Testimony of

Mr. David Beier

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I. INTRODUCTION

Mr. Chairman and Members of the Subcommittee, I am David Beier, Senior Vice President for Global Government Affairs for Amgen Inc. I am pleased to be with you today to discuss the challenge of establishing an approval framework for follow-on biotechnology products. Amgen is the world's largest biotechnology company and is headquartered in Thousand Oaks, California, with locations in South San Francisco, Washington state, Colorado, Massachusetts, Rhode Island, Puerto Rico, Australia, Japan, and throughout Europe. Amgen has seven marketed products in the United States, including two of the most recognized biotechnology products, Epogen® (epoetin alfa) and Neupogen® (filigrastim). Last year, we invested 1.7 billion dollars in research and development on new therapies.

Amgen is a pioneer in the development of biotechnology-derived proteins, with experience covering the fields of molecular and cellular biology, target discovery, safety assessment, therapeutic delivery, and biotechnology process development. Few organizations in the world can claim to have Amgen's technical experience, and few have been able to deliver safe and effective biotechnology products to patients for so long with so few adverse events. Amgen's innovations have helped millions of people worldwide who have medical conditions for which there are few effective treatments. Our biological products help fight these diseases and improve the quality of people's lives. It is from this perspective that I comment on behalf of Amgen on the issue of what some call "generic" and others, like the Food and Drug Administration (FDA), call "follow-on" biologics.

My testimony today will focus on the public policy and legal principles that are central to the debate on this issue. In particular, I will discuss five points:

? The ways in which biotechnology products are different from chemically-derived drugs;
? The landmark Hatch-Waxman amendments that created the generic drug approval process, and why it is not applicable to biotechnology products;
? The potential risks to patient safety posed by follow-on biologics;
? The need to protect and promote innovation in the biotechnology industry; and
? The need for a structured public process to explore the science of follow-on biotechnology products.

Before I address these points, I think it is important to frame what I believe are the defining principles in this discussion.

Amgen believes that patients and physicians deserve the best and safest medicines that technology can deliver. And, we believe that patients deserve access to the most cost-effective, competitively-priced therapies available. As we have learned from the landmark system for the approval of small-molecule, traditional drug products, these twin goals are not mutually exclusive. They do, however, require exquisite balancing. For innovation to thrive, the needs and rights of pioneer manufacturers must be preserved, and the system as a whole must - without compromise or fail - ensure that patient safety is protected.

Thus, in developing any process for expanding the availability of biotechnology products, we believe there are three principles that trump all others:
? Always put patient safety first;
? Ground the process in sound science; and
? Fully respect innovator rights.
We believe that if these fundamental principles are maintained, through a sound public process, Congress, FDA, patients, and industry can develop a sensible roadmap for the approval of safe and effective follow-on biologics.

II. BIOTECHNOLOGY PRODUCTS

Biotechnology holds the promise of treating or curing the most devastating human illnesses, many of which remain almost completely untreatable today. In fact, almost half of the new products approved by FDA last year were biological products, and nearly 300 biotechnology products - for over 150 diseases, including cancer, Alzheimer's disease, heart disease, chronic kidney disease, diabetes, multiple sclerosis, AIDS and arthritis - are currently in Phase III clinical trials. To the 325 million patients who have been helped by these products, and to those waiting and hoping for a treatment or cure, biotechnology represents a beacon of hope in a dark night.
To understand the promise of these therapies, and to foster their continued development, we first need to understand what they are and how they are different from traditional drugs. Thus, I will briefly review - from the lay perspective only - the nature of biological products and, in particular, biotechnology products.
To begin, biological products are significantly greater than traditional drugs in size, structure, and complexity. Because they consist of large molecules, most biological products must be administered intravenously or by injection, usually in a doctor's office or hospital setting.
Biological products and, in particular, therapeutic proteins, are manufactured from living cells. This is an elaborate process, spanning several months and involving numerous steps. The process generally begins with the "programming" of a unique cell line (by genetic engineering or recombinant technology) to produce a certain protein. These cells may be derived from bacteria (like E. coli) or mammals (like Chinese Hamster Ovary cells). The use of cells in production requires highly controlled manufacturing environments, and the process must be kept sterile and free of pathogenic microorganisms to ensure proper growth and safety of the desired protein.
The end product of this biotechnology manufacturing process is, most often, a complex mixture of heterogeneous proteins and impurities. Each of the closely-related proteins in this mixture contributes to the biological activity, efficacy, and safety of the product. The mixture in any one biological product is defined largely by its manufacturing process. This is because living cells are, in essence, the factory. While the cell can be programmed to produce a very specific protein, the cell is still a living organism; it cannot be controlled in the same manner that pharmaceutical engineers can control the synthesis of small-molecule drugs.
The protein molecule itself is a three-dimensional structure, often in the form of a long amino acid backbone with strands of carbohydrates appended in all directions. This structure can be described using an array of tests, but they can only describe specific parts of the protein structure. We have tools such as amino acid sequencing and peptide mapping, which provide some information about the product's structure. We can gain additional information on the identity, structure, heterogeneity, and biological activity of the product using additional tests such as chromatography, immunoassays and biomimetic tests.

However, the picture that can be drawn of a biotechnology product based on these types of measures is, unquestionably, incomplete. Animal studies and pharmacokinetic (PK) data can add to the picture, but it is not a picture from which a complete determination of safety or effectiveness can be made. Most important, and in contrast to experience with small-molecule drugs, it is Amgen's experience that physico-chemical testing cannot establish "sameness" with regard to either the identity or the composition of one manufacturer's biologic to that of another. In other words, the chemical characterization of active ingredients in these products is inadequate to ensure sameness of efficacy (i.e., "biological activity") and sameness of safety (i.e., no unexpected adverse reactions, including immunogenic responses).

With these concepts in mind, it will be evident why - under current law - most biotechnology products are subject to a different approval process than small-molecule drugs and are not amenable to a true "generic" drug approval process.

III. LEGAL BACKGROUND

A. Hatch-Waxman

In 1984, Congress - under the leadership of the Chair of this Committee - amended the Food, Drug, and Cosmetic Act (FDCA) and U.S. patent law to establish an abbreviated application process for drug products that are in the twilight years of their patent protection. These amendments - titled the Drug Price Competition and Patent Term Restoration Act of 1984, but affectionately known as Hatch-Waxman - authorized FDA to approve generic copies of innovator drugs without requiring an independent showing of safety and effectiveness. Instead, the new law allowed generic companies to rely in full on data developed by pioneer manufacturers, provided the generic could show chemical "sameness" to the pioneer's product.

Prior to Hatch-Waxman, and with some exceptions, a pioneer company's clinical data were considered to be proprietary in perpetuity. With Hatch-Waxman, the pioneer industry relinquished certain of its data protection rights to generic manufacturers in return for patent term restoration, various forms of data exclusivity, and a structured process for litigating patent disputes.

More specifically, under section 505(j) of the FDCA, a generic drug is considered to be the same as the pioneer - and is considered to be as safe and effective as the pioneer - if the generic has the same: (1) active ingredient, (2) dosage form, (3) route of administration, and (4) strength as the pioneer, and if the generic is shown to be bioequivalent to the pioneer. A bioequivalence study typically involves no more than two to three dozen healthy subjects, who often receive only one dose of the proposed generic and one dose of the pioneer drug.

With this showing of "sameness," the safety and effectiveness of the generic product can be assumed. And, in fact, for small-molecule drugs, the science supports this assumption. Physical and chemical comparisons of small-molecule drugs are sufficient to assure that one manufacturer's version will provide the same clinical benefit, and same risk profile, as another manufacturer's version.

For this reason, FDA considers generic drugs to be interchangeable with the pioneer, allowing substitution with the full expectation that the generic has the same clinical effect and safety profile as the listed drug. The agency assigns an "A" level therapeutic equivalence (TE) rating to such products and publishes these ratings in the Orange Book. Most state and federal health care systems rely on FDA's TE ratings when substituting lower cost generics for brand name prescription drugs.

Finally, a handful of recombinant DNA products (e.g., human growth hormone (hGH) and insulin) are, for historical and administrative reasons regulated solely as drugs. Nonetheless, follow-on versions of these complex protein products have not been approved under section 505(j) because it is not possible to determine that the active ingredient in one manufacturer's version is the same as in another. In other words, the chemical characterization of active ingredients in these products is inadequate to ensure sameness of efficacy (i.e., "biological activity") and sameness of safety (i.e., no unexpected adverse reactions, including immune response reactions). The agency's experience with naturally-derived complex drugs such as Premarin® (conjugated estrogens) illustrates the difficulty of showing sameness for products where the specific active ingredients are not well-characterized.

Again, Hatch-Waxman is based on "chemical" sameness - the idea that one manufacturer can make an exact chemical copy of another manufacturer's active ingredient. With complex substances, including certain products that are regulated as drugs, we simply do not have the assurances we need to establish the safety and effectiveness of a proposed "generic" product.

B. The Public Health Service Act

For many of the reasons already discussed, biological products are subject to a separate premarket approval system from traditional drug products. Most biotechnology products are "analogous to" or derivative of live cellular products and, as such, meet the definition of a "biological product" under the Public Health Service Act (PHSA). They often target a specific aspect of the body's immune system, and most biotechnology products themselves are large enough to trigger an immune system response.

For example, Amgen's leading biotechnology products, including Epogen® (epoetin alfa), Neupogen® (filigrastim), Aranesp? (darbepoetin alfa), Neulasta? (pegfilgrastim), and Enbrel® (etanercept), are produced from gene-altered cells to form complex proteins. Like the body's own erythropoietin, Epogen® stimulates the production of red blood cells in the body by triggering the division and differentiation of erythroid progenitors in the bone marrow. Neupogen® is a recombinant DNA version of a human protein that stimulates the growth of white blood cells, and Enbrel® targets tumor necrosis factor to reduce inflammation in patients with severe and debilitating rheumatoid arthritis.

Amgen is required to maintain a license under the PHSA for each of these products, and for each license, Amgen is required to meet the manufacturing and labeling requirements applicable to all therapeutic products under the FDCA. To obtain a license under section 351 of the PHSA, sponsors must submit a biologics license application (BLA) and demonstrate that: (1) the biological product is "safe, pure, and potent;" and (2) "the facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent."

The emphasis in the PHSA licensing standard on the manufacturing process and the "facility" is not to be overlooked; it reflects the long-held view that the manufacturing process has a significant potential to affect the quality of biological products, and the limitations in the ability to unambiguously characterize these molecules using current testing methodologies. While the Secretary of Health and Human Services is authorized to establish, by regulation, all requirements "for the approval, suspension, and revocation of biologics licenses," the Secretary has never authorized the approval of biological products under an abbreviated application process. Rather, it is FDA's longstanding position that original, product-specific, clinical data are required for each approval of a biological product. Much of the data innovators submit constitutes trade secrets or confidential commercial information.

IV. HATCH-WAXMAN DOES NOT PROVIDE A MODEL FOR THE APPROVAL OF BIOLOGICAL PRODUCTS

For small-molecule drugs, where sameness generally can be established to a chemical certainty, Hatch-Waxman represents a valid approach from a scientific perspective. It is quite another matter for biologics.

As I noted at the outset, on a relative basis, biotechnology products are significantly greater in size, structure, and complexity than small-molecule drugs. Biotechnology products are difficult to characterize with precision and impossible to characterize with certainty. They are made in cultures from living organisms, rather than synthesized from purified materials. These products (as well as the cells used to produce them) can react to imperceptible changes in temperature and light; and they can be affected by new processes, new solvents, and new methods of fermentation and purification.

A would-be sponsor of a follow-on biologic would be using a different cell line and different media to produce the protein, and would likely use different fermentation methods, purification processes, and specifications. Because of the inherent differences in these materials and processes, a generic sponsor cannot produce the same product as the pioneer. For example, even if the would-be generic sponsor and the pioneer both used Chinese Hamster Ovary cells to produce the biologic, each manufacturer's cell line would have its own sensitivity to the fermentation process. Each manufacturer would use its own proprietary cell culture or media to "feed" the cells, and each manufacturer would "feed" the cells at a different rate for a different period of time.

All of these factors bear on the composition, quality, and structure of the finished product. Given that the process depends on cellular metabolism, and that metabolism is sensitive to environmental factors, it is impossible for two manufacturers to produce identical protein products. In addition, it is impossible to determine - with only analytical and bioequivalence testing - that a follow-on biological product will be just as safe and effective as the pioneer product.

Thus, it is FDA's current position that an abbreviated generic approval process for follow-on biologics (akin to the Hatch-Waxman pathway for generic drugs) is simply not appropriate. Amgen agrees with this position. We believe that, as the science evolves and reaches a consensus, there may be opportunities to abbreviate certain of the requirements (likely not with respect to safety or manufacturing-related data) for follow-on products. Even then, we believe that legislation is required before FDA could formally adopt any sort of abbreviated approval process for any biologic. In the meantime, the scientific issues distinguishing biologics from small-molecule drugs, and the challenges of showing the "sameness" of biologically-derived products, must be explored.

V. PATIENT SAFETY

Biologics are some of the newest, most effective treatments for battling serious diseases. At the same time, biotechnology products interact with the body in new and unique ways. They often operate within the body's immune system and, unlike small-molecule drugs, they are large enough to be recognized by the body's immune system. Taken together, this means that biotechnology products raise a qualitatively different set of risks than most small-molecule drugs.

For example, the antibodies that may be formed against a therapeutic protein can trigger serious clinical effects, including loss of efficacy and neutralization of the body's own essential biological functions. Many biotechnology products are designed to replace a deficiency in the body's own native or "endogenous" proteins. An immune response to such a product may result not only in the body neutralizing the therapy, but also in neutralizing its own native supply of the protein. While such events are very rare, they are rare because of the elaborate controls and extensive safety database systems that have been established to support all of the approved biologic products today.

The incidence of Pure Red Cell Aplasia (PRCA) in patients taking Eprex® (Epoetin alfa), an erythropoietin product, illustrates one such rare event. Erythropoietin is produced in the kidney and stimulates the production of red blood cells in the body. Eprex® is a recombinant DNA version of erythropoietin manufactured by a subsidiary of Johnson & Johnson for use outside of the United States. Based on a longstanding agreement between Amgen and Johnson & Johnson, Eprex® is made using the same basic technology that is used to make Amgen's own Epoetin alfa, known as Epogen®. However, in the late 1990s, it was reported that Johnson & Johnson made several changes to the manufacturing process for Eprex®. Those changes have been linked in time to an increase in immune reactions in Europe to Eprex®.

Since 1998, more than 160 Eprex® patients have developed neutralizing antibodies to the product and to their own naturally occurring erythropoietin. These patients were unable to stimulate the production of new red blood cells, even after Epoetin alfa treatment was discontinued. Some of these patients were required to take immunosuppressive drugs, and others required blood transfusions or kidney transplants. Many of these patients could be dependent on blood transfusions for the rest of their lives. Since its market introduction in 1989, only five cases of antibody-mediated PRCA have been reported in relation to Amgen's version of the product, Epogen?.

This type of immunogenicity is one example of the potential for significant safety concerns related to follow-on biologics. It illustrates how a manufacturing change may - and I emphasize may, because the cause of these incidents is still under investigation - result in unpredictable and potentially irreversible adverse reactions.

Such reactions may be a function of glycosylation and the unique folding of the protein structure, each of which is specific to the particular manufacturing process. Minor species and impurities, which are also present in biological products and are specific to the manufacturing process, can also contribute to immunogenicity. Unfortunately, neither analytical testing nor testing in animals can predict whether, or at what rate, a biological product may trigger a serious immune response in humans. It is also unlikely, if not impossible, that two biological products produced by different manufacturers would have the same immunogenicity profile.

In short, biotechnology products present numerous challenges from a patient safety perspective. Before we begin to expand the market for such products, through the introduction of follow-on products, we need to fully understand the nature of these risks and evaluate the science that would be needed to assure that these risks can be managed across a wider array of manufacturers. It is imperative that these safety issues are addressed by Congress and resolved by the relevant medical experts before we can responsibly support a system for the approval of follow-on biological products.

VI. INNOVATION: PROTECTING AND STIMULATING ADVANCES IN RESEARCH AND DEVELOPMENT

In 1984, when the Hatch-Waxman amendments were passed, there were tens of thousands of marketed drug products, many of which had been safely used for dozens of years. FDA, the medical community, and the public had decades of experience with these products. By contrast, today there are only about 155 approved biotechnology products, most of which were approved very recently. While the entire biotechnology industry doubled in size between 1993 and 1999, biotechnology is still very much in its infancy compared to the state of the larger drug industry when Hatch-Waxman was first being debated.

In looking ahead at expanding access to biotechnology products, we must be sure to retain the incentives for pioneers and investors to take the enormous risks that are needed to sustain innovation in the industry. Put differently, in creating new policy, we must maintain an incentive structure that stimulates the level of innovation that has driven the United States to be the leader in research and development up to this point.

For example, the development of just one pharmaceutical drug costs an innovator at least $800 million on average - and the cost of developing a biological product could be even more. Moreover, in 2002, research and development spending by the United States pharmaceutical industry was approximately $28 billion - almost 41% more than R&D spending in Europe. In the same year, the U.S. biotechnology industry spent $20.5 billion on research and development. These figures are just one indication of the United States' position as the world leader in terms of research and development, innovation, and job creation in the pharmaceutical and biotechnology industries.

Thus, a critical issue in creating any sort of follow-on biologics approval process must be: How can the law encourage innovation and competition? How can Congress assure access to biological therapies while preserving patent protections and other market incentives for the development of new therapies? Without keeping one eye on the innovation side of the issue, patients ultimately will lose if there is no longer sufficient incentive for companies to engage in the expensive and risky new drug development process.

This is especially critical in the area of biotechnology, where success represents the exception rather than the rule, and where 40 to 50% of candidates fail in Phase III studies. The vast majority of biotechnology companies are not profitable today, and are highly dependent on the flow of venture and investment capital to complete the research needed to bring their first product to the marketplace. To remove or undermine incentives for new research and development at this time, while we are on the cusp of so many exciting biotechnology breakthroughs for so many diseases, would be a terrible blow to innovation and the public health.

The good news is that we know Congress can have a profound impact on the stimulation of innovation. The Orphan Drug Act of 1983 may be the best example of this. Before the Act, there were less than ten approved orphan drugs. Today, there are nearly 250. These new orphan treatments are helping more than 12 million patients in the United States. The Act achieved this by offering a seven-year period of market exclusivity after approval, as well as government grants, tax credits, and other incentives, for any new orphan drug.

This type of legislation illustrates the clear cause-and-effect connection between economic incentives and innovation. Just as congressionally-created incentives were critical to attracting companies to invest in orphan drugs and pediatric studies, so, too, will such incentives be critical to keep biotechnology companies investing in new, ground-breaking biologics research and development.

VII. INNOVATION: PROTECTING INNOVATOR TRADE SECRETS AND PROPRIETARY DATA

Strong intellectual property and data protection laws are a cornerstone of any innovation-driven industry. Innovators must be able to rely on the protection provided by patents and trade secret law. When a biotechnology innovator submits a BLA, it provides FDA with extensive trade secret and other confidential data, encompassing years of research and clinical studies. This information is provided specifically for the approval of the innovator's biologic and should be regarded as proprietary and strictly confidential unless the innovator consents to its public release or as required by law. Current law governing biologics does not give FDA the authority to infringe on these innovator rights.

Thus, as FDA recently noted, the data required for the approval of any new product (even a follow-on product) "must be in the public domain. FDA does not have the legal authority to reference information in an innovator company's BLA submission." This principle is also reflected in FDA's regulations, which memorialize the agency's longstanding position that summaries do not constitute full reports of investigations. Even if summaries of clinical studies are available in medical journals, for example, these are clearly not sufficient to establish substantial evidence of safety and efficacy. Only Congress can change this paradigm to strike a balance between protecting innovator rights and establishing guidelines for follow-on biologic approval.

Finally, the Fifth Amendment of the Constitution prohibits the government from taking private property - including intellectual property, such as proprietary data - without just compensation. FDA has consistently maintained the position that a manufacturer cannot directly rely on data from another without authorization from the owner. Thus, biotechnology innovators have reasonable, investment-backed expectations that their data will not be shared. If this information is shared - by federal regulators - it is a government taking and requires just compensation.

Some may argue that a taking of innovator data is justified because it is in the public interest to lower healthcare costs and increase access to biologics. Without doubt, these are important public policy goals. But, we must not lose sight of the goal of finding new cures and developing new, innovative therapies. Thus, FDA, Congress, and the biotechnology industry should work together to ensure that innovation is encouraged and proprietary rights are respected. With these incentives, investors and companies will be willing to accept the bold risks associated with developing new biological products - in other words, to invest the "cure capital" necessary to discover and produce breakthrough treatments for serious diseases.

The European Union (EU) - which, admittedly, operates in a very different regulatory environment - has begun to tackle the issue of how a political community secures the right balance between innovator incentives and innovator rights, while also providing patients with as many market-based options as possible. The recently passed "pharmaceutical review" legislation in the EU illustrates one attempt. For newly approved products, the EU has established a protection period of eight years (during which no application for a generic version can be accepted), and a marketing protection period of ten years (during which no application for a generic version can be approved), which can be increased to eleven years if a new therapeutic indication is approved. These data and market exclusivity provisions represent an increase over the previous protections that existed in most European nations, and represent a careful balance between the rights and opportunities of innovator and follow-on companies, in a regulatory environment that - historically - has had less robust trade secret protections and fewer procedural

rights than in the United States.
We must commit to a deliberate examination of the incentives that drive our industry, so that we can preserve our position as the seat of pharmaceutical and biotechnology innovation.

VIII. A STRUCTURED PROCESS IS NEEDED TO ADDRESS THE SCIENCE

Patients deserve safe, effective, and affordable treatments. No cost savings, however, is worth placing patient safety at risk. Amgen is committed to bringing new therapies to patients in the most efficient manner possible while keeping patient safety as the primary consideration. Thus, Amgen supports a process that explores the development of follow-on biologics, but only if there is a robust public process and clear, science-based legal authorization.
In particular, Amgen believes that:
? Patient safety is paramount;
? There is no such thing as a "generic" biologic because identity cannot be established with the innovator product;
? Pre-clinical and clinical data will need to be provided by a follow-on company, with a post-marketing safety commitment required;
? Immunogenicity is a serious concern and should be carefully evaluated;
? Follow-on biological products must be held to the same high standards of safety, efficacy, quality, and manufacturing requirements as innovator products to ensure safety and efficacy for patients; and
? Any follow-on biologic approval process must respect and encourage innovation.
Amgen also believes that as legislators, FDA, and the public begin to think about a follow-on approval pathway, we must start with the recognition that follow-on biologics are truly unique products - and not carbon copies. As discussed above, follow-on biologics cannot be considered therapeutically equivalent to the innovator product (as is possible for small-molecule drugs, where the active ingredients in such products may be regarded as copies). Instead, while one can think of follow-on biologics as expanding the number of options in the marketplace for patients and healthcare providers, and as adding to the therapeutic armamentarium, it does not give rise to a true generic system.
From that principle, a reasonable set of pre-conditions to regulatory approval of follow-on biologics will flow. For example, the development of a follow-on biologic approval pathway must begin with a structured, public process to first resolve the myriad scientific questions implicated by follow-on biologics. Thereafter, any regulatory scheme ultimately developed should be transparent, science-based, predictable, and product-specific. The standards that are developed should be established only after comment by all interested persons, including legislators, scientists, doctors, patient groups, innovator companies, and healthcare associations. Moreover, in the interest of transparency, and to ensure that the knowledge and experience of the industry and the scientific community is harnessed, it is imperative that a follow-on approval system allow for case-by-case premarket comment on the standards for specific categories of products. The science is simply too complex, and the patient safety risks too great, to proceed in any other way.
This is illustrated by recent developments in Europe. The "pharmaceutical review" legislation, discussed above, permits the European regulatory authorities to approve follow-on biologics, or "biosimilars." The legislation is far from presenting a clear legal framework, however. Still unresolved are the critical issues of how much data will be required for the follow-on applicants,

and the extent to which regulators can rely on innovator data contained in agency files to approve follow-on applications. Furthermore, although the EU determined that, because of the risk of immunogenicity and other safety problems, pre- and post-approval safety data, including immunology data, will always be required for follow-on products, it did not establish clear parameters for these tests. As a result of these unresolved issues, the European authorities have been urged to issue additional guidance documents, including product- or class-specific guidelines, which would offer more transparency to all stakeholders.

If we are to learn from this example, we will determine the relevant scientific and safety standards before implementing a sweeping approval process for follow-on biologics that, at this point, would raise more questions than it would answer. This process must include product-specific or category-specific opportunities for comment prior to review and approval of follow-on products. As well, adequate safety data must be provided in the pre-approval stage for any proposed follow-on biologic, and these clinical data should be adequate to evaluate the immunogenicity of the follow-on biologic in comparison with the innovator product. In addition, robust post-marketing surveillance systems must be in place to monitor the safety aspects of the product.

Amgen supports competition among products proven to promote health. We believe that follow-on biologics, as new biologic products approved based on pre-clinical and clinical data substantiating their safety and efficacy, can expand physician and patient choice. Thus, once patent rights expire, and assuming remaining innovator rights are appropriately recognized and protected, we are open to the creation of a legal and regulatory framework for follow-on biologics. We are committed to working with regulatory authorities to provide any expertise that we can share in this ongoing process to expand patient access to more treatment options.

IX. CONCLUSION

It is Amgen's considered view that the present-day generic drug paradigm cannot be applied directly to biologics. This is based on the fundamental differences between small-molecule drugs and biologics, including size, structure, and sensitivity to manufacturing processes. Most importantly, follow-on biologics raise the possibility of serious immunogenicity responses in patients, and these reactions are extremely difficult to predict. Thus, we believe it is imprudent, if not dangerous, for one manufacturer to receive approval for a biological product based solely on the clinical data produced by another manufacturer. Such reliance, without authorization by the data owner, would negate trade secret rights and pose a compelling question under the Fifth Amendment. In addition, an approval system for follow-on products must preserve sufficient incentives for innovative organizations to invest in the continued research and development of new, life-saving therapies.

Amgen believes we should work together to explore whether a viable follow-on paradigm can be developed that would, as a matter of science, allow one sponsor to utilize analytical testing to demonstrate basic similarity, to apply an appropriate but flexible standard to establish efficacy, and to conduct robust pre- and post-market studies to assure safety. Even then, however, it would be inappropriate as a scientific and medical matter to consider the follow-on product to be the same or identical to, substitutable for, or interchangeable with, another sponsor's biological product.

The specific standards by which follow-on products should be tested and approved should be determined through a structured public process, with input from all relevant stakeholders,

including the medical and scientific communities. If these stakeholders, together with Congress and FDA, commit to put the patient first, base decisions on sound science, and respect innovator rights, we believe a sensible policy regarding follow-on biological products will result.

Thank you for the opportunity to discuss these important issues with you, and I will be happy to answer any questions you may have.