning first with the notice issues and then continuing to timing, moving to patent inclusion, then additional patents and approvals, discussing a sue or lose provision, so what sort of penalties should be in place, because there are penalties in some of the bills, and ending really because, this is the end of the day with a summary, by all panelists of what you think should be included in a patent resolution scheme and how you think that should work so we'll reserve 20 minutes at the end for that.

But to begin, with the beginning, when should a follow-on biologic applicant provide notice of its application to the sponsor company in relation to when any data exclusivity period ends? You're the first one.

MR. KUSHAN: I won one. I think there's been a

lot of discussion, which I think has been very constructive over the past couple years about how to figure out what patents matter, and I think when you look at the nature of the biologic approval, you're going to have to time the notice and the information exchange close enough in time to the potential approval to make sense because at the end of the day, you need to walk down the process technology.

And you're not going to want to do that eight years before you're on the market. You will want to do it two or three or four years before you're out, so something which is kind of aiming at the back end of the data exclusivity window is necessary so that you can get the relevant technology identified and resolved.

I think as a practical matter from the discussion this morning, the take away I have of the discussion this morning is that it may be that we will get a patent that covers through the claim language of the patent the exact molecule that's in the follow-on producer's product.

It may be that we don't, but then we may have process technology, and we may have other types of technology that's been patented, so there needs to be some kind of an exchange where the relevant patent owners can identify patents that they have that relate

to what is actually going to be marketed and how the product is going to be made.

And that's I think a big differentiation from the orange book Hatch-Waxman model where you might have a bit more certainty knowing the characteristics of the product, and second, the process variable in the approval system is the other differentiation.

The goal is to really not have disruptions once the follow-on product is on the market. Since the process technology used to make your product becomes integrated into the approval basis, you're going to want to resolve the process technology issues as well. Otherwise you're face the same kind of market disruption.

So I think as a practical matter, the only way to kind of navigate these two variables, the two unknowns is what patents matters and what technologies implicated by the follow-on producer. You're going to have to set up some kind of information exchange where the technology that's being used by the follow-on producer is communicated to some body of patent owners that are going to be having or holding relevant patents.

It's difficult because I don't know that it's so simple, and Rochelle's introduction makes it clear. You're dealing with a larger population of interested

patent owners, and you're dealing with a more granular type of relationship between the patents and the technology that's implicated, so it seems to me there needs to be some sort of flexible window during which you can figure out what patents matter, which ones are implicated, and once that's over, then you can go through the conventional dispute mechanisms that you might create.

MS. DRENNON: Christine?

MS. SIWIK: I think Hatch-Waxman included obviously the amendments because basically in part because what had you without it is we couldn't start doing the R&D without infringing the patent until the patent expired, and so you ended up with what they called the de facto patent exclusivity or, I'm sorry, a de facto patent extension because you couldn't infringe.

So the monopoly continued, again I'm not using that in a negative way, but the monopoly continued while we did the R&D, and they stopped it. They said that's not a good idea, let's get the research done now.

If we have the notice patent process start too close to the end of whatever data exclusivity period is, we're just going to create something new. We've going to create a de facto data exclusivity period because data exclusivity means people should be able to go when

that's over, whatever that date is, and the goal should be to set it so that we can definitely be done, and it can't start near the end.

Anyone that does Hatch-Waxman litigation knows it's -- there are courts that aren't giving us summary judgment any more. Trials are taking 48 months to get through court on a simple case, so it needs to happen early. It needs to happen right away. We need to start the process.

And with respect to the notice, I know your question asked us, are there any anti-competitive consequences to the notice. I think there could be significant anti-competitive consequences to this notice if it's not done carefully, which is under some of the pending bills -- we have to give over our entire, we'll refer to it as an ABLA for purposes, plus manufacturing information to anyone who wants it.

If you say you've got a patent, we've got to turn it over, and we have to turn it over with no real confidentiality provisions, and the brands say our data is really important, we deserve X amount of exclusivity to protect it. Our data is going to be important. We're going to be able to protect that too.

I guess the anti-competitive consequences from my perspective are: If you are going to do all this

work and spend the tens of millions of dollars it's going to take, you can't be forced to turn that stuff over to anyone who asks for it on insufficient confidentiality terms.

MS. DRENNON: Thank you. David, I think you had something.

MR. MANSPEIZER: Well, I don't think the three or the two people who have spoken so far and me are necessarily all that far off from each other. I think that we've got to have a resolution mechanism that starts early enough that we can completely resolve the issues before the end of the data exclusivity but late enough so that the process is set.

Now, if the data exclusivity is long enough, there's plenty of time to do that, and I'll just use the example that's up on the screen behind us. If you had 14 years of data exclusivity, and I'm using the term data exclusivity loosely, because true data exclusivity for 14 years would mean that you couldn't file an ABLA for 14 years, so let's use data exclusivity correctly.

Ten years of true data exclusivity followed by 4 year period of market exclusivity, in which there would be 48 months to resolve a litigation, would certainly seem to be enough time to allow the ABLA filer to have fully defined its process and what its product is and

yet give sufficient time -- and I recognize that we have some courts today who are not perhaps handling our cases as expeditiously as both sides would like. I think there are some ways to deal with that.

So I don't think that we're as far as off on the timing as people might think. I think the true dispute here is whether it should only be a limited number of patents or everything that both sides want to bring to the equation.

And I come back to the point I made before about fairness and complete resolution, and I think in order to get that, there needs to be some mechanism by which both sides can lay their cards on the table completely, and when I say both sides, I mean the innovator and the ABLA filer, recognizing that there may be some circumstances in which there are third party licenses.

There can be mechanisms worked out to deal with those, but once we get a basic structure in place, those are fine points, if we can agree on the basic structure.

MS. SIWIK: Just to be clear, I agree maybe conceptually we have some framework to talk about, but I just want to be clear that I'm not saying that we shouldn't -- eight years of data exclusivity is acceptable and that we should sit idly for eight years doing nothing.

I think we would want to be able to file our applications much sooner. And data exclusivity are filing moratoriums for the generics. That's what they are. We can call it whatever we want. It's a filing moratorium. You can't submit an application and get the review process started.

So the idea of basically double what we have in Hatch-Waxman as a filing moratorium, I don't think a lot of generics are going to find that particularly competitive, so I agree that we can probably talk about a structure, but I certainly wouldn't want to leave anyone here with the impression that we need eight years to file.

MR. WROBLEWSKI: Let me ask you a quick question: Say you had said -- say you had a data exclusivity period of X numbers of years and you would back out some period of time, you had said 48 months. Is it that you are waiting for an appeals court review to provide the certainty? Is that what you're looking for? If there were numbers say from a 2002 Generic Drug Study that showed that District Court resolution for all Hatch-Waxman cases up to that point took 24 months and that when you added in an appeals court, it added another 14 months, so you add the District Court plus the 14 months for an appeals court decision on average,

then you subtract it from whatever the data exclusivity period would be. Is that what you're thinking?

MR. MANSPEIZER: Yes, I was thinking Federal Circuit because the Federal Circuit, although obviously there's always the possibility of someone higher taking a look at one of the cases, but the Federal Circuit tends to be in these cases the less word, and that would give both sides the certainty.

I would back it out from the end, but recognizing again this is in the context of a fully defined system that has adequate data exclusivity.

MR. WROBLEWSKI: Sure, sure. I just wanted to make sure I understood what the time would represent, and it would represent an appeals court decision, and if you had average numbers, you could kind of make that calculus on average.

MR. MANSPEIZER: And I built in extra time because I think that everybody here who practices in this area recognizes that 30 months doesn't cut it.

MS. SIWIK: You can't get it out of District Court.

MR. MANSPEIZER: So we need to have an adequate period of time. You have to figure out what adequate means and ways in which we can expect courts to enforce that or live up to that end of the bargain.

MS. DRENNON: And we're actually going to come back to the litigation issue, but I think I'll ask one more question on the notice and, Ken, I know you had your card up, so both with respect to the question we just asked of when you should have notice, I also want to turn to: What should be included in that notice because we talked about it a little bit, but in a little bit more detail, what would you include in your notice.

And then also with respect to your notice should that just be to the sponsor company or as we have here, we have universities and third parties that are also involved with their own series of rights, how would you corporate those issues?

MR. GOLDMAN: All right. I wanted to -- the last conversation was quite a bit about data exclusivity and the interplay of the expiration of data exclusivity with patent exclusivity.

First of all, I don't believe data exclusivity is a filing moratorium. Obviously you can file a full drug application for a follow-on molecule. It's not a filing moratorium. It's only a moratorium on the use of data, and I don't think there's -- I mean, eight plus two is -- you can also think of that as ten minus two. It's ten years of market -- of data exclusivity and two years -- but you can start two years early in filing

your application.

You just can't get approved for two more years, so I think that whole calculus, there's no artificial data exclusivity extension I think in that system. You're going to come -- we're all going to come to some agreement about what the appropriate term is, and you're going to be able to have time to file your application and get it approved after the expiration of that term, but to tie it back to -- I'm going to first try and get back to the hypo and then violate my own promise in that regard.

The question is: When does patent exclusivity and with relation to data exclusivity, and I think this time language shows the impossibility of coming to any sort of reasonable conclusions about how those two are going to interplay. Let's assume that we have ten-year exclusivity. If you just look on the timeline, you have some patents expiring at five years, some patents at 7, some 9, 10, 11, 12, 13, 14 years.

Some of them obviously are going to expire within the data exclusivity. Some of them are going to expire outside of the data exclusivity. There's no way you can make any sort of reasonable legislative decisions on whether -- on what's going to control, whether you're going to need to -- whether people are

going to be able to file -- whether generics are going to be able to file before or after the data exclusivity.

The patent system should be separate. This is where I know we're assuming there's a patent resolution system, but it doesn't seem that you can make any reasonable conclusions on whether you need to have this system in place based on whether the patents are going to expire before or after the data exclusivity because even in this one situation, you're all over the map.

So Novartis believes that you don't need to have a notice provision when you file the FOB application. It would require disclosure of confidential data at a point which is inappropriate, and that the only notice that's necessary is after the approval and only to the extent that notifies the innovator that an FOB has been filed based on the innovator's delay.

MS. DRENNON: The other Ken?

MR. DOW: The one point I was going to make is obviously the longer the data exclusivity period, the less this becomes a problem because most of its patents -- a lot of the patents will expire, and so you're going to have less of an issue, but if the data exclusivity period is short, there are a lot more patent issues to be resolved in a very short period of time, and that it's unlikely that that is likely to occur.

MS. DRENNON: Turning to Jeff, both what should be included, and I would like to hear people's thoughts on whether notice should be given to anyone besides the sponsor company?

MR. KUSHAN: First of all, let's kind of step into the real world and realize that all the patents are published, and so the universe of what patents you're probably going to have to run into is not going to be an unknowable fact. You're the follow-on producer, you can do a patent search like anyone else can.

The universe of implicated potentially implicated patents is not infinite. It's going to be finite, and it will be a list of people that you can find.

I think the universe is also going to be a manageable one, once you understand what technology is being used by the follow-on producer to produce their product. Obviously the longer the data exclusivity window is, the fewer people you have to deal with, so I think there's not an intractable problem to figure out what patents have to be resolved based on which patents are going to be infringed.

I completely subscribe to the idea that you need to have the confidentiality bubble around the exchange of information. I don't think anybody would suggest

that you have to open up your manufacturing technology and let everybody see it, so you can implement a relatively straightforward type of mechanism to make sure that any information that is exchanged under this process will be done so without any risk of it going outside -- going to the public sector.

At the end of the day, the information has to identify what technology is going to be implicated so if you look at a typical manufacturing process, you will have to figure out the wholesale type, the sequence you might be producing, the nucleic acid sequence, maybe some of the expression technologies you're employing, so there's some process technologies, some of the manufacturing processing information will have to be conveyed.

The molecule structure, the formulation, the stuff that you typically might find corresponding to some of your Orange Book stuff, the molecule's identity and it's intended use. I think a lot of it will be captured in the biologically abbreviated application. There will be more that's needed beyond the typical application such as some of the process technology for manufacturing.

I think there's a way of figuring out how to provide a mechanism to let interested patent owners know

that there's a process that has to be started and give control to the applicant to determine when to convey information, and that may be the mechanism that you use to ensure who gets the information and barring them by any appropriate confidential restriction.

But we do have to figure out who make that official. We don't want to have to make that a game plank element of the system, but you do need to get into some of the technology used to make the product in order to figure out what patents you have to resolved.

MS. DRENNON: All right. Turn to Bruce and then Hans and Rochelle.

MR. LEICHER: Actually Jeff just made a number of points I was going to make, which I think one of the problems with the hypothetical, which is great for doing the analysis we are doing from a theoretical point of view, but from a policy making point of view, I think it overly complicates the circumstances of many products in the sense that it asks us before asking these questions.

So, for example, I would propose that the notice should only go to the sponsor, that with many products that any company launches, whether it's generic or brand, there are patents out there that you're going to do a clearance process, you're going to identify, and there are patents that are not controlled by your future

competitor, and you negotiate an agreement or a license with the university or with whoever holds that patent, and there's an example here on that.

And it's really the patents that are controlled by or are under common control with and some mechanism by the sponsor that I think you should give the notice to. We think that a notice mechanism needs to be kept as simple as possible.

I think that's sort of the view we have, something maybe along the lines of the PIV kind of notices now with some kind of reasonable confidential access provision so you can just get things dealt with, and I would also like to say, I agree with David, you need to do this early enough so that you don't end up -- and this is maybe where Ken and I disagree.

We think it's important you don't end up with a process that extends the data exclusivity period as a result of litigation. It's not so much the patent term, but the data exclusivity, but essentially I think if you limit it to the key patents that are built around the product that the brand company controls, I think you've got it simplified, and I also agree, you have the ability as a generic company to go and see what's out there because you know your process. You know your product.

MS. DRENNON: Thanks. Hans?

MR. SAUER: Everybody of course is striving for simplicity. I think you know what, Bruce, as you said, giving the notice only perhaps to the sponsor of the reference product, the ABLA would also be in synchrony with what was done under the Hatch-Waxman Act where third parties are largely excluded from the Hatch-Waxman specific patent resolution process.

I think certain -- to some degree I think we have to account to the fact that there is some more technology stacking going on in biotech than in the small molecule space. So I think maybe some accommodations can be found for the kinds of patents that would be exclusively licensed into the innovator's portfolio, and to even account for situations where the innovator himself may not have the first enforcement rights for such in-license patents.

I think as a basic proposition, I think innovators typically license them with enforcement rights. It sometimes does happen, that when they're in-license from certain academic institutes, that those retain first enforcement rights. And a way would have to be found to accommodate that. I don't think it's going to be an insurmountable obstacle.

At the end of the day I think the purpose of all

of this of course is to identify the patents that are going to be part of this pre resolution process, and in the Hatch-Waxman context, we do it with an Orange Book, and here the only reason why we talk about a notice is that we're obviously not contemplating an Orange Book like process.

I think probably for good reason in that the approval standard is not going to be one based on sameness, so you're going to be less clear about what kinds of patents you're supposed to be listing. The assumption can be to the same extent that is under Hatch-Waxman, that you list the patents you are going to be covering, the follow-on product, and the second difference I guess is product process patents, which aren't part of the Orange Book process.

And it would have to be included. Again it's going to be easier to do this through a notice process, and the third I think is a structural problem with the Orange Book process, and that once you start requiring people to list patents, you're presumably going to build in disincentives for not listing patents, penalties for listing wrong patents, and as we've seen in the Hatch-Waxman context, it tends to drive people to over-list or to start putting things in there for fear of being penalized and not having put them in there.

So for all these reasons that we see that in other contexts cropping up through the legislative proposals do, but forfeiture provisions and all that kind of stuff. I think keeping it simple and as close as possible to normal patent litigation I think is going to be beneficial, and therefore I think a notice process under appropriate confidentiality and not everybody who thinks they have a patent that covers the follow-on product can show up from outside is going to be helpful and more appropriate.

MS. DRENNON: Thank you. Christine and Rochelle and Esther, and as you're answering this, I would be interested in other thoughts that you have with respect to the Orange Book because technically I have that coming later but I think it's a good time to talk about it now.

MS. SIWIK: It fits in. There are obviously -- in Hatch-Waxman there are third parties that own patents. We do give notice to people who are other than the brands. We give notice to the patent holders. It's easier to figure out with the Orange Book, but we routinely do give out the notice letter to companies that are not the brand.

It happens I just did it this week. It happens -- it does happen a lot, so I think that

starting with the brand I think makes sense. They know what patents they've licensed. I don't as the person who is submitting it, so I do think it's only realistic to think there's going to be people other than the brand who are going to need notice.

I mean, especially -- I know we'll get to this at the end so I'll throw it out. If there are sue or lose type penalties, the people that the brand is licensing from are going to need to be part of that process in some respects.

Again I agree simplicity is important, but if there's going to be a sue or lose, there has to be someone that knows that might be happening, I hate to use the word fair because it so rarely counts in these things, but you need to be fair.

And I think that the idea of the Orange Book, I think Hatch-Waxman works. I think it could be better. I think it could be a lot worse, but I think we can look at that -- I don't know if Liz Dickinson is still here. I love talking to her all the time about the Orange Book, multiple times a week, but there's going to be a better way to do it.

I don't know if listing -- I think the concerns are right. There's over listing. There's under listing, how are you going to figure it out. I think

the idea behind the Orange Book, the idea of identifying key patents and litigating those early is not a bad idea at all. It's a good idea, but an FDA should be doing what FDA does which is reviewing and approving applications.

Like I said, I love talking to the office of chief counsel, it's fun, but their time is going to be better spent not figuring out what patents should have been listed, and to take it even a step further, none of the bills that I've seen tie any type of exclusivity to the generics actually submitting a patent. It's a challenge. It's been tied to approval.

And that takes even more of a burden off the FDA, the idea of collateral litigation I think Bruce touched on earlier, I haven't seen a proposal where that would happen because FDA is being pulled out of the picture, and I think to the extent we can let them focus on what they're good at and what they should be doing, I think it helps everybody.

MS. DRENNON: Thanks. Rochelle?

MS. SEIDE: I think some of the points that I was going to address have already been addressed. Particularly in this area, process patents are of importance, and they are specifically excluded, and the drugs situation from the Orange Book. You do not --

there's a separate method under 271(g), pursuant to 271(g) that you go and ask the sponsor or the brand company for any process patents that might cover their product because they are not listed in the Orange Book.

The same kind of situation occurs in regard to producing generic antibiotics which are not also listed in the Orange Book, and I would venture to say that generic companies that are looking to make a generic antibiotic have a very difficult time of identifying what patents are important in regard to that because if they are not listed on the label, there's a very difficult way of going to find who owns those patents.

And it may again -- the same kind of thing, it may be that the patentee is not the drug sponsor, and when you're looking -- when you give notice to say the patentee, it may not be the brand company that's the drug sponsor, and I've seen this in a lot of situations.

I again think the notice, the whole issue of notice should be as simple as possible, but some of the issues are more complex than we see even in the more complex drug situations.

MS. DRENNON: Thanks. Esther?

MS. KEPPLINGER: Just a couple of points, but the example that we created was not just an arbitrary hypothetical but actually Hans pulled together an amount

of data from actual situations and drugs, and so we compiled the example trying to base it on the kinds of situations that are actually out there. We threw a couple of additional curve balls in, but this is the kind of situation that might be typical in biologics.

Secondly, it seems like one of the lessons from Hatch-Waxman, and many people have talked about it, is that there's quite a lot of litigation, and it seems like in designing the situation, we should be looking to try to reduce the litigation because it is just a lot of money that could probably be better spent on other things, like designing more pharmaceuticals.

Lastly, with respect to the Orange Book, it seems that it should also be a simple process, one in which you reduce the number of errors that could possibly be made by someone so a different kind of mechanism for identifying what patents would be appropriate should be looked at.

MS. DRENNON: Ken Goldman?

MR. GOLDMAN: I'm sure everyone is going to be shocked to hear that Novartis does not believe that there needs to be Orange Book listings. I wanted to address -- in that regard, I wanted to address something that Bill said with regard to Hatch-Waxman, which is that the purpose of Hatch-Waxman is so that when valid

patents expire, competition can begin. That's fair, right?

And I just wanted to say that Novartis completely agrees with that, that when patents expire, competition should begin. That's absolutely our fundamental principle for us. The problem of course is: What does pre approval patent resolution due to achieve that?

I mean, again I wish Doug was back on this panel. He said if you look at the history of drug litigation in the last 20 years, you would believe that the PTO has failed to issue one single valid patent that covers a drug. Every single patent gets challenged. So the point being that the pre-approval patent resolution process is an opportunity to bounty hunt. Of course everyone is going to -- all the generic companies are going to challenge every patent under the rubric that otherwise there will be a patent extension because of patents -- because they won't be able to launch because of the existence of illegitimate patent. But I say that that's not true.

The way to achieve that for generics is exactly the same way that innovators that launch drugs deal with that, which is you make an assessment, and you launch at the time that you believe that you don't infringe any

valid patents.

It's the same for innovators as it is for generics, and you don't need any sort of pre approval resolution procedure to do that. The generics would be in exactly the same place as every other drug company is when they go to launch a product biologic product.

MS. DRENNON: Ken Dow.

MR. DOW: We were talking a little bit about this possible exchange of information earlier on, so well I was going to mention that there are some precedence for that, and Rochelle mentioned one, under 271(g), that the process patent requests.

The other is early in the Hatch-Waxman context when there is a patent certified filed, oftentimes the issue might be around infringement or whether the generic actually will infringe the product, and often early in that process there is an exchange of information under an appropriate protective order so that the brand can make an evaluation as to whether or not the product will actually infringe these -- sometimes the later formulation patents and that sort of thing.

And so we know how to do this. We've done it, we do it in other contexts, and I don't see any reason why we couldn't it, we design the same kind of system

here.

MS. DRENNON: Thank you. And I would like to switch gears a little bit and still follow up with what we've been talking about, but ask if the timing of FDA approval should be tied to the outcome of the patent resolution process, and what are the marketing and competitive consequences of this decision. I guess Christine would like to go?

MS. SIWIK: I'll start and then Jeff should go next.

MS. DRENNON: Let's go to Hans. It looked like you were raising your hand. Either way, I'm happy Hans, why don't you start.

MR. SAUER: Your question sounds again a bit like linkage so what about lineage, should there be linkage or not? Under Hatch-Waxman I think people understand linkage to mean different things. We've heard one definition, and others under -- others think the 30-month stay when they hear that. Something is delayed in the FDA approval process if litigation starts.

Others see other elements there, so I think if we dissect that so there's this one element, a 30 month stay that kicks in that delays the approval of the ANDA, and that happens solely by virtue of the reference drug

holder having filed a lawsuit and pressing a lawsuit, so it's not about winning, it's about litigating, which results in an exclusivity benefit.

I think that has been necessary because -- for various reasons I guess. It's been built into the Hatch-Waxman Act from its inception, but it's been subject to a lot of criticism too. I think it's been remarkable that nobody has been -- on this panel so far has been arguing for a 30 month like stay provision to be built into this follow-on pathway, where approval is stayed solely by being virtue of being in litigation or where litigation itself is something that's valuable.

The other linkage concept I guess that's built into the Hatch-Waxman is that once patent litigation is resolved, if everything works as planned within Hatch-Waxman and within 30 months you get to a final judgment and the patent is upheld and found to be infringed, then the secretary won't make the ANDA approval effective until the expiration of that patent.

That kind of linkage seems to be quite rational, and it seems to be the logical consequence of having any pre approval patent resolution mechanism, so that I guess is something that we would all agree to at BIO as an appropriate element. Nobody is really asking for delaying approval pending litigation, which many BIO

members don't.

MR. WROBLEWSKI: To make sure I understand, that if the FOB, the follow-on application, the ABLA were to lose at the District Court level, should the FDA stop its review?

MR. SAUER: No, no, I don't think it should stop its, just like it doesn't stop its review under the Hatch-Waxman.

MR. WROBLEWSKI: How far do you go? Federal Circuit, Supreme Court? If there's linkage, what is the stopping point?

MR. SAUER: The stopping point of final resolution of litigation? I think that's open to discussion. Under the MMA it's District Court judgment and it is falsely -- and that would be kind of a logical symmetry to what we might want to adopt here.

MS. DRENNON: Christine?

MS. SIWIK: I think I'll agree with half, not the second half. I think, like I said, we've learned a lot from Hatch-Waxman, and I think one of the things that the generic side has learned is that linkage doesn't expedite market entry. The 30 monthly litigation stay linkage encourages litigation.

That's a significant financial incentive to file a suit, regardless of whether or not -- what you value

your chance of success. Someone has made the point, well, if we launch and you get damages four or five years later, that's not sufficient. That might not be sufficient. The same is true for us.

If we get sued from a frivolous lawsuit, our approval is delayed for 30 months and a day, and I try to get antitrust damages and good luck, but if I do that's another five years away, and that doesn't make up for the competitive harm.

So I think linkage in that sense of the initiation of a lawsuit somehow is going to delay approval or somehow impact approval, I think that we should avoid that. I think it does have anti-competitive -- I'm not saying antitrust but anti-competitive consequences because it creates an incentive to file lawsuits that you might not otherwise have filed.

And I think linkage between the outcome of the patent litigation and the approval, in this context in particular, is not necessarily going to be appropriate. We've heard a lot that there's all these different types of patents. I mean, for example, let's pick one from the hypothetical tech platform patents. We saw in the assumptions that that's not exclusively licensed to the brand. It's not exclusively licensed to many other

companies for many other products.

If I am found to infringe that patent, they're not going to get a permanent injunction, to block my approval because they're more likely than not not going to be able to establish that standard given their licensing history. Why should I get stayed for my approval until patent expires simply because -- in other words if the brand can prove a permanent injunction, get a permanent injunction. Don't give it to them automatically with linkage because there isn't -- there's going to be patents that exist that they're not going to be able to make that standard.

Yet if there's automatic linkage we're going to get blocked even in they can't meet the standard.

MR. WROBLEWSKI: Can I ask you a follow-up question? What you said intrigued me. You said a 30-month stay encourages litigation.

MS. SIWIK: Yes.

MR. WROBLEWSKI: What's the difference between that and a data exclusivity period minus X numbers of years? In my example, David had earlier in the discussion said 48. When you are coming the other way, isn't that the same thing? Couldn't a data exclusivity minus X numbers of years have the same economic affect as the 30 months stay in terms of encouraging litigation

that may otherwise not occur?

MS. SIWIK: Yes, and that's why there should be no data exclusivity either. It's all bad.

MS. DRENNON: Christine, if you could move a little closer so we can get it recorded.

MS. SIWIK: Yes, but yes and no. Yes and no. I mean, they're going to get their data exclusivity period whatever that number is, regardless of the patent litigation. If there's no linkage, I don't see what extra incentive they have necessarily to bring that suit. Do you see what I'm saying?

So they're going to get eight or nine, four, three, five, whatever those years are, and if in theory we set it up such that the litigation would necessarily be complete, whatever that means, by the end of that period, what extra incentive do they have because it's not going to get them anything else? Under Hatch-Waxman it gets you 30 months no matter what.

MS. DRENNON: Jeff or Ken?

MR. GOLDMAN: Can I just make one quick comment about linkage because I'm not confused about what linkage means, and usually that of course means that I'm not thinking about it hard enough, but linkage in my mind is the creation of an artifical act of infringement by the filing of that FOB application. Now you'll prove

me right.

MS. DRENNON: Jeff?

MR. KUSHAN: I think the question that you are asking is whether a valid patent is infringed by a follow-on producer, the FDA should defer the approval of their application until the expiration of that valid infringed patent, and I think for many people in the biotech community, the answer has got to be yes, and it's not a complicated question, and it resolves itself in two ways.

If it's an elective technology, which you have elected to use and therefore have infringed, the consequence of not using the technology is logicalness that is what a lot of businesses are based on in terms of the biotech community.

I think the practice of licensing does go into the question of whether you'll get an injunction. I think it's not a black and white question. I think there are many instances where you can enforce and get an injunction against a party notwithstanding the fact that you have a non exclusive license to somebody else.

There's a variable that goes into the equation of a conventional litigation that dictates whether you're going to get this injunction or not. In this environment, if we're going to be designing it to signal

which patents should be avoided and which ones should not be, the logical connection is that you come in and say, if you elect to use the technology, then you're going to have to have a deferral on when you can get onto the market using that technology.

It may be that if do you things right and you have an initial fight about technology you don't have to use to make good product, you do what everybody else does and you change your method before it has a big consequence on you getting on the market.

That's the way it should be, and that resolves the patent dispute by not admitting the issue of infringement, and this is all going to happen before there's any liability because you're talking about pre approval.

So there seems to me a logical symmetry of saying let's drill down to the patents that do present the conflict, resolve the status of those patents, if the resolution is that patent is invalid and infringed, the linkage should flow from that, that you should have a deferral of the product that has deployed the technology that you've infringed.

I think if you go to a more subjective standard that basically says you can litigate and then there's just whatever outcome you get is going to come, that

does erode the confidence that you're trying to create in the market equation that the innovators is looking at.

So there should be -- this doesn't have to be black and white. I think maybe you need to look at the types of patents that are at issue, but conceptually it makes sense that if you're making the investment to do the litigation upfront, you should tie the outcome as it makes sense into the linkage structure.

MS. DRENNON: All right. And Ken Dow?

MR. DOW: One issue that concerns me is that if you don't have some kind of linkage, then you get a sticky situation at the end of the -- if the patent is determined to be valid and infringed, what do you then do if the generic has already launched and you wind up with the same kind of compulsory license situation which we've never really been in favor of in this country, or you have to pull the drug from the market, which is not going to be something that you want to subject consumers to pulling drugs off the market that have been put out there.

I think that's a really bad idea so that I see early resolution of these disputes the only answer.

MS. DRENNON: Bill Schultz?

MR. SCHULTZ: Personally I'm not persuaded that

there should be any filing moratorium. In other words, I'm not persuaded that the generics shouldn't be able to litigate these patents as early as they want after they've filed their application.

MS. DRENNON: What do you mean by filing moratorium?

MR. SCHULTZ: I mean a period of time during which the generic cannot file an abbreviated application, I'm not persuaded of that, but if there is to be one, then you need to figure out how long the litigation is going to take. This is the point I want to make.

I don't think we should be looking at the average time because if you pick the -- if the average is 48 months and you pick that, then they're going to be roughly half, half of the time the litigation is actually going to delay the generic from getting on the market, so if you were going to pick this period of time you really need to look at the upper end and say, What's the upper end amount of time litigation is likely to take because the whole goal ought to be so that litigation is not delaying approval of the generic.

MS. DRENNON: Thank you, and, Hans, I see that your tent is up. We're also planning on talking about -- okay, excellent. Because we have about 15

minutes to cover a couple of other issues before we get to our final summary point, and the next issue I want to talk about is: We have this spreadsheet here with all these other patents and then when you look at the timeline, you have the second approval and third approval and all of that.

Once the resolution process has begun, assume it's begun, how should the process handle additional patents that are applied for and/or granted that claim the reference product? And then also I'm tying these together. Let's do that quickly and then I have a follow-up question, so does anyone have any thoughts on that. Bruce?

MR. LEICHER: From our perspective it seems there should just be a DJ right or an artifical act of infringement so you could actually integrate it into the litigation that's occurring at that point in time so you can actually have the clarity in the same timeframe.

MS. DRENNON: Christine?

MS. SIWIK: I think that works fine in theory a little bit, and I think maybe my experience with Hatch-Waxman has taught me a little bit different, which is you can't keep going. You can't be 30 month s into your litigation, have a new patent issue and start from scratch, get 15 more months into your litigation, have

another patent issue and then stop everything.

You will never get done, and there is a remarkable opportunity to stager patent issuance. It's not an exact science any more than you can predict the day your approval is going to pop out of FDA, but there are a lot of things that can be done to stager patent issuance. We've seen it happen a lot.

So the idea -- like I said in theory you would want to resolve the key disputes, but as time goes on, the chances of those patents also covering the product seems slim because that, in theory, is what we heard is the first patent you get, not the 15th patent you get 15 years after approval.

So as time goes on, the patents get more narrow. The patents get further away from the brand product or something we infringe, so the idea of folding in every new patent that comes out right away is going to drag the litigation out way, way too long.

MS. DRENNON: David and then Jeff?

MR. MANSPEIZER: Confining myself to your hypothetical --

MS. DRENNON: If you have major changes that would affect your answer, the hypothetical is just a hypothetical.

MR. MANSPEIZER: Because you directly were

questioning about the second and third edification, and the answer there seems to me is defined by: Is the biosimilar applicant seeking approval for that indication. If they are, then there should be a mechanism to include that. If they aren't, and they're not allowed to promote for that and they're not allowed to sell for that and there's no substitution, then it shouldn't be included.

MS. DRENNON: Thank you.

MR. LEICHER: Let me say that we would also agree with that point as well.

MS. DRENNON: Jeff?

MR. KUSHAN: I don't have a lot to add. I think the one thing that I have found in my experience is that the patents that come out later you can't really make any conclusions about, whether they're going to be narrower, broader. It may be that the first patent that came out of the gate is the picture claim because that's the one that was easiest to demonstrate patentability.

The one that took an appeal, an inference to come out of the system may be broader. The converse may be true, and it may be that maybe you get a late issuing extremely narrow claim which lands directly on the follow-on's product, so I think you need a little bit of flexibility in your thinking about the patents might be

that come out and why they might come out late.

And I also wish, maybe you are more powerful than I am in controlling exactly when the patent office will give us a patent, but usually it's never, but it's another question, but it's not a process that you can carefully predict. I think the basic mechanism is when the patent comes out, determining if it's going to be infringed, and if it needs to be resolved, it goes into the existing litigation.

MS. DRENNON: What if the existing litigation has ended?

MR. KUSHAN: You may need to bring a new suit. Again, at some level, the mechanism, if it's embedded within the data exclusivity period, is self resolving, if it's a patent that issues the day after the follow-on launches, that's an undesirable scenario, but it's one where you're just going to have to fight it out, and it may have that less desirable outcome of disrupting what happens on the market.

But the idea is that if everybody is trying to get everything resolved with this early notification process, you get as many of it done as possible, that's the optimal model. I just want to make sure people appreciate that you can't make these kind of general assumptions about what the patents are that might come

out late and why they might have come out late.

MS. DRENNON: Hans, I think you have your something?

MR. SAUER: Jeff largely said it. As a practical matter, with appropriate periods of data exclusivity, I think as a practical matter, the issuance of patents that run into the back end of data exclusivity, that innovators might get so late in the game is -- it can't really be predicted what kind of patents those might be, but if they issue that late, and that's again a business risk that the innovator will have to live with as well, at some point this data exclusivity period is over, and if there's an ongoing lawsuit, the FDA is still going to make the approval effective of what we're seeing.

And then things will work themselves out the way they do in normal patent litigation in that context. Also I think there's some element of being able to stir issuance of patents. The PTO has a much tolerated accelerated review program, accelerated review program that you can take advantage of.

So everybody has some business risk, and if your patent issues, whatever, 12 years into the market, I think that's probably a business risk that innovators live with today and they can live with under this system

as well.

MS. DRENNON: Ken Goldman and then Ken Dow.

MR. GOLDMAN: Just real quickly on the issue of the later filed, the later issuing patents, I agree with Hans that these are normal litigation issues, and title 35 and judge made law surrounding that are perfectly adequate to deal with issues of whether you can add patents to ongoing litigation or not.

And I see no reason why this particular issue has any particular valiance in this context so it's just another reason to keep there whole issue out separate from the FOB approval process.

MS. DRENNON: Ken?

MR. DOW: I wanted to make a point about subsequent indications.

MS. DRENNON: That was my follow-on.

MR. DOW: And why we need to deal with that in the data exclusivity, because you need to provide that incentive to investigate newer indications.

If you rely solely on patents and your patent is only on the secondary indication and the generic comes on the market for the primary indication, the first approval, there's nothing that that second patent will do. You can't use that patent to prevent doctors from using the generic drug for the secondary indication, and

so you lose that incentive if you don't deal with it in -- by tacking it on to the original data exclusivity period.

MS. DRENNON: Christine, and then I would like to move to the issue of penalties.

MS. SIWIK: Well, quickly I think the problem I would throw out maybe, and I wasn't trying to suggest it was possible to pinpoint when new patents are coming out, but I think the idea of the problem of these late arriving patents is going to be exacerbated depending on the number of third-parties that allowed to come into the process.

So while the brand might say, I'm only going to get ten patents on this, if any third-party that wants to is allowed to jump in, it just raises a whole new host of issues for these late patents if they're automatically allowed to be brought in.

MS. DRENNON: Thank you. Now turning to the idea of kind of an enforcement issue: If any party fails to participate in the patent resolution process, should there be regulatory penalties? To whom should the penalties apply? Again we've got the sponsor company, the university and the third party follow-on applicant, and what is the competitive effect of a sue or lose provision? Ken, you're up.

MR. GOLDMAN: Oh, no, but since you asked, I think obviously sue or lose is a -- sounds very penalty oriented and in fact seems to detract from Constitutionally appointed patent rights, and we would oppose the insertion of any type of sue or lose provision.

MS. DRENNON: Would you have any enforcement provisions other than what's in title 35?

MR. GOLDMAN: I'm sorry?

MS. DRENNON: Would you have any enforcement provisions?

MR. GOLDMAN: Enforcement provisions of?

MS. DRENNON: Such that if a party doesn't participate in the regulatory process, and later then asserts rights under just title 35?

MR. GOLDMAN: There's case made law about how long you can delay in filing your lawsuit, and we believe those are the adequate protections.

MS. DRENNON: Thank you.

MS. SEIDE: I was going to say the same thing in the sense that those situations exist, even though in a sense Hatch-Waxman has that kind of penalty. If you don't sue in 45 days after the Paragraph IV situation, and the ANDA is approved, there is really not a penalty because the innovator or the branded can sue under

271(a). There's no preclusion against bringing a regular patent lawsuit at this point in time.

MS. DRENNON: What if you didn't have that 45 day -- what if that wasn't part of the regulation? How would that affect things?

MS. SEIDE: It's a matter of whether the penalty applies to pre or post approval. I think that would be an issue. Are you making the penalty -- if you don't sue pre approval, do you lose the right to sue post approval, and I don't think you can -- that's a property right. The issues maybe different. You have a property right in your patent and don't have to sue on it at a particular time, and then you're sort of taking away a property right from the innovator from the patent holder.

MS. DRENNON: If you're doing that and it's not a matter of the regulatory process, how do achieve certainty through the regulatory process?

MS. SEIDE: In that situation you can't. And I don't think you can.

MS. DRENNON: Okay. So you wouldn't be able to have certainty?

MS. SEIDE: No. The certainty is when the patents all expire.

MS. DRENNON: Christine and then Bill?

MS. SIWIK: I think that's part of the issue is that the whole purpose of this system, let's just say it's pre approval, the whole point is to get certainty and if you can hold back patents, if the brand, a third-party, whoever, if you can hold back patents until just near the end of litigation or just to launch, if the point is to litigate early to get certainty, everyone has to play by that.

And if it doesn't happen, then the whole point of the process is lost so whether or not the generics will hold up their end of the bargain, whether or not the brands will hold up their end of the bargain, what those penalties need to be are going to be in large part a function of what the overall scheme looks like.

If the overall scheme is fair and balanced, maybe we don't need to worry about huge sticks to make people participate, but in Hatch-Waxman we learned that there are rules, but if there are no sticks, the rules are going to go out the window. There were statutory definitions of what patents could go in the Orange Book, and there were a few companies that abused that, and a list of other patents triggered a lot of 30 month stays and a lot of litigation delays, but there were no penalties for doing it.

The courts refused to enforce it. FDA wouldn't

enforce it, so just we ended up with an untenable situation until that was corrected, what, 20 years later so people need to participate and do the system or else what's the point.

MS. DRENNON: Bill and then David, and then I see we have a bunch of people over here, and then we'll do our sort of summary what should the goals be.

MR. SCHULTZ: Christine said what I wanted to say because it's really important.

MS. DRENNON: Do you have to because we've got 12 minutes?

MR. SCHULTZ: Yes. This is really fundamental. I mean, if the basic idea is that at the end of valid patents, the day after valid patents expire you get to go on the market, then you have to have a system that allows that to happen, and if you don't have some mechanism for forcing these lawsuits to be resolved early, then effectively the brand gets a patent extension or an extension of its monopoly for however long it takes to litigate.

So we've now pushed all the incentive to the end of the process, and the incentive is to bring the cases late and litigate them late, and this isn't anything against the brands because everyone in this business is going to operate in a financial interest, and that's the

last thing you want to do.

MS. DRENNON: David?

MR. MANSPEIZER: If we design the system the right way, such that it's based on principles of certainty and principles of full disclosure, then I don't have a problem in the right system with a sue or lose provision because I think under traditional principles of laches and estoppel, you're probably going to be excluded anyway.

Now, there have to be -- kind of the unfair play role on both sides, so if -- I'll give you an example. If the biosimilar applicant were to change its process, such that in the middle of the processing of its application at FDA, were to change its process such as to bring a patent that was otherwise not infringed by the old process, but now has become relevant by virtue of their change, you shouldn't be precluded from asserting that patent.

I would also put some incentives on the table for the biosimilar applicant to want to fully disclose, and one example would be perhaps a requirement that they have to certify to FDA that they have in fact fully disclosed.

I don't think anybody in this business would like to -- on any side wants to be on FDA's bad side by

putting in a statement that's not truthful and accurate, but I think again it all comes down to, in many ways, what does your system look like, and is it adequately and fairly balanced.

MS. DRENNON: And then I think Bruce and Jeff. Bruce is down?

MR. LEICHER: I think the points have been made.

MS. DRENNON: Okay. Jeff?

MR. KUSHAN: Yeah. I think in large part the going in and abrogating a property right is a very serious event, and I think by looking at that as a sanction is kind of like the only sanction to think about is a little bit unsettling to many people because given the flavors of the process we've seen so far, there's a lot of administrative risk. There's a lot of procedural risk that you then see translating into lost profit rights.

So that's why there's just a general reluctance to say, If you don't comply with the process, your property rights disappear, and so maybe the right way of thinking is not necessarily focusing on kind of the loss of right patent sanctions, but I tend to believe that if you set up the process and everybody participates thoroughly in it, and despite that you get notice of the infringement and you take no action, the first thing

that you will have as a biosimilar is the right to have the right to file yourself.

And in the case of Novartis it makes it pretty clear that you're going to have DJ jurisdiction, and if it's a patent that the other side really wants to fight about, it will start the fight, and maybe you need to bless that, the right way given that standing.

The second variable is if neither side starts the fight and you're out eight years later, the idea that I'm going to walk into a court and get an injunction on this patent that I've been sitting on for eight years is a pretty tough sell. I know there's no hundred percent certainty but that's a tough case.

So there's a self policing variable in the equation as to the amount of disruption you can cause to the follow-on's conduct once they're on the market if you don't participate in the system.

So I think at the end of the day, my two points are really, when people focus on the patent sanction as the mechanism, it's a very big sanction, especially when there's a lot of different products that might be implicated by that one patent.

The second variable is that there's ways short of that patent sanction to give relief to the party that needs to fight and resolve patent suits, and those

certainly should be included in the equation of any kind of system.

MS. DRENNON: And, Ken, can you include your points in a wrap up? Would that be okay if I turned it on you?

MR. DOW: Okay.

MS. DRENNON: Thank you. Because I want to thank everyone for spending -- Christine as well, I'm sorry I missed you. Thank everyone for spending two hours on a Friday afternoon talking about patents. I was really looking forward to this, but I know that.

MR. KUSHAN: Most exciting thing ever.

MS. DRENNON: I do honestly think that. I know that other people might not share in my joy.

MR. WROBLEWSKI: Also I wanted to thank Suzanne for -- this is something new for the FTC to try to do a hypothetical like this and to craft an open discussion, so this was kind of testing the waters, and I think Suzanne and all of the folks here on this panel did a fantastic job. So I appreciate your taking the leadership role and getting this initiative off the ground and have it so well received.

MS. DRENNON: I guess to wrap up, based on our discussions today, what should be the main goal of a regulatory patent resolution system? And, Ken, since I

cut you off last, I'm going to go to you first, and I think I'll just go around and see what people have to say.

MR. WROBLEWSKI: I'm going to add to Suzanne's point about what the main goal should be and achievable?

MS. DRENNON: That's a good point.

MR. DOW: First of all, I want to thank you for allowing us to come here and be heard and have this discussion. I think it was great.

The one point I wanted to make was that I think in terms of the sue or lose provision, I think that was one thing that Hatch-Waxman might have gotten a little bit right, but there was a linkage there, and if the patent was put into play, then you had a chance to resolve the patent litigation, and as long as that was done, you had linkage that the generic wouldn't be approved.

If you didn't sue, you lost the linkage. And you could still sue later on, but the generic could be already launched. So that was one thing I thought was conceptually right. Whether we do that, whether we have 30 months stays or not, I don't know if that's the right answer, but at least something like that.

I do think that the goal of the patent resolution process should be to resolve the patent

issues during the exclusivity period so that everyone has certainty as to when the generic can launch, and I do think that it's achievable. I think it's something that we can -- there are some good proposals out there. I think we can work with them. I think in the end I think we can design something that will work for all the parties involved.

MR. GOLDMAN: I also would like to thank you for inviting the Novartis group of companies, which includes Sandoz, to speak here, and I just -- it's obviously a very complicated issue.

The question of early resolution I believe is tied to the art. You can't have early resolution unless you create the artificial act of infringement, which is the filing of an ABLA, which is I think what linkage -- despite the fact that I think people seem to agree with me, I think the court would disagree with me.

The core of early resolution is the creation of the artificial act of infringement, and everything follows from there, and Novartis believes that there's no need to do that, to achieve the -- first of all, there's no -- we've seen it. The only way to achieve certainty is to make sue or lose so that -- every part of the deal so that every single patent that could possibly be a problem gets put in.

You would have to have enough time to start so that you could finish litigation, and that litigation is as long as the longest possible litigation you could imagine, which is 10 or 12 years. There's no way you're ever going to achieve that certainty. We believe that the launch at risk is the appropriate remedy, appropriate way to deal with the situation.

MS. DRENNON: Thank you. Bruce?

MR. LEICHER: I think in the end I think we actually disagree with the last point just because from a financial perspective, for the smaller companies, it's just not financially feasible to raise capital by waiting until the end to get clarity and resolution.

We actually think the proposal that we've been talking about for the last hour was to set up a timeframe where this can be done before the patents expire, to have a mechanism that protects for the brand companies valid patents, but also makes available for the generic and follow-on companies the opportunity to clear out of the way in an appropriate sometime the invalid patents.

I also share Jeff's comment which I was going to make earlier, which is if need be, the remedy should be DJ jurisdiction if you have a valid notice mechanism so you can just get in there and make it happen because

that gives everyone due process.

And the one lurking issue that is sort of behind all this, and I'm not sure that that gets resolved today, is: Is everyone's caveating what they're saying on, what's the date of protection period, and for me -- and it's probably where I disagree with a number of the members on the panel, if that turns on your belief system about the strength of the ultimate patents themselves, if you believe that the biotech patents provide a significant level of protection, then you have one view of the data protection period.

If you believe they don't, you have another view. We tend to look at what the current -- if we're going to look at the current proper products that are out there for the next ten years, they have very broad claims. They seem to have -- and it's not clear to us at least why the lengthy data protection period is necessary.

MS. DRENNON: Esther?

MS. KEPPLINGER: Well, I think the objective is to get the follow-on onto the market at the point that the patents end, but following on to what Bruce was saying, I think that while those early patents may be broad, I think that they will be getting more narrow as we move forward.

And the problem is that you need the system that will create the incentives for the innovators to innovate. Without that you will have no competition, and so you have to create the system that really rewards them and provides a long enough period of data exclusivity to cover it, because I'm not sure as we move forward that patents will.

MS. DRENNON: Jeff?

MR. KUSHAN: So first I would like to request that I can sit right next to the left of Christine. I really appreciate the discussion today. It's been very constructive, and I think it just helps you see that there are a lot of legitimate needs that need to be addressed in designing any kind of a system.

I do believe that the pre-approval mechanism for resolving patent issues is viable and should be implemented. I think what we're going to see is that there may be an initial noisier interchange at the outset of figuring out what patents do matter to the follow-on product and which ones have to be resolved.

But once that kind of initial noise ends, and you figure out which patents are relevant, you're going to see a relatively conventional picture of resolving those patents that are in dispute.

I think one thing you also have to keep in mind

is within the biotech community culture, there has been a far greater tendency of licensing practices, so when you can identify the patents that are relevant, particularly for the universities, they're more inclined to come in and want to get money without litigation.

So it's probably better for everybody to make sure that you keep this initial identification process inclusive and flexible with the hope that at the end of the day you're not going to see some significantly different picture of how to resolve the patent fights.

The last thing I would mention, I didn't touch on this earlier, but I think one of the critical questions is: At what point does the linkage kick in, and I think when we were talking before, there's a desire to get late enough in the -- toward the end of the data exclusivity period so you can see what the real processes are that are going to be used by the follow-on producer, not too early, not too late.

But at the end of the day, when you're looking at kind of a two or three, four years out from launch time point, you are going to want to make sure that once you've identified the relevant patents and fought to a conclusion, the conclusion really should be at the District Court level, at that point that should dictate whether you're going to cause the FDA to stop or go

forward on approval.

I think it's fair to do it at that point because that's an outcome. That's a judgment. You have already made a resolution. It may get flipped on the appeal, but if you're looking at a T minus two commencement of litigation, you're never even going to get a District Court judgment by the second year, and I think there's some good faith believes in the equation that we need a balance.

So I think that the system is definitely viable to create, and I think it ultimately will prove to be beneficial to both sides.

MS. DRENNON: Thank you. David?

MR. MANSPEIZER: Well, first, we've heard a lot of talk today about the products that are out there waiting today ready to be picked, and let's not get too distracted by them because if we were going to design a system that would deal only with the patents that were going to go off patent, whatever that means by 2014, it probably would look nothing like what we've all been discussing here for the last two hours.

We've got to remember that whatever gets legislated here is going to be a system we have to live with for the next 20, 25, 30, 50 years, however long it is, and it's got to be adequate to deal with all of the

issues that we're going to face over that time period, and it's got to be fair and balanced to both sides of the equation.

I think we all recognize that there's a lot more common ground between us than we thought there was I think when we all walked in here today, and there's a lot more agreement if fact than there is disagreement. The devil is always in the details, but I do think that it is certainly achievable.

The biggest -- and I don't know if Bruce said it, the biggest difference seems to be how do we factor data exclusivity into this all and what role does data exclusivity play, and for us again it's not about the strength or the weakness of a patent or whether you believe it's a strong patent or a patent that's going to permit you to retain your position.

It's about certainty, and it all comes back to you have to have enough certainty to balance innovation and competition, so you have to design your system with that in mind, and the other stuff I think we've discovered will fall into place.

MS. DRENNON: Thank you. Hans?

MR. SAUER: We didn't much talk about patients and providers and payors, all of whom want certainty too. It's not just us and you guys, but also the guys

out there in the market, so in that sense when you think of it, Plavix maybe isn't even a great idea or a example to analyze this situation under.

We're talking about biologics for really serious diseases, which for the most part as we've talked about earlier in these panels are not going to be interchangeable so we're talking about products that would be in the market where the FDA already said, you can't switch them back to the innovator product. There's no immediate obvious substitute.

So what are you going to do if there's litigation that's unresolved? Do you want to take away the drug from these people, tell them to switch when the FDA has said they're not really interchangeable and so on?

Nobody really wants to do that, and at the same time nobody really wants to live under a compulsory license too. I don't think that's the way the case law is going, and compulsory licenses just from a business perspective anywhere, like compulsory marriage. It's not what you would want, being in a licensing relationship with somebody.

So I think there are just a lot of good reasons that we should all try very, very hard to put together a reasonable pre approval litigation and patent resolution

half way. Conceptually it doesn't sound that difficult. During the innovator's exclusivity a window would open that's long enough to get it all done before the follow-on approval can be made effective.

I think we also shouldn't forget that for the most part, it's going to take many follow-on applicants probably four or five years to begin with to put an application together, and the first -- maybe it's quicker. I don't know, some products are going to be more difficult.

So all that, if you piece that together, that's going to -- as you said, the elephant in the room. How long is this data exclusivity going to be in the end? I think we have some building blocks that we've been working with that already give us a dimension of where it's going to rationally end up, and I think we optimistically can look forward to a process that we can craft that's going to be rational and work for all.

MS. SEIDE: Well, without belaboring the analysis because I agree with a lot of what's said, and I think what we have to realize is that there is a very much symbiotic relation between the innovator company and the follow-on or the generic companies because without any innovation, there wouldn't be any follow-on.

For that point, then the follow-on would have to

become an innovator, and there's an interesting dynamic there, so whatever situation, I think there's some rudimentary -- our discussion today leads to certain ways of developing that, and I think it's a workable -- there's a workable pathway ahead.

I think the issue is again, there has to be some kind of certainty, that whatever happens, the innovators will still be allowed to innovate and develop new biologics that could be very useful for treating all these horrendous diseases, and that lower cost follow-on biologics come on the market because that also benefits to the population that will be benefitting from them.

And again like everybody else said, the other issue is how does data exclusivity factor into this particular resolution. My perspective is that the resolution should come at some point in time before launch, but again what is the window and when does it appear and when does it -- what are the consequences for not going in that window. Are there details that still have to be worked out?

But again I also want to thank the FTC for at least addressing these issues. I think it's very timely and hopefully some useful proposals will come out of it.

MS. DRENNON: Especially at this time with a new Congress, who's going to be grabbling with this, and

this is going to be a big issue in healthcare so it's very timely.

MR. SCHULTZ: I think the goal is that the first day that the generic or biosimilar or biogeneric is ready to be approved, all issues regarding patents that it has identified this would preclude it from marketing have been resolved. I think it's doable. I think there's probably a range of ways to do it, but I absolutely think it's doable.

And I agree with what other people said. I think if it were this group resolving it, I think there's a way to resolve it. I hope it wouldn't be unduly complicated, and I think this has been a terrific session. Thank you. Everybody.

MS. DRENNON: Christine, you get the last word. The downside of being last is everybody wants you to be quick.

MR. SCHULTZ: And they don't listen.

MS. SIWIK: I guess I want to make the point -- two points. One, I would certainly hate for anybody to leave here thinking that the generics are out to stick it to the brand industry in any sense. Without a strong brand industry, there is no generic industry, by definition.

We need a strong, robust, innovative brand

industry or there is nothing to file a generic version of, so I think it's all about balance. It's about balance on the approval pathway. It's about balance on whatever brand exclusivity there is going to be, and on the patent piece, the balances, we need to resolve the key patent disputes early, and we have to avoid a system that is going to make the rate limiting step, if you will, of marketing a patent dispute.

And to a large extent I think we should try to avoid some of the things we've seen before and help expedite that process by not linking the patent process to the approval process.

Finally, I would like to again echo the thanks of everyone else that's been on the panel. This has been very helpful, and we really appreciate your time.

MR. WROBLEWSKI: This concludes our marathon day of the issues and we appreciate everyone sticking around.

The one thing I do want to make clear is that the record is still open for another 30 days. So if there are topics that we addressed today or questions that were raised and you didn't feel like you got an ability to make a point, you're welcome and we encourage you to file comments, and it's until -- the closing date is I think Monday December 22. So thanks again.

(Whereupon, at 5:13 p.m. the workshop was concluded.)

CERTIFICATE OF REPORTERS

CASE TITLE: FTC ROUNDTABLE ON FOLLOW-ON BIOLOGIC DRUGS

DATE: NOVEMBER 21, 2008

WE HEREBY CERTIFY that the transcript contained herein is a full and accurate transcript of the steno notes transcribed by us on the above cause before the FEDERAL TRADE COMMISSION to the best of our knowledge and belief.

DATED: DECEMBER 1, 2008

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CERTIFICATION OF PROOFREADER

I HEREBY CERTIFY that I proofread the transcript for accuracy in spelling, hyphenation, punctuation and format.

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SARA J. VANCE