



**The Trans-Pacific Partnership
and Innovation in the Bioeconomy:**

***The Need for 12 Years
of Data Protection for Biologics***



Executive Summary

- The biotechnology industry is one of the most research-intensive industries. It spends tens of billions of dollars throughout the world each year on vital research to improve the lives of people across the globe. It has a remarkable track record of delivering life-saving biological treatments for patients with serious unmet medical needs, as well as a wide range of vaccines that contribute substantially to global public health.
- The vast majority of biotechnology companies are small, start-up companies that are heavily reliant on private investment capital, lack revenues from marketed products, and operate in financial loss positions. They are engaged in highly risky and costly endeavors that take, on average, more than a decade and in excess of \$1.2 billion to bring a biological product to market. Accordingly, they are highly sensitive to changes in market risk.
- Biologic pharmaceutical products are complex and challenging to manufacture. They present unique considerations relative to pharmaceutical products containing active ingredients made by traditional chemical synthesis. These distinctions translate into different kinds of challenges – both with respect to the regulatory approval of these products and how they can be effectively protected by intellectual property standards.
- One important distinction is that, unlike generic drugs, a biosimilar product is not identical to the innovator product. Among other things, this means there is greater uncertainty as to whether an innovator's patent rights will cover a biosimilar version of the innovator's product, as compared to a traditional generic drug. Without the certainty of some substantial period of market exclusivity, innovators will not have the incentives needed to conduct the expensive, risky, and time-consuming work to discover and bring new biological products to market.
- In 2010, Congress created a pathway for approving biosimilar versions of biological products. Under this law, biosimilar products must be highly similar to earlier approved innovator biological products. This requirement enables FDA to rely on its earlier findings of safety and efficacy with respect to the innovative product to decrease the development requirements for subsequent market entrants with highly



similar products, thus reducing the cost, time, and uncertainty in gaining approval of the biosimilar product.

- The legislative process that produced the U.S. system was deliberate, thoughtful, and driven by rigorous analysis. Extensive research by noted economists demonstrated that developers of innovative biological products require a period of market exclusivity of between 12 and 15 years simply to break even on their investments in developing a new biological product.
- This economic evidence was reinforced by practical insights of every sector of the community involved in development of biological products – ranging from investors to patient groups to research universities and the full spectrum of companies that make up BIO (including many that make or plan to make biosimilars). The unified message from this community was that, in addition to strong IP protections, an extended period of regulatory data protection – beyond that given to traditional, small molecule drugs in the generic drug context – was essential to properly incentivize the development of new biological products and new uses of those products.
- Patents and regulatory data protection, while complementary, serve two distinct purposes. Patents protect inventions ranging from the foundational inventions that underpin new drugs and biologics to the incremental advances necessary to bring those products to market and manufacture them at the scale needed by patients. Patents provide such protection even where a third party conducts its own, full research and development program to develop the same or similar product. Data protection, on the other hand, is intended to incentivize biomedical innovators to invest the enormous amount of resources and time necessary to conduct the complex development work required to prove a new drug or biological product is safe and effective, and to secure regulatory approval of that new product. Data protection does so by requiring third parties seeking to gain approval of a same or similar product to independently generate the full range of pre-clinical and clinical evidence for their own product, or to wait a defined period of time before seeking a regulatory shortcut to approval based on the innovator's prior approval. Data protection thus prevents parties from unfairly "free riding" on the investments and efforts made by the innovator to secure original approval of its product.



- For small molecule products, the period of data protection – five years in the United States – is less important, because the regulatory approval standard for generics requires a generic to have the identical active ingredient. This requirement allows for patents to predictably provide effective market exclusivity – that is, patents on the innovator’s product will cover the generic product as well. In addition, the U.S. Hatch-Waxman Act provides patent term restoration to compensate new drug and biologic developers for periods of lost effective patent life consumed by the regulatory approval process. Through term restoration, a patent covering the product or its use or manufacture may be extended up to 14 years post-FDA approval. Thus, studies show that the interplay of these extended patent rights and the stringent regulatory standard for approval of generics combine to provide innovator products protection against premature generic competition for, on average, 12 years.
- As noted above, the regulatory approval standard for a biosimilar product does not require identity with the innovator product it references. This creates a potential “patent protection gap” that – without an extended period of data protection – could create a situation in which it is possible to rely on the innovator’s regulatory approval while eluding an innovator’s patents. That likelihood is exacerbated by two critical facts. First, because of the nature of biologic products – large molecules produced by living cells and organisms through highly specific processes – patent protection is often narrower than that of small molecule drugs. Second, the creation of an abbreviated pathway for approval of similar biological products creates new and strong incentives for competitors to exploit this patent protection gap.
- Recognizing these challenges, Congress, with broad bipartisan support, adopted a system that provides at least 12 years of regulatory data protection for innovative biological products – essentially creating parity in market exclusivity between small molecule and biological products, though utilizing a different mix of protections to achieve that comparable result. Under the U.S. system, FDA will not approve a biosimilar that relies on the prior FDA approval of the innovator’s product until at least 12 years following innovator approval. Congress found this period of data protection necessary to mitigate the risks and uncertainty described above, and to preserve robust incentives for continued investment and development of innovative biological products.
- During the legislative process, the U.S. Federal Trade Commission (FTC) presented an outlier view that data exclusivity was wholly unnecessary for



biological products, as patent protection would remain strong and be sufficient to incentivize innovators. This view was shown to be based on serious errors and faulty assumptions, and was consequently rejected by a broad spectrum of experts and stakeholders. Congress also overwhelmingly rejected legislative proposals based on the FTC's position.

- There are many sound reasons why Congress did not adopt the FTC's recommendations. One was the important recognition, seemingly ignored by the FTC, that regulatory data protection runs *concurrently* with patent protection. As a result, data protection will not defer entry of a biosimilar except in those instances in which a biosimilar manufacturer is able to design around the innovator's patents while still relying on the innovator's prior regulatory approval. Thus, if the FTC is correct that patents alone are able to provide effective market protection against early entry of a biosimilar that is comparable to the protection patents provide small molecule drugs against generics – i.e., roughly 12 years post innovator approval – then a 12-year data protection period would have no effect on when biosimilar products could reach the market. But if the FTC's key assumption about the strength of biologic patents is wrong – as many experts believe – then the 12-year data protection period becomes critically important. Specifically, it becomes the only mechanism to prevent premature biosimilar market entry that would undermine the incentives necessary for innovators. Properly understood, then, the 12-year data protection period serves only as an insurance policy against the uncertainty of patent rights preventing premature market entry by biosimilars.
- To encourage continued development of innovative biological vaccines and therapies, it is critically important to implement effective standards of IP protection within the TPP region. The realities of modern research and development in this industry demonstrate that each TPP member has the potential to participate in the discovery and development of new biological products, or new uses of existing products. The highly leveraged and disseminated nature of the biotechnology industry enables research institutions and small start-up companies in any TPP country to be the seed of this process of discovery, innovation, and development.
- This innovative potential requires an IP infrastructure that is certain and consistent throughout the TPP region. As we move to more tightly integrate the economies of the TPP countries and to promote collaborations throughout this region, discrepancies in the IP infrastructure will become substantial obstacles to collaboration. For this



reason, we believe it is imperative that the TPP create a set of strong intellectual property standards – particularly those governing data protection, patents and trade secret protection – that are relevant to biological products. BIO believes this approach will help achieve the TPP's vision of promoting high standards that integrate the trade and investment climate in the region.

I. The Biotechnology Industry

BIO is a not-for-profit trade association representing more than 1,100 companies, universities, research institutions, investors, and other entities in the field of biotechnology across the United States and in more than 32 countries, including TPP participants Australia, Canada, Japan, New Zealand, Singapore, Mexico and Malaysia. The biotechnology industry is one of the most research-intensive industries in the world. In 2008 alone, biotechnology companies spent more than \$30 billion on R&D. Between 2004 and 2008, the biotechnology industry raised more than \$100 billion in private investment. Between 2009 and 2012, the industry averaged more than \$15.2 billion/year in private investment or approximately \$60 billion.

These investments are paying off. The biotechnology industry has developed hundreds of innovative products that are helping to heal, feed, and fuel the world. In the healthcare sector alone, this industry has developed and commercialized more than 300 biotechnology therapies, cures, vaccines and diagnostics that are helping more than 325 million people worldwide who are suffering from cancer, HIV/AIDS, diabetes, hepatitis C, and numerous other serious and debilitating diseases and conditions. And there are hundreds of more promising products in development.

The biotechnology industry is also a dynamic, job-creating industry, and presents opportunities for every country in the TPP region. Indeed, the vast majority of biotechnology companies are small- and medium-sized enterprises. What these companies share is a philosophy that is critical to the task of developing biotechnology products – a willingness to take huge risks and invest in development of new technologies that will lead to new products and services that will improve peoples' lives.

The vast majority of biotechnology companies do not market any products. Instead, what these companies focus on is identifying and developing new technology. Research and development of biotechnology products, particularly new biological products, requires substantial investments of time, resources and capital. Given the high-risk and long-term nature of their



development efforts, biotechnology companies face significant challenges in raising capital. They must compete with other, less-risky investment choices that the capital markets have. Experience has demonstrated that, in order to attract funding, biotechnology companies must be able to leverage their only asset – their intellectual property – to deliver market success for their products and services, if and when those products make it to the market.

Standards that enable biotechnology companies to protect and leverage their intellectual property are of critical importance to BIO and its members. This is particularly true for development of new biological products, which we understand is the subject of recent discussions within the TPP negotiations. With this letter, we hope to provide you with a better sense of the challenges biotechnology companies face in developing new biological products, and how those challenges translate into the need for effective intellectual property standards within the TPP region.

II. Introduction to Biological and Biosimilar Products

We understand that, in recent TPP deliberations, a number of questions have arisen about biological products.¹ Biological and small molecule pharmaceutical products both are used to treat disease, but there are some fundamental differences between the two. Small molecule drugs, the principal domain of traditional pharmaceutical companies, are made by chemical synthesis procedures that in some cases have been understood for over a century.² Small molecule drugs are relatively small in size.³ In contrast, biologics are vastly larger and more complicated.⁴ Biologics are not made by simple chemical synthesis, but rather are produced by living organisms.⁵ For example, rDNA biological products are manufactured through biological

¹ In the U.S., a “biological product” is defined in the Public Health Service Act (PHSA) as a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings. See PHSA § 351(i) (42 U.S.C. § 262(i)).

² Deloitte, “Avoiding no man’s land: Potential unintended consequences of follow-on biologics” (March 2009) (“Deloitte”) at 3.

³ *Id.* at 12.

⁴ *Id.* at 12; PriceWaterhouseCoopers, “Biotech: Lifting Big Pharma’s Prospects with Biologics” (2009) (“PwC Report”) at 5, available at <http://www.pwc.com/ar/es/publicaciones-por-industria/assets/biotech-final.pdf>.

⁵ Henry Grabowski, “Data Exclusivity for Biologics: What is the Appropriate Period of Protection?” American Enterprise Institute for Public Policy Research (Sept. 2009) (“Grabowski 2009”) at 1.



processes involving manipulation of genetic material and large-scale cultures of living cells. They have the potential to act only on a desired target and thus often present a reduced risk of side effects.⁶

Biological products are complex products, not only because of the inherent variability and complexity of the active constituent of them, but because the product as a whole often cannot be completely and objectively characterized by available scientific techniques. This complexity of biological products has a number of important implications.

First, because biological products often cannot be completely characterized, regulatory agencies, such as the U.S. Food & Drug Administration (FDA), use a different model for evaluating these products relative to drugs containing active ingredients manufactured using chemical synthesis. Specifically, the approval of a biological product is accompanied by a review of the particular manufacturing processes used to make that product.⁷ This differs from the regulation of drugs containing active ingredients made by chemical synthesis, which permit changes to the manufacturing process for those drugs, or even use of a different supplier of the active ingredient.

One reason for this different regulatory model is that a protein made by expression of rDNA in a host cell actually is a heterogeneous mixture of related proteins. By contrast, a chemically synthesized active ingredient of a drug product is typically a homogeneous collection of identical molecules. This distinction is an important one for approaching regulation of the two types of pharmaceutical products. Specifically, because two chemically synthesized active ingredients in a drug will be identical, both drug products can be presumed to work in the same manner. Indeed, this assumption – that two drugs that contain an identical active ingredient will work the same in the body – underlies the basis of approving generic versions of innovator drugs. As long as a generic manufacturer can establish that the active ingredient of its product has the same chemical structure as that in the innovator's product, and that its product, when administered to healthy volunteers, behaves the same way in the body (is "bioequivalent" to the innovator product), FDA may approve the generic product without a requirement for independent clinical testing of the generic drug. See 21 U.S.C. § 355(j).

This "identity" presumption is not true for biological products. The developer of a biological product must prove, using pre-clinical and clinical

⁶ Deloitte at 12.

⁷ Biologics are regulated under the Public Health Service Act, § 351 *et seq.*



evidence, that its product is safe, pure and potent, which is equivalent to the “safe and effective” standard for a new drug. However, regulatory approval is linked to the product as it is manufactured by a particular process. If the developer of a biological product changes an aspect of the manufacturing process used to create the biological product, FDA often will require new evidence that establishes the product made by the changed process is still safe and effective.⁸ This practice has been based on the FDA’s recognition that even minor changes to an established manufacturing process can have unforeseen consequences to the safety or effectiveness of a biological product.

Second, regulatory agencies cannot use the generic drug regulatory model to evaluate the safety and effectiveness of purported “copies” of biological products that reference an earlier approved innovative biological product. The premise of the generic drug approval process is that the generic version of a product will contain an identical active ingredient, and therefore will produce the same safety and efficacy profile as the innovator product. This permits FDA to approve the generic drug without independent clinical evidence, and permits substitution of the generic version of the drug for the innovator product in the marketplace. However, existing scientific techniques make it impossible to prove two complex biological products are identical, making the traditional generic approval regulatory model unworkable for biologics. Simply stated, it is scientifically impossible to make a “generic” version, or exact copy, of a complex biological product – hence the internationally accepted name “biosimilars” (rather than biogenerics).

These regulatory distinctions have important consequences for the types of companies that may pursue production of biosimilar products. Specifically, the biosimilar manufacturer will face substantially greater upfront costs and complexities in securing approval than a generic drug manufacturer contemplating production of a generic version of a new drug. For example, a biosimilar manufacturer will have to conduct some amount of clinical investigations of the product to establish the biosimilar product is safe and effective.⁹

⁸ See, e.g., Food and Drug Administration, Guidance for Industry – Q5E Comparability of Biotechnological/Biological Products Subject to Changes in Their Manufacturing Process (June 2005), available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073476.pdf>

⁹ See, e.g., PHSA § 351(k)(2)(A)(i)(I)(aa); see also Food and Drug Administration, Guidance for Industry – Scientific Considerations in Demonstrating Biosimilarity to a Reference Product (Draft Guidance) (February 2012) at 12-19.



Similarly, the biosimilar manufacturer must develop a viable and scalable manufacturing process for the product and subject that process to FDA review.¹⁰ The costs of manufacturing facilities can run several hundred million dollars, and often these facilities are designed for product-specific purposes and tied to approval of the product being produced.¹¹ If a manufacturer has to change its production methods for the product after approval, it generally will be required to conduct additional clinical investigations, which are time-consuming and expensive.

For these reasons, the generic drug business model is largely inapplicable to biosimilars. According to one analyst, a biosimilar product is likely to take eight to 10 years to develop at a cost of \$100 to \$200 million.¹² In contrast, small molecule generic drugs require much less time and money to go to market (approximately three to five years to develop, at a cost of \$1 to \$5 million).¹³

The recent experience of the United States reveals the inherent complexities of regulating biologics. In 2010, the Congress created an abbreviated regulatory approval process for biosimilar products. This regulatory pathway, established in the Biologics Price Competition and Innovation Act (BPCIA), authorizes the FDA to approve a biosimilar product that references an earlier approved innovative biological product after a set period of time post innovator approval – 12 years.¹⁴ Importantly, Congress recognized that FDA will ordinarily require clinical evidence for a biosimilar product. The BPCIA

¹⁰ See, e.g., Food and Drug Administration, Guidance for Industry – Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product (February 2012) at 4-5 (“All product applications should contain a complete and thorough chemistry, manufacturing and controls (CMC) section that provides the necessary and appropriate information (e.g., characterization, adventitious agent safety, process controls, and specifications) for the product to be adequately reviewed. This guidance describes considerations for additional CMC information that may be relevant to the assessment of biosimilarity between two protein products.”).

¹¹ See, e.g., Food and Drug Administration, Guidance for Industry – Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product (February 2012) at 4-5 (“This guidance should be used as a companion to other guidances available from FDA that describe the CMC information appropriate for evaluation of protein products. We encourage early interaction with FDA to discuss specific CMC issues that may arise for an applicant’s proposed biosimilar product.”).

¹² Sumanth Kambhammettu, *The European Biosimilars Market: Trends and Key Success Factors* (Oct. 27, 2008), available at <http://www.obbec.com/specialreports/20-biopharmaceuticals/2152-the-european-biosimilars-market-trends-and-key-success-factors>.

¹³ See CBO Cost Estimate (S.1695), *Biologics Price Competition and Innovation Act of 2007*, As Ordered Reported by the S. Comm. on Health, Education, Labor, and Pensions on June 27, 2007 (June 25, 2008), available at <http://www.cbo.gov/ftpdocs/94xx/doc9496/s1695.pdf>.

¹⁴ See 42 U.S.C. § 262(k), enacted in Title VII, Patient Protection and Affordable Care Act, Pub. L. 111-148 (March 23, 2010).



nonetheless creates a pathway that decreases the burdens on the developer of a “highly similar” biological product by permitting that applicant to rely, to some extent, on the prior approval of the referenced biological product. Similarly, the European Medicines Agency (EMA), which has approved numerous biosimilar products, generally has required fairly extensive clinical dossiers in stark contrast to the traditional generic drug approval process.

Third, the scientific complexity of, and inability to objectively characterize, most biological products also translates into greater commercial uncertainty for innovators and the investors that support them. Specifically, the scientific differences between the biologic and biosimilar products create uncertainty as to whether the innovator’s patents will cover the biosimilar product. As explained in more detail below, this presents a significant risk for companies considering development of biological products, particularly given that companies and investors make the “go/no-go” decision two decades or more before the advent of a potential biosimilar competitor. Over that time, scientific and regulatory evolutions can fundamentally impact the risk of premature biosimilar competition preventing an adequate return on innovator investment.

Each of these issues presents unique challenges in developing intellectual property standards that will govern biological products. We believe it is critically important to understand these challenges as you work to create a trans-Pacific regime for protecting intellectual property. A strong intellectual property regime will ensure strong incentives throughout the trans-Pacific region that will stimulate discovery and development of innovative biological products, which in turn will benefit patients throughout this region and elsewhere.

III. The Economic Challenges of Developing New Biological Products

Like any other pharmaceutical product, a biological product must be thoroughly tested in pre-clinical and clinical studies before it can be approved for use in human patients. Those studies take years of effort, and cost hundreds of millions of dollars to complete. For example, studies have shown that the average cost of developing and bringing to market a new biological product is in excess of \$1.2 billion dollars.¹⁵ The costs of bringing a new biological product to market are comparable to those faced in developing other types of human

¹⁵ See Joseph A. DiMasi & Henry G. Grabowski, “The Cost of Biopharmaceutical R&D: Is Biotech Different?” *Managerial and Decision Economics*, 28(4-5), at 469-79 (2007) (“DiMasi & Grabowski”) (finding average cost of new biological entity development to be approximately \$1.2 billion).



pharmaceutical products.¹⁶ How these costs arise and some of the steps that development of biological products require present a number of distinct challenges, however. The inherent complexities of biologic therapies compared to small molecule drugs create additional uncertainties related to taking an invention from the laboratory to commercial scale production.

The industries that develop these two types of products are very different as well.¹⁷ The traditional pharmaceutical industry is mature, composed of large, publicly traded companies that are capable of financing their own research and development without resorting to outside sources of capital. By contrast, the majority of innovator biologic firms are small companies.¹⁸ As such, the biologics development sector is highly dependent on venture capital to fund research and development.¹⁹

Economists have studied the process of development of biological products extensively.²⁰ New biologic therapies typically "originate in a start-up company financed through venture capital financing."²¹ A high percentage of potential biologic therapies fail during the long development cycle from initial research through animal testing and human clinical trials, and often do so late in the development process²² – meaning that more money is invested into such candidate treatments before they are found to be ultimately unsuitable.²³ Even successful biologic therapies typically have a development time of a decade or more.²⁴ For example, Genentech/Roche's biologic therapy Avastin

¹⁶ See Henry Grabowski, "Follow-on biologics: data exclusivity and the balance between innovation and competition," *Nature Reviews: Drug Discovery* (June 2008) ("Grabowski 2008") at 483.

¹⁷ Of course, there are many established pharmaceutical companies developing both types of pharmaceutical products.

¹⁸ Deloitte at 11 (describing the biotech sector as "fragmented," "barely profitable" and composed of numerous start-up companies); see also Joseph Golec *et al.*, "Data Exclusivity Period Length and Federal Government Savings from Enactment of the Biologics Price Competition and Innovation Act of 2007" (Jan. 2008) ("Golec") at 15 n.16; National Venture Capital Association, "Cost of Capital for Early-Stage Biotech Start-Ups Found to be In Excess of 20 Percent" (2010) ("NVCA"), available at http://nvca.org/index.php?option=com_docman&task=cat_view&gid=71&Itemid=93.

¹⁹ Deloitte at 11, 15.

²⁰ Grabowski 2008 at 481.

²¹ *Id.*

²² *Id.*

²³ *Id.* ("[B]iologics that fail in clinical trial often do so only after high development costs have been incurred.").

²⁴ *Id.*



(bevacizumab) stemmed from a discovery made by a Genentech researcher in 1989, but was not approved by FDA until 15 years later, in 2004.²⁵

Because biologic developers face a long and uncertain path to product approval, investors are less willing to give them capital – or, put more simply, biologic developers have a hard time getting a loan.²⁶ Borrowing money (*i.e.*, the cost of capital) is more expensive for these companies than it is for established companies, or other industrial sectors presenting less risk of loss.²⁷ This cost of capital can have a dramatic effect on the economic viability of these companies. The largest and most successful biologic innovators have discount rates of 11.5% to 12.5%, which reflects their costs of capital.²⁸ At a discount rate of 11.5%, Professor Grabowski estimated that a new biologic therapy would just break even 12.9 years after sales begin; increasing the discount rate to just 12.5% showed the same product would need 16.2 years to simply break even.²⁹ Smaller firms are unlikely to be able to obtain comparably low costs of capital, and their times to break even on a product would be even longer.³⁰ Indeed, the appropriate discount rate for small biologic innovators has been calculated by other economists to be 13.25%, 14%, or even 23.7%.³¹ The National Venture Capital Association (NVCA) also commissioned a study by noted academics from Harvard and Boston Universities providing unprecedented access to relevant investment data. These scholars found that the cost of venture capital for small private biotech companies was at least 20%.³² The study also found that partial or total loss of capital investments occur in 44% of the investments in biotech.³³

Given this risk backdrop, biotechnology companies must present far more than a “break even” business proposition to compete against less risky investment opportunities. The fact that, until recently, successful innovator biologics did not have to worry about “generic” competitors eroding their markets certainly helped offset the higher risk/higher cost of capital surrounding biologics development. The advent of biosimilar pathways, however, has eliminated what used to be, essentially, infinite regulatory data protection for

²⁵ *Id.*

²⁶ *Id.* at 482.

²⁷ *Id.*

²⁸ *Id.* at 486.

²⁹ *Id.*

³⁰ *Id.*; DiMasi & Grabowski at 474.

³¹ Henry Grabowski, Genia Long, & Richard Mortimer, “Data Exclusivity Periods for Biologics: Updating Prior Analyses and Responding to Critiques” (Dec. 2008) (“Grabowski, Long, & Mortimer”) at 16-17.

³² NVCA at 2.

³³ *Id.*



biologics – meaning, that any biologic competitor used to have to engage in the same, extensive biologic development program that the original innovator did, but now has a regulatory shortcut to market. This changes the economic and marketplace incentives for both innovators and biosimilar competitors in fundamental ways.³⁴ While more expensive than a traditional generic drug program, biosimilars will nonetheless be a far cheaper and less risky path than innovator biologic development.³⁵ Accordingly, a new abbreviated regulatory pathway for biologics must be accompanied by a substantial regulatory data protection period.

The risk of getting this new balance of economic incentives wrong is quite high. The success of innovative biotechnology companies is essential to realizing the future potential of biotechnology innovation to help prevent, treat and even cure so many life-threatening diseases afflicting millions of people around the world. This research and development of new biologic therapies is funded by the profits of past successful biologic therapies.³⁶ Indeed, biologics developers reinvest an average of 38% of their profits into research and development.³⁷ The ability of a biologic innovator to enjoy commercial success for a sufficient period of time ensures that additional clinical investigations of this product to discover new uses can occur, and additional research to discover and develop other new biologic products will be undertaken.³⁸ Without sufficient market protection for such innovative products and uses, there will, quite simply, be less of them in the future.

IV. The Unique Intellectual Property Issues Presented by Biologics and the U.S. Response to Addressing those Challenges

As noted above, the ability of the prospective innovative biologic developer to overcome this daunting economic picture is of critical importance to public health. In simple terms, governments must devise and implement policies that create an environment that induces companies to undertake the risky and uncertain effort of developing new biological products. If governments do not do so, reduced investments in developing biological products to address unmet medical needs will result, and thus patients will have fewer options. All of the countries in the trans-Pacific region share an interest in developing policies that encourage development of new biological products to meet unmet

³⁴ *Id.* at 3.

³⁵ *See supra* at nn. 12-13.

³⁶ Golec at 4.

³⁷ *Id.* at 16.

³⁸ *Id.* at 4.



medical needs. Patients in every one of these countries will benefit from the scientific advances and products that flow from these development efforts, and there often are country-specific health needs that will only be addressed if local markets are supportive of such innovation.

While not the only critical factor, effective intellectual property standards are the primary variable affecting the environment governing research and development of new biological products. Intellectual property is particularly important to the small businesses that make up the majority of the community engaged in early-stage development of new biological products. Indeed, intellectual property is the primary, and often the sole, asset of these small businesses. As a result, predictable and enforceable intellectual property protection is crucial for these companies to secure funding, forge collaborations with research universities or other corporate partners, and undertake the risky and difficult process of biological product development.

Three types of intellectual property are critical to developers of new biological products:

- *Data protection* refers to a period of time during which a follow-on manufacturer referencing an innovator product cannot rely on the earlier approval of an innovator biological product to obtain regulatory approval. Data protection essentially serves as a temporary ban on free-riding on the efforts of the first company that undertook the task of discovering, developing and clinically testing the new biologic product.³⁹ Importantly, data protection does not confer market exclusivity for the innovative biological product – it simply prevents reliance by another company on the earlier approval of the innovator's product for a defined period of time. Other entities may conduct their own, independent clinical testing of their products, and gain market entry (subject to patent rights) for those products, at any time.⁴⁰
- *Patents* are granted for inventions, and provide a limited period of exclusive rights to that invention – 20 years from the filing date of

³⁹ Grabowski 2009 at 2.

⁴⁰ Companies developing a biosimilar product will invariably weigh the costs and benefits of using an expedited approval pathway for their product against the added cost of conducting complete clinical investigations of their products. If they choose the former, they must wait for a specified period of time for data protection to expire. If they wish to market their products sooner, they can conduct full clinical testing of their product and submit their applications under PHSA § 351(a), rather than § 351(k).



the patent application. Patents can protect the active ingredient or formulation of the biological product, the products use in treating a particular disease, or the materials and processes used to manufacture and produce the biological product. Patents undergo rigorous examination before grant, often are subject to post-grant challenges, and the scope of rights granted by any particular patent will vary significantly across jurisdictions.

- *Trade secrets* are legal protections given to information that is kept confidential. Examples of trade secrets that are important to biologics developers are details of manufacturing conditions and processes, formulation techniques for their products, and the like.

The existing international trading system regulates each of these types of intellectual property protection through the Agreement on Trade-Related Aspects of Intellectual Property (TRIPS), and numerous free trade agreements between the United States and its trading partners (including many individual TPP countries).

A. Unpredictability in the Science of Biologics Has Made It Difficult To Secure Broad Patent Protection

Over the past 20 years, the legal standards governing patentability of biotechnology inventions, and how the U.S. Patent and Trademark Office (USPTO) apply them, have become increasingly stringent. The consequence of this trend is two-fold. First, patents emerge from the examination process at the USPTO with a narrower scope. This means the patent, as granted, often will not extend to structural variants of a protein or nucleic acid that was not actually made and tested. Second, courts have used more stringent standards to invalidate patent claims or to narrow their scope. Court decisions, of course, often occur long after the patent is granted and commercial products of the innovator are on the market, making those findings particularly disruptive and difficult to manage.

The unpredictable nature of biologics affect three standards under the patent law: namely, the utility requirement under 35 U.S.C. §101, and the written description and enablement requirements under 35 U.S.C. § 112(a).

- The utility requirement mandates disclosure of a “practical utility” for the invention. Practical utility is a shorthand way of attributing real-world value so that others may use the invention in a manner that provides some immediate benefit to the public. In the leading



Supreme Court case construing the utility requirement, *Brenner v. Manson*, 383 U.S. 519 (1966), the Court held that a utility of a process for making a compound that was disclosed to be *useful* only as a possible object of scientific inquiry or research is insufficient. As a result, the USPTO instructs examiners to assess whether an application discloses a use for the invention that meets the *Brenner* Court's tests for a specific, substantial, and credible utility.⁴¹

- The USPTO and courts use the written description and enablement requirements for biotechnological inventions to limit the breadth of patent claims. Under 35 U.S.C. § 112(a), a patent applicant must satisfy two different disclosure requirements: (i) the application must describe the claimed invention with sufficient detail and precision to demonstrate the inventor had possession of what is being claimed, and (ii) the disclosure must enable a person skilled in the art to make and use the claimed invention without undue experimentation.

Innovators face substantial challenges in securing claims covering a range of variations of an original or reference protein or nucleic acid sequence. Those challenges stem from the unpredictability of changes to the sequence and structure of a protein on its activity and behavior in the body.

For example, an inventor may have generated experimental evidence showing a protein with a particular sequence exhibits properties that make the protein useful. However, the inventor may not have tested variants of that protein. Without experimental data proving those variants also share the essential properties as the tested protein, a patent examiner usually will not grant the inventor rights extending to those variants. One reason is that the examiner may conclude that creating and testing those variants will require an "undue" amount of experimentation if there is not sufficient guidance in the patent application for overcoming the unpredictability.⁴² A second reason may

⁴¹ In 1995, and again in 2001, the USPTO issued guidelines relating to the "utility" standard of 35 U.S.C. §101. See *Utility Examination Guidelines*, 65 Fed. Reg.1092 (Jan. 5, 2001). The USPTO has supplemented these guidelines with training materials that illustrate how to apply the standards. See <http://www.uspto.gov/web/menu/utility.pdf>.

⁴² For example, in *Amgen v. Chugai Pharmaceutical Co.*, 927 F.2d 1200 (Fed. Cir. 1991), *cert. denied* 502 U.S. 856 (1991), a court significantly limited the scope of a patent claim covering a gene by claiming variations of the gene's DNA sequence. The decision held that, unless the inventor could reliably predict the effect of the variation on the activity of the encoded protein, the inventor was not entitled to a claim covering all functional equivalents of the protein.



be that the examiner believes the variants covered by the claim do not share sufficient similarities to justify grouping them together. The examiner may, for example, limit the claim to a subset of protein sequences that were actually tested or which can be shown to have a common structure proven to correlate to a desired functional behavior of the protein.⁴³ A third reason may be that the examiner concludes the variants will not exhibit the same profile of functional properties that the protein that was actually tested will exhibit – that these other proteins do not have the same “utility” as the actually tested protein.⁴⁴ All of those theories rest on the scientific unpredictability of proteins and their behavior in vivo, and any one of them can function to limit the scope of patent rights granted by the USPTO.

The unpredictability in the connection between a protein sequence and the functional properties of that protein, in particular, has led the USPTO to limit the scope of claims covering DNA or protein sequences. For example, USPTO guidelines direct examiners to refuse to grant claims that broadly define groups of related nucleotide or amino acid sequences (*e.g.*, a protein having as little as 1 to 5 % variation relative to a defined reference sequence).⁴⁵ For such claims (called “genus” claims), the USPTO will require a description either listing a “representative number” of species within the definition of the claim, or one which describe the structural features common necessary for the molecules to exhibit a specified functional property. The USPTO, in particular, has explained that this approach is important where there is substantial variation in the properties of the proteins falling within the scope of this genus.

A more relaxed standard for finding inventions “obvious” over the prior art compounds the pressures to narrow the scope of patent claims. The U.S. Supreme Court established this trend following the decision in *KSR International*

⁴³ For example, the Federal Circuit in *Ariad Pharmaceuticals, Inc. v. Eli Lilly & Co.*, 598 F.3d 1336 (Fed. Cir. 2010) (*en banc*), held a claim covering many thousands of molecules sharing a functional property invalid, based on a finding that there was no established correlation of specific chemical structures to molecules that exhibit that functional property. Indeed, the USPTO and courts often reject efforts of an inventor to use “functional” definitions of a protein or DNA sequence to define the scope of their patent claims. As the Federal Circuit has held, a “description of what a material does, rather than what it is, usually does not suffice.” *Enzo Biochem Inc. v. Gen-Probe, Inc.*, 323 F.3d 956, 968 (Fed. Cir. 2002).

⁴⁴ See also *In re Fisher*, 421 F.3d 1365 (Fed. Cir. 2005).

⁴⁵ Manual of Patent Examining Procedure (M.P.E.P.) § 2163; see also Written Description Training Materials, available at <http://www.uspto.gov/web/menu/written.pdf>. The training materials, which supersede an older set of training materials issued by the Patent Office in 1999, assist patent examiners in applying the “Guidelines for Examination of Patent Applications Under the 35 U.S.C § 112, first paragraph ‘Written Description’ Requirement,” which are incorporated in the M.P.E.P. at § 2163.



Co. v. Teleflex Inc., which announced a new, flexible standard that made it easier to claim that patents were obvious and undeserving of patent protection.⁴⁶ For example, following *KSR*, the Federal Circuit has found a biotechnology claim covering a range of nucleic acid sequences obvious, even though the field of the invention was unpredictable, by reasoning that a person of ordinary skill would have believed it was “obvious to try” to produce the invention.⁴⁷ Under such cases, there exists a justifiable concern that, as the art of biotechnology continues to mature, the Federal Circuit may find other inventions “obvious to try,” and therefore unpatentable.

Courts also have limited the scope of patent claims for biotechnology inventions using other patent law concepts. For example, the Supreme Court recently held that patents may not cover isolated genomic DNA (although complementary DNA, or cDNA, was held patent eligible).⁴⁸ The Federal Circuit recently limited the scope of a patent claim covering use of antibodies to a particular cell receptor. Specifically, in *Biogen Idec, Inc. v. GlaxoSmithKline LLC*, the Federal Circuit relied on the examination record of the patent to conclude that the patent should be limited to use of the specific antibody product of the innovator, rather than other antibodies that bound to the same cellular target and behaved similarly, reasoning that the only evidence used during examination to secure the patent was linked to the specific product of the patent owner.⁴⁹ As another example, the Federal Circuit held that the reverse doctrine of equivalents could be used to find that patent claims to isolated factor VIII:C did not cover recombinantly produced factor VIII:C where the inventor had obtained factor VIII:C by purifying it from plasma.⁵⁰

The combined effect of these changes in legal standards and examination practices has made it increasingly difficult for an innovator to secure patent claims that grant broad rights beyond a specific protein sequence that was tested and evaluated. Importantly, none of these doctrines question whether a valuable invention deserving of patent protection has been made. Rather, the doctrines question what rights beyond the specific example should be covered by the patent. Under these various doctrines, the answer is that the

⁴⁶ *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007).

⁴⁷ For example, the Federal Circuit upheld a decision of the USPTO to deny a patent by reasoning it would have been obvious to try to obtain a nucleic acid molecule encoding a known protein using conventional techniques for finding nucleotide sequences. *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009).

⁴⁸ *Ass'n for Molecular Pathology v. Myriad Genetics*, 569 U.S. ____ (2013).

⁴⁹ *Biogen Idec, Inc. v. GlaxoSmithKline LLC*, __ F.3d __ (2013), 2013 U.S. App. LEXIS 7550 (Fed. Cir. Apr. 16, 2013).

⁵⁰ *Scripps Clinic & Research Found. v. Genentech, Inc.*, 927 F.2d 1565, 1580-82 (Fed. Cir. 1991).



scope of rights will be narrowly defined. This conclusion is relevant to the regulation of biosimilars, given that protein sequence claims are the closest – yet still highly imperfect – analog to the traditional composition of matter patent covering a small molecule drug active ingredient.

B. Intellectual Property Issues Addressed in the U.S. Biosimilar System

Congress recognized the challenges facing biotechnology innovators in connection with securing effective patent protection for new biological products when devising a biosimilars approval regime. Congress also recognized these products could not be regulated under the same regime used for small molecule drugs, particularly with respect to the appropriate mix of market protection mechanisms and the system for resolving patent disputes over new drugs relative to the existing Hatch-Waxman Act generic drug system. Consequently, Congress devised a new scheme to accommodate these unique issues.

There are two key intellectual property elements of this new U.S. biosimilar regime.

First, innovator biological products are provided a 12-year period of data protection.⁵¹ This period may be extended by six months, to 12.5 years, if FDA requests that the innovator company conduct pediatric clinical investigations of the product.⁵² Second, Congress provided a system for identifying and permitting enforcement of patents before approval of a biosimilar application. Key elements of that regime include:

- The biosimilar applicant must provide a copy of its biosimilar application and associated manufacturing information to the innovator who holds the reference product biologic license application (BLA) and other patent owners to enable the BLA holder and third-party patent owners to identify relevant patents that would be infringed by the product, its approved use, or the process or materials used to manufacture the biosimilar product.⁵³ This must be done within 20 days of the FDA accepting the biosimilar application for review, with provisions for confidential access even earlier.⁵⁴

⁵¹ PHSA § 351(k)(7)(A).

⁵² *Id.* at § 351(m).

⁵³ *Id.* at § 351(l)(2)(A).

⁵⁴ *Id.*



- For each patent identified by the BLA holder to the biosimilar applicant, that applicant must state either that it will defer its commencement of marketing of the biosimilar product until the patent expires, or provide detailed reasons to the BLA holder/patent owner why the biosimilar product does not infringe the patent or why the patent is invalid.⁵⁵
- Patents that are contested may then be litigated before FDA approves the biosimilar application.⁵⁶ This is provided by creation of a right of action for patent infringement similar to that used in the Hatch-Waxman Act system.⁵⁷
- If the litigation results in a final determination of infringement before the 12 or 12.5 year data protection period following approval expires, the court must grant an injunction under the infringed patent. If that final result occurs after the data protection period ends, then the court may grant injunctive relief under the ordinary criteria used in patent litigation.
- The biosimilar applicant must provide notice to the BLA holder 180 days prior to commencement of marketing of its product.⁵⁸ The primary purpose of this measure is to enable the patent owner to assert any patents that could not be asserted earlier (*e.g.*, those patents issuing after the original patent identification process concludes, or which were precluded from being asserted under § 355(l)(5)).

Thus, Congress recognized it was necessary to ensure that original biological products were effectively protected, both by providing a different, longer form of data protection and by providing a mechanism for the enforcement of patents before FDA approval of the biosimilar application occurred.

The enactment of the biosimilars pathway did not require changes to the U.S. legal regime governing trade secret protection. Under pre-existing law, FDA is precluded from disclosing to the public any trade secret information provided to it, unless doing so is necessary to address public health

⁵⁵ See *id.* at § 351(l)(3)(B)(ii).

⁵⁶ See *id.* at § 351(l)(6), (8).

⁵⁷ See 35 U.S.C. § 271(e)(2)(C).

⁵⁸ See PHSA § 351(l)(8)(A).



requirements.⁵⁹ Of course, measures that effectively protect trade secrets are of critical importance for developers of biologics, as they must provide FDA highly detailed descriptions of manufacturing processes in order to secure approval of a new biological product. Policies and regulations that require FDA to carefully manage this information are of critical importance.

C. Legislative History of the Biosimilars Pathway in the United States

The process for designing an abbreviated approval process for biosimilar products began in the late 1990s with discussions between FDA and industry about whether biosimilar products could be approved given the state of scientific knowledge surrounding biologics, and if so, whether new statutory authority was necessary to do so.⁶⁰

Congress began introducing legislation on biosimilar approval concepts beginning in 2002.⁶¹ The legislative process of developing a biosimilars pathway became more focused in 2006.⁶² For example, Congressman Henry Waxman (D-CA) introduced a biosimilars bill in the House of Representatives in September of 2006.⁶³ The Waxman bill provided *no* data protection for innovator biologic products, and was not considered by the then-Republican-led House of Representatives.⁶⁴

After Democrats took control of both Houses of Congress following the mid-term election of November 2006,⁶⁵ legislative movement on a biosimilars bill began in earnest. A Senate committee led by Sen. Ted Kennedy (D-MA) crafted a biosimilars bill in 2007, and approved it in June of that year with strong bipartisan support.⁶⁶ This Senate bill provided for 12 years of data protection for innovative products, short of the 14 years advocated by BIO and other stakeholders.⁶⁷ A different bill introduced by Senator Judd Gregg (R-NH)

⁵⁹ 18 U.S.C. § 1905.

⁶⁰ Krista Hessler Carver *et al.*, "An Unofficial Legislative History of the Biologics Price Competition and Innovation Act of 2009," 65 *Food & Drug L.J.*, 671, 697-702 (2010) ("Hessler").

⁶¹ *Id.* at 704.

⁶² *Id.* at 716.

⁶³ *Id.*

⁶⁴ *Id.* at 717.

⁶⁵ John M. Broder, "Democrats Gain Senate and New Influence," *The New York Times* (Nov. 10, 2006).

⁶⁶ Hessler at 724.

⁶⁷ *Id.*



provided for essentially 14 years of data protection.⁶⁸ Congressman Waxman also introduced a second biosimilars bill in 2007, which again would have provided no data protection for innovative biological products.⁶⁹

Data protection was the subject of several Congressional hearings.⁷⁰ In those hearings, noted economists testified that innovator companies required “more than a decade” to achieve “[b]reak-even returns on R&D for” a typical “biological product.”⁷¹ Other witnesses provided figures of 15 years and \$1.2 billion as typical.⁷² Multiple witnesses pointed out that data protection was necessary to mitigate the risk that patent protection may not be sufficient to protect an innovator’s investments from the encroachment of a similar but not identical follow-on product.⁷³ Others noted the importance of creating parity with the roughly 12 years of market protection afforded to innovator small molecule developers through the various provisions of the Hatch-Waxman Act.⁷⁴

Following these hearings, Congresswoman Anna Eshoo (D-CA) introduced a bill in the House in 2008, which provided 12 years of data protection, with extensions available for situations such as supplemental indications.⁷⁵ She reintroduced a substantially similar bill in 2009.⁷⁶ Congresswoman Eshoo’s approach was co-sponsored by scores of Congressmen from both sides of the political aisle and supported by an incredibly broad spectrum of the research, university, and patient advocacy communities, among others.⁷⁷ Congressman

⁶⁸ S. 1505, § 2, 110th Cong. (2007). The Gregg bill provided for 12 years of data exclusivity followed by two additional years during which FDA could not approve a biosimilars application. S. 1505, § 2.

⁶⁹ H.R. 1038, 110th Cong. (2007).

⁷⁰ See, e.g., *Examining Food and Drug Administration Follow-On Biologics, Generally Referred to as a Biotechnology-Derived Protein Drug (or Biologic) that is Comparable to a Novel, Previously Approved Biologic and that is Approved with Less Supporting Data than the Innovator Biologic: Hearing Before the S. Comm. on Health, Labor, and Pensions*, 110th Cong. (2007); *Safe and Affordable Biotech Drugs: The Need for a Generic Pathway: Hearing Before the H. Comm. on Oversight and Government Reform*, 110th Cong. (2007); *Assessing the Impact of a Safe and Equitable Biosimilar Policy in the United States: Hearing Before the Subcomm. on Health of the H. Comm. on Energy and Commerce*, 110th Cong. (2007); *Biologics and Biosimilars: Balancing Incentives for Innovation, Hearing Before the Subcomm. on Courts and Competition Policy of the H. Comm. on the Judiciary*, 111th Cong. (2009) (“Biologics and Biosimilars Hearing”).

⁷¹ *Safe and Affordable Biotech Drugs*, 110th Cong. at 162.

⁷² *Id.* at 92.

⁷³ *Id.* at 92, 183.

⁷⁴ *Biologics and Biosimilars Hearing* at 8.

⁷⁵ H.R. 5629, 110th Cong. (2008).

⁷⁶ H.R. 1548, 111th Cong. (2009).

⁷⁷ See Letter from 162 Signatories to Congressman Kennedy and Congressman Enzi (June 23, 2009). Signatories included the Association of American Universities, the Association of University



Waxman also introduced another bill in 2009, although this one proposed three- or five-year data protection in some situations.⁷⁸ As Congress increased its attention on the issue of data protection, additional draft provisions circulated with varying subsidiary provisions, but generally retained the 12-year baseline for data protection.⁷⁹

U.S. regulatory agencies also were involved in the process. The FDA expressed its approval of substantial data protection provisions.⁸⁰ The FTC, on the other hand, issued a report that deemed data protection wholly “[u]nnecessary.”⁸¹ The White House and the Office of Management and Budget jointly proposed seven years of data protection as a compromise.⁸²

Congress continued to internally debate data protection periods of various lengths up to 14 years.⁸³ Additional hearings brought in the views of other witnesses, including, importantly, those of the venture capital community, which funds the vast majority of biotech companies and supported the longer time periods under consideration as necessary to ensure continued investment in biologic innovation.⁸⁴

Technology Managers, Johns Hopkins Institutions, the National Kidney Foundation, and several members of the Pennsylvania state legislature. Other groups sent similar letters. *See, e.g.*, Letter from 39 Signatories to Congressman Reid and Congresswoman Pelosi (Jan. 14, 2010) (“Unlike so many of the issues that remain unresolved in health reform, this issue was resolved with the vast majority of Senators and Representatives, both Democrat and Republican, in agreement. In addition, the university community is aligned that 12 years is the appropriate number to ensure continued research. . . . 150 Members of the House supported legislation that included twelve years of data exclusivity. Amendments that included twelve years of data exclusivity passed overwhelmingly in the House Energy and Commerce Committee (47-11) and Senate HELP Committee (16-7) during the mark-ups of health care reform.”); *see also* Letter of Association of American Universities to Congresswoman Eshoo and Congressman Barton (June 10, 2008) (“To ensure that these discoveries will benefit the public, innovator companies and venture capitalists must have sufficient economic incentives to commit the substantial investments necessary to conduct clinical trials and develop such discoveries into new, breakthrough biologic treatments. Your bill accomplishes this objective by providing innovators 12 years of data exclusivity.”).

⁷⁸ H.R. 1427, 111th Cong. (2009).

⁷⁹ Hessler at 785-86.

⁸⁰ Letter of Frank M. Torti, FDA Chief Scientist, to Congressman Frank Pallone (D-NJ), Chair, Subcommittee on Health, Committee on Energy & Commerce, U.S. House of Representatives (Sept. 18, 2008) at 11.

⁸¹ Federal Trade Commission, *Emerging Health Care Issues: Follow-on Biologic Drug Completion* (June 2009) (“FTC Report”) at vi. *See infra*, at pp. 24-29, for detailed discussion of flaws in the FTC Report.

⁸² Letter from Nancy-Ann DeParle & Peter Orszag (June 24, 2009) at 1.

⁸³ Hessler at 791-96.

⁸⁴ Biologics and Biosimilars Hearing at 183.



After more than two years of competing legislative proposals, economic analyses, reports, debates, and in-depth hearings, in July 2009, the House Energy and Commerce Committee held a legislative mark-up to consider a bill creating a biosimilars pathway.⁸⁵ Congressman Waxman (then Chairman of the House Energy and Commerce Committee) offered his version of a biosimilars bill that, once again, provided for *no* data protection whatsoever, consistent with the FTC's recommendation.⁸⁶ Congresswoman Eshoo offered a comprehensive amendment to the Waxman bill that, among other things, provided for 12 years of data protection.⁸⁷ During mark-up of the bill, the Committee adopted Congresswoman Eshoo's amendment and rejected Chairman Waxman's position by an overwhelming vote of 47 to 11.⁸⁸

The Senate version of this bill, which was highly similar to the Eshoo amendment and contained a 12-year base data protection period, ultimately was joined to a larger healthcare reform bill.⁸⁹ Although there were a handful of attempts to amend the data protection period during subsequent progress of the bill, none were adopted.⁹⁰ The larger healthcare bill that was eventually enacted into law with President Obama's signature provided for 12 years of base data protection for innovative biologics.⁹¹ There has been no serious effort by Congress or the Administration to change this result, which had strong, bipartisan, bicameral backing throughout the legislative process.

D. Congress' Rationale for Finding that 12 Years of Data Protection Was Essential to Promote Innovation in Biologic Products

As described above, a central focus of the deliberations of Congress in enacting the U.S. biosimilars approval pathway was determining the appropriate period of data protection for biological products. Congress recognized that, by creating a new, abbreviated pathway, it would be fundamentally disrupting a key economic assumption of the industry that was engaged in developing new biological products – namely, the assumption that every entrant to the biologics market would face the same challenge of undertaking original and complete pre-clinical and clinical investigations of its product. This assumption was well-

⁸⁵ Hessler at 802.

⁸⁶ H.R. 3200, 111th Cong. (2009).

⁸⁷ Hessler at 802.

⁸⁸ *Id.* at 803.

⁸⁹ *Id.*

⁹⁰ *Id.* at 803-06.

⁹¹ PHSA § 351(k)(7)(A), (B).



founded because FDA had stated long ago that there was no such thing as a “me too” biologic.⁹² Stated another way, Congress recognized that it would be decreasing the period of data protection for innovative biologic products from, effectively, infinity to a limited period.

Congress also recognized that the impossibility of proving identity between two complex biological products – the central predicate of the generic approval pathway – raised unique patent issues. Specifically, under the Hatch-Waxman Act system, a new drug developer will know, at the time it begins its drug development efforts, that patents that cover its own innovator product also will cover the generic product. This is because any generic version of the innovator drug will and must have an identical active ingredient. With biologics, the patents an innovator may hold at the start of their development process, however, may not cover the biosimilar product, which invariably will be different – as expressly permitted by the biosimilars statutory scheme.

Compounding this problem was that the same scientific issues that preclude use of a “generic” type approval process led the U.S. and other patent offices to adopt stringent standards for granting patents. Often, as described above, those standards would limit the innovator to a very narrow claim covering only its particular protein product. Consequently, due to the unpredictability in the science governing the biological activity of proteins, patents often could not be secured by innovators that would cover all possible variations of an original biological product. In other words, a biosimilar product that differs from the innovator product but that is “biosimilar” enough could be approved through an abbreviated pathway, while also evading patents the innovator might hold.

Congress considered the needs for data protection for innovator biologic products in light of this unpredictable patent landscape, and concluded that a longer data protection period was necessary for biologics than had been provided under the Hatch-Waxman Act scheme for small molecule drugs.

Importantly, in reaching its conclusion about what length of data protection was necessary for innovative biologic products, Congress considered experiences under the Hatch-Waxman Act. Research has shown that, under that law, new drugs containing a new molecular entity (NME) typically enjoy a

⁹² Federal Register, v. 39, no. 248, p. 44641 (December 24, 1974).



substantial period – 11.2 to 13.8 years⁹³ – of marketing free from generic competition.⁹⁴

Equally as important, this period of market exclusivity was delivered through patent exclusivity for the new drug or an approved use of the new drug. As explained above, the active ingredient of a generic drug must be identical to that in the innovator product. This requirement makes it possible for new drug developers to more confidently predict that their patent rights will cover potential generic products at the point in time when the new drug developer undertakes pre-clinical and clinical testing of its new drug. The periods of market exclusivity that were observed by this research are obviously longer than effective data protection periods provided under the Hatch-Waxman Act for new drugs, which demonstrates that patent rights are playing an important role in providing the necessary market incentives for new drug development.⁹⁵

This result did not occur by accident. Congress recognized in the Hatch-Waxman Act that an effective period of patent exclusivity was important to encourage new drug development, but that – because of the lengthy development cycle between invention and marketed product – effective patent life for new drugs was woefully inadequate. This is why Congress included provisions in the Hatch-Waxman Act that permit an innovator to restore the lost “effective term” of a patent for a new drug product or its method of use. Specifically, under 35 U.S.C. § 156(c), the owner of a patent may secure an extension of a patent on a new drug or its method of use or manufacture of up to five years in duration, with an overall limit of 14 years of “effective” patent term (*i.e.*, the period starting on the day a drug is approved and ending when the extended patent expires). In other words, Congress devised a scheme that would deliver to new drug developers an “effective” patent life of up to 14 years post-FDA approval, recognizing these patents would deliver freedom from competition by generic versions of new drugs for that period.

⁹³ This 11.2 to 13.8 year period runs from the commencement of marketing of the drug until generic competition begins.

⁹⁴ See, *e.g.*, Grabowski and Kyle, “Generic Competition and Market Exclusivity Periods in Pharmaceuticals,” *Managerial and Decision Economics*, 27:1-12 (2007) at 7 (showing that the average market period for NME drugs was 11.2 years for drugs approved between 2002 and 2005, and 13.8 years for drugs approved between 1995 and 2001).

⁹⁵ The Hatch-Waxman Act provides, effectively, 7.5 to 8 years of data protection for a new drug containing a new molecular entity. This is the consequence of the structure of the Act, which provides that an abbreviated new drug application (ANDA) may not be filed earlier than four years after NDA approval, but, if patents are available and challenged, FDA will defer approval of the ANDA for up to 30 months while litigation over those patents is proceeding.



Congress arrived at the 12-year data protection period for new biological products by evaluating their unique scientific, regulatory and patent issues, and determining what length of data protection would create parity between small molecule and biologic products in terms of effective market protection. That is, Congress used a different mix of data protection and patents to achieve the same end result – approximately 12 years of protection from biosimilar competition. In this way, a longer data protection period only serves as an “insurance policy” against the possibility that the differences in patent and regulatory schemes for biologics and biosimilars could result in a shorter period of protection for biologics as compared to small molecule drugs. If the patents for a biological product “hold” against biosimilar competitors, then the innovator can expect roughly 12 years of market protection from those patents (based on the studies noted above); but if the patents fail to provide effective protection due to the narrowness of biological claims and the lack of an “identity” standard for biosimilar approval, then data protection serves as the backstop to create a similar 12-year period. This powerful argument was made repeatedly to Congress by economists, academics, the investment community, and others, including BIO.

Congress also considered exhaustive, objective economic studies of the development process for biological products. As described earlier, those studies established that a period of data protection in excess of 12 years was needed to provide sufficient economic incentives for privately-funded research into new biologic therapies. Protection of this duration was found necessary to attract venture capital to fund long-term research projects that are neither guaranteed to succeed nor be profitable. Indeed, Congress reached its conclusion about the minimum period of data protection for biologic innovators after considering the evidence that biological developers will not recoup their development investments for between 12 and 14 years, on average. One empirical study based on internal data from the biologics innovators estimated that one new approved biologic therapy represented a cash outlay of \$559 million, or \$1,241 million if considering time costs, in 2005 dollars.⁹⁶ Professor Grabowski, in a paper published in *Nature Reviews*, demonstrated that biologic innovators can expect to break even in about 13 to 16 years after they first begin selling a biologic.⁹⁷ Similarly, Professor Golec and colleagues noted that biologic innovators can expect to need about 17 years just to break even on a product.⁹⁸ Professor Golec concluded that a data protection period of less than 14 years “is

⁹⁶ DiMasi & Grabowski at 477.

⁹⁷ Grabowski 2008 at 486.

⁹⁸ Golec 2008 at 3.



counterproductive with respect to encouraging innovative, new breakthrough biologics.”⁹⁹

In sum, Congress did not arbitrarily select the number 12, but rather had substantial justification for devising the biosimilars scheme that it finally enacted in 2010, after years of thoughtful deliberation and consideration.

E. Congress Decided to Use “Soft Linkage” for Biologics

Adopting data protection provisions of at least 12 years for biosimilars also gave the United States more flexibility in addressing the attendant patent issues. This is in contrast to the patent framework established for small molecule drugs under the Hatch-Waxman Act, which created what is known as “hard linkage” between patents and FDA approval.

During the debates that led to the passage of the Hatch-Waxman Act, generic manufacturers pushed for the ability to begin marketing and distribution of a drug the day after the relevant innovator’s patents expired. The realities of testing, scale-up, and regulatory approval necessarily required a generic manufacturer to make and use the patented product years before sales could begin, but doing so would constitute an act of patent infringement under 35 U.S.C. § 271(a).

The resolution of these issues required instituting “hard linkage” between the patent system and FDA’s approval process. To resolve patent issues before patent expiration, and to give generic manufacturers the ability to conduct a product launch the day after patent expiration, two changes were made to the patent laws. First, a statutory exemption to patent infringement was created so as to allow generic manufacturers to conduct activities “reasonably related to the development and submission of information” to FDA.¹⁰⁰ In other words, generic manufacturers were allowed to do things such as conduct formulation studies and set up manufacturing processes for the purposes of obtaining permission from FDA to sell a generic drug. Second, the submission of such an application to FDA was deemed to be an act of patent infringement.¹⁰¹

Generic manufacturers were not required to notify innovator companies that they were conducting activities that were exempt from infringement by § 271(e)(1). However, generic manufacturers were required to notify innovator

⁹⁹ Golec 2008 at 21.

¹⁰⁰ 35 U.S.C. § 271(e)(1).

¹⁰¹ 35 U.S.C. § 271(e)(2).



companies that they had applied to FDA for permission to market a drug and were not planning to wait until patent expiration to begin marketing.¹⁰² The Hatch-Waxman Act gave innovator companies incentives to early and expeditiously resolve patent issues in such cases. For example, an innovator company must list all patents covering a drug with FDA.¹⁰³ If the innovator company sues the generic company within 45 days of receiving notification of intent to market before patent expiration from the generic company, FDA is precluded from approving the generic application for 30 months (subject to a few exceptions).¹⁰⁴

Such a system of hard linkage is necessitated by the compressed timeframe between expiration or invalidation of applicable patents and the practical ability of generic companies to begin marketing generic small molecule drugs immediately thereafter. In contrast, the 12-year data protection period in the biosimilars law obviates the need for such a hard linkage for biologic drugs. Patents play a different role for biologic innovators under the BPCIA, protecting early investment in an area, but unlikely to determine the period during which an innovator has exclusive sales from which to recoup development costs. Instead, data protection is the primary mechanism for ensuring that such innovators have the ability to recover their substantial investments in research and development, and thus have the incentive to undertake such investments years and decades before they begin to bear fruit.

That is not to say the patent system is wholly disconnected from the FDA approval process for biologic products. The BPCIA requires notification of filing and intent to challenge patents on innovator biologic products, and provides mechanisms for early resolution of any patent suits that arise.¹⁰⁵ However, there is no listing of patents on biologic products with FDA, and no bar on FDA approval of a biosimilar application triggered by a patent infringement lawsuit (unless ultimately successful). As a result, the connection between the patent system and FDA with respect to biologics is termed “soft linkage.”¹⁰⁶

¹⁰² 21 U.S.C. § 355(j)(2)(B).

¹⁰³ *Id.* at §§ 355(b)(1), (c)(2).

¹⁰⁴ *Id.* at § 355(j)(5)(B)(iii).

¹⁰⁵ PHS 351(k), (l).

¹⁰⁶ The FTC report stated that any special procedures for patent issues between innovator and follow-on companies were unnecessary, could undermine patent incentives, and would harm consumers. Here, the FTC again ignored the realities of the marketplace. Both innovator and follow-on companies agreed that certainty is a key component to making good business decisions, and that both needed certainty with respect to patent issues. The Hatch-Waxman Act was created to resolve patent issues for small molecule drugs before a follow-on company undertook the



It also should be noted that the substantial data protection provisions of the BPCIA are likely to lead to less patent litigation for biosimilar products compared to small molecule drugs, since fewer patents are likely to remain in force 12 years post-FDA approval.

F. Congress, Academia, and the Biotech Community Reject the Federal Trade Commission Report

As noted above, during the debate on a biosimilars pathway, the FTC released a report suggesting that *no* years of data protection were necessary for biologics.¹⁰⁷ Criticism of the methods underlying the FTC report, and disagreement with its conclusions, came swiftly and from across a wide spectrum of interested and disinterested parties, including Congress. Academics pointed out critical flaws in the FTC methodology and assumptions,¹⁰⁸ and one researcher whose work was cited in the FTC report as support for its position, subsequently explained that the FTC's conclusion "was based in part on a misapplication of the results of [his] study."¹⁰⁹ In fact, even research funded by Teva Pharmaceuticals (a global leader in biosimilars and key opponent of the 12 years provision) found that seven years of data protection was necessary to maintain appropriate incentives for biologics innovation, not zero as the FTC concluded.¹¹⁰ Clearly, the FTC's report represented an outlier view compared to credible academic and economic opinion on the subject.

A House of Representatives subcommittee held a hearing on the FTC's report, exposing several of these flaws.¹¹¹ The FTC was forced to admit that it had not even considered the effect of data protection (or the lack thereof) on investment in new biologic therapies.¹¹² The

commercial expense of a full-scale product launch. A similar regime for biosimilars is eminently reasonable.

¹⁰⁷ FTC Report.

¹⁰⁸ Grabowski, Long, & Mortimer at 10, 15-19.

¹⁰⁹ Christopher Holman, "Maintaining Incentives for Healthcare Innovation: A Response to the FTC's Report on Follow-On Biologics," 11 *Minn. J. of Law, Sci. & Tech.* 755, 756 (May 2010) ("Holman").

¹¹⁰ Alex M. Brill, "Proper Duration of Data Exclusivity for Generic Biologics: A Critique" (Nov. 2008) ("Brill"), available http://www.tevad.com/Brill_Exclusivity_in_Biogenics.pdf

¹¹¹ See *Hearing on Emerging Health Care Issues: Follow-On Biologic Drug Competition, Hearing Before the Subcomm. on Health of the H. Comm. on Energy and Commerce*, 111th Cong. (June 11, 2009) ("Hearing on Emerging Health Care Issues"), available at <http://www.gpo.gov/fdsys/search/pagedetails.action?browsePath=111%2FHOUSE%2FCommittee+on+Energy+and+Commerce&granuleId=CHRG-111hhr73747&packageId=CHRG-111hhr73747&fromBrowse=true>

¹¹² *Id.* at 181.



subcommittee also questioned the FTC's assumptions about the interplay between patent protection and biosimilar approval, given the lack of certainty about what form any biosimilar approval pathway would take and how the regulatory standard of similarity would evolve.¹¹³ Members of the subcommittee criticized the report's conclusions on data protection, going so far as to describe them as "fantastically unrelated to the realities of the marketplace."¹¹⁴

As a representative for NVCA explained, the biotechnology industry is funded primarily by venture capital, yet venture capital firms had no opportunity to provide input for the FTC report.¹¹⁵ NVCA also testified that the FTC should have asked, but did not ask, "whether reliance on patents alone continues to be justified even under a new abbreviated biologics approval pathway that completely changes the business incentives for pioneering developers and subsequent competitors alike."¹¹⁶

To summarize, the major substantive critiques of the FTC report are as follows:

- *The FTC report stated that data protection was unnecessary because competition between biologic and biosimilar manufacturers will resemble brand-to-brand competition rather than brand-generic*

¹¹³ *Id.* at 73, 167 (issue raised by Representatives Eshoo ("We have absolutely no experience with the similarity standard that will be used for biologics for the approval of biosimilars, so how can you be sure that a new and untested standard would not facilitate a path for patent workarounds for biologics?") and Christensen ("If there are no biosimilar pathways that exist, how could there be any evidence as to how patents could be worked around?")).

¹¹⁴ *Id.* at 179. The subcommittee's condemnation of the FTC's determination on data exclusivity was bipartisan and extensive. See Hearing on Emerging Health Care Issues at 15 ("The scenario outlined by the FTC would, I believe, unfairly tilt competition in favor of bio-similars by allowing them to capitalize on innovators substantial research and development efforts at any time."), at 39 ("I am quite concerned by the report's assertion that no period of data exclusivity is necessary for pioneer or brand biologics because patents and market pricing should provide sufficient protection and incentive."), at 40 ("Data exclusivity provides the certainty brand biologics need to spend hundreds of millions of dollars and years investing in the research, development, and approval of new drugs, and the assurance that this investment can be recouped."), at 43 ("I am convinced that shortening the time of patent and data exclusivity would adversely impact needed innovation."), at 117 ("You also state that data exclusivity is only justified for products that are unpatentable, but I see no substantiation at all for these positions in your report."), at 133 ("I just cannot fathom how you make this argument that removing data protection is going to create greater incentive for investors to put money into products that will truly respond to this condition in a new way. I just think you have turned reality on its head in that regard.").

¹¹⁵ Biologics and Biosimilars Hearing at 182.

¹¹⁶ *Id.*



competition. While there is some truth to this argument, this new competition is NOT brand-to-brand competition in one critical respect that the FTC all but ignores. Brand competitors have to engage in the same lengthy and costly R&D process, from basic invention, through proof of concept, through clinical trials, and full regulatory review and approval, that the initial brand innovator did. Biosimilar manufacturers, on the other hand, have been given a scientific and regulatory shortcut that, while still more demanding than small molecule generic drug entry, is considerably shorter and cheaper than the process that the initial innovator had to go through. There is a huge difference between the \$1.2 billion that is invested on average to produce true innovation, versus the \$100-200 million (or less over time) that the FTC suggests a biosimilar manufacturer would have to invest. In no other industry outside of pharmaceuticals does government affirmatively permit (let alone encourage) such “free riding,” and to suggest – as the FTC does – that this fact is essentially meaningless in terms of economic incentives for future innovation is baffling.

- *The FTC report stated that patents alone are likely sufficient to support biologic innovation without any data protection period necessary.* This remarkable conclusion is based on an unfounded assumption that the strength of a biologics composition of matter patent would be as protective against early biosimilar entry to the same degree as an active ingredient patent would protect a small molecule innovator against generic competition. The FTC report acknowledges two instances where biologics composition of matter patents were indeed designed around by competitors, but points to six specific cases to support its contrary assertion.¹¹⁷ Research by patent scholar Christopher Holman, however, indicates that a close examination of four of these six cases reveals that they do not actually support the FTC’s conclusion, and that the remaining two cases were decided at the lowest levels of U.S. courts (no appellate decision cited) and are atypical based on his extensive research.¹¹⁸ The FTC also ignored or overlooked a number of other instances where there had indeed been a design-around of an innovator’s patents on a biologic product.¹¹⁹

¹¹⁷ FTC Report at 37 & n.153

¹¹⁸ Holman at 771.

¹¹⁹ See *Hormone Research Found v. Genentech, Inc.*, 904 F.2d 1558 (Fed. Cir. 1990); *Genentech, Inc. v. Wellcome Found. Ltd.* 29 F.3d 1555 (Fed. Cir. 1994); *Novo Nordisk v. Genentech, Inc.*, 77 F.3d 1364 (Fed. Cir. 1996); *Amgen Inc. v. Hoechst Marion Roussel*, 314 F.3d 1313 (Fed. Cir.



Holman also points out that, in the United States, biologics innovators have had difficulty obtaining composition of matter patents due to many of the products being recombinant versions of what naturally occurs in nature. Indeed, the recent U.S. Supreme Court decision in the *Myriad Genetics* "gene patent" case and eroding patentability standards for basic biotech inventions around the world only make obtaining composition of matter patents for biologics even more difficult. As a result, biologic innovators are often forced to rely on secondary patents on particular processes or uses involving the new composition of matter. And Holman's research found numerous examples of competitors who successfully designed around these other types of patents.¹²⁰ Even the FTC acknowledges that designing around such secondary patents by competitors is "prevalent."¹²¹ The uncertainty of patent protection for both biologic composition of matter patents and biologic secondary patents requires additional innovation incentives to prevent premature biosimilars entry.¹²²

- *The FTC claimed that data protection was not necessary because biosimilars market data in Europe revealed that innovators would retain 70-90 percent of their market share years after biosimilar entry.* However, the reality is that, as of 2012, the biosimilar market share for one major biological innovation, EPO, in Germany stood at 45% of the overall market, while the reference product only had about 20% due to other competition with non-reference products.¹²³ The FTC's methodology also suffers from the wide variance among EU countries of biosimilar uptake. For example, a December 2011 IMS report found that biosimilar uptake varies when

2003); *Genzyme v. Transkaryotic Therapies, Inc.*, 346 F.3d 1094 (Fed. Cir. 2003); *Biogen v. Berlex*, 318 F.3d 1132 (Fed. Cir. 2003).

¹²⁰ Holman at 773.

¹²¹ FTC Report at 45.

¹²² The FTC also relied on Holman's research on the written description requirement to support its conclusion that biotech patents were sufficiently strong. Yet Holman points out that the FTC's reliance was misplaced and based on a misunderstanding of his work, as the written description doctrine has resulted in a tightening of patentability standards for composition of matter patents. See Holman, at 777; *see also id.*, where Holman argues that the FTC Report relied on the ability of patent applicants to obtain broad 70 percent identity claims on protein sequence patents, even though by the time of the report's issuance, the PTO was requiring percent identity claims of 95 percent or greater in many cases. Further, Holman notes the recent decision of the Board of Patent Appeals in *Ex parte Kubin*, which demonstrates that "inventions relating to biologic drugs may be afforded substantially narrower patent protection than they have in the past." *Id.*

¹²³ IMS Health, "Biosimilar Accessible Market: Size and Biosimilar Penetration," April 2012. Found at http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/biosimilars_imsstudy_en.pdf



therapeutic areas are considered according to type. For example, filgrastim biosimilar uptake stood at 80% of the commodity market in the United Kingdom.¹²⁴ In addition, IMS Health projects the U.S. market penetration of biosimilars to reach 50% by 2020.¹²⁵ Clearly, the updated data on the biosimilars market shows that biologic innovators will not retain 70-90 percent of the market years after biosimilar entry, which was a major assumption underlying the FTC's erroneous conclusion about the lack of any need for data protection.

- *The FTC report found that granting 12-14 years of data protection for biologics would harm rather than promote innovation.* However, the FTC's arguments in this vein are demonstrably incorrect. At the time of the FTC report, with no biosimilar pathway in the United States, innovators effectively had infinite data protection, and yet there was widespread recognition of the amazing amount of healthcare innovation occurring due to the scientific developments surrounding biotechnology and biologic drugs. Under the FTC's theory, however, such infinite exclusivity should be even less likely to encourage true innovation. Further, Professor Holman points out that, precisely because of the infinite data protection available prior to the BPCIA, innovators often have brought biologics to the market that they otherwise would not have due to the absence of effective patent protection for the products. The notion that providing 12-14 years of data protection would actually harm, rather than maintain, innovation incentives flies in the face of marketplace realities the FTC simply chose to ignore.¹²⁶
- *The FTC disregarded the cost of capital model to determine the appropriate data protection period.* The FTC inexplicably disregarded this economically rationale approach to determining an appropriate return on investment period, and instead looked at then-recent trends in biotech stock prices and investment rates as indicating a solid investment climate that would continue even with an abbreviated pathway for biologic competitors and no data protection period.¹²⁷

¹²⁴ IMS Health, "Shaping the Biosimilars Opportunity: A Global Perspective on the Evolving Biosimilars Landscape, available at http://www.imshealth.com/ims/Global/Content/Home%20Page%20Content/IMS%20News/Biosimilars_Whitepaper.pdf

¹²⁵ *Id.* at 6.

¹²⁶ Holman at 772-773.

¹²⁷ Hearing on Emerging Health Care Issues at 158.



Yet even those economists supporting a shorter period of data protection and funded by the biosimilars industry accepted Professor Grabowski's cost of capital approach as a sound basis for determining an appropriate data protection period. For example, as noted earlier, a report authored by Dr. Alex Brill and funded by Teva Pharmaceuticals agreed with the methodology employed by Dr. Grabowski, but found that, under a more favorable set of assumptions of the cost of capital and other variables, the break-even point for new biological products would occur between 9.5 and 12.5 years after approval, thus supporting, in Dr. Brill's analysis, a seven-year data protection period for innovators rather than the 12-14 years found by Dr. Grabowski.¹²⁸ Notably, Dr. Brill's paper focused not on small and medium-sized biotechnology companies, which make up the vast majority of the biotechnology industry, but on large, established publicly traded companies with a much lower cost of capital. Indeed, other economists found the Brill report unrealistically assumed a discount rate of 10%, a figure far too low a cost of capital in the biologics sector for even the largest, most successful companies.¹²⁹ A study commissioned by NVCA found that the cost of capital was much higher than Dr. Brill estimated, and was at least 20% for small private biotech companies.¹³⁰ The Brill report also used other faulty assumptions, such as a contribution margin of 60%, which is not representative of the sector as a whole, but rather would be in line with only the largest and most successful biologic innovators.¹³¹ NVCA also pointed out a "survivor bias" in Brill's analysis, as the paper only looked at companies that successfully transitioned to the public markets,¹³² and explained that a seven-year data protection period would preclude investment in new biologics research because it would be impossible to break even on such investments.¹³³

As Dr. Grabowski concluded after considering the Brill report:

Data exclusivity periods of twelve years or more provide an "insurance policy" to stimulate innovation in cases in which

¹²⁸ See Brill at 9.

¹²⁹ Grabowski, Long, & Mortimer at 10, 15-19.

¹³⁰ NVCA at 2.

¹³¹ Grabowski, Long, & Mortimer at 15-19.

¹³² NVCA at 1.

¹³³ *Id.* at 2-3.



effective patent protection is limited in scope or time, or uncertain in nature. If the data exclusivity period is only a nominal five to seven years, many products with limited patent protection, regardless of clinical value and importance to patients, will not enjoy sufficient exclusivity time to recover R&D costs and earn positive returns. Smaller, early-stage innovative firms will be most adversely affected, given their dependence on external financing with high costs of capital. Furthermore, biotech firms may elect more often to invest in lower-risk biosimilar manufacturing opportunities, rather than to pursue innovative pioneer positions. The net result would be a shift from an aggressively innovative industry to an imitative one.¹³⁴

Even if – despite all the rebuttals cited above – one accepts the FTC’s assumptions and findings, 12 years of data protection is still the most prudent course. Professor Holman points out that “the FTC Report apparently fails to recognize that the data exclusivity period would run concurrently with the patent term...”¹³⁵ Therefore, if a biologic patent is strong enough to preclude premature competition for as long as a patent typically does in the small molecule world (roughly 12 years), as the FTC argues it is, then no additional market exclusivity is provided by the 12 years of concurrent data protection. However, if the FTC is wrong and the biologic patent provides inadequate protection, then the incentives to innovate in this space would be at great risk.¹³⁶

It also should be emphasized that overreliance on patent protection, instead of the full complement of regulatory and other protections, will often lead to less innovation and less cures. Firms evaluate the strength of patents for pharmaceuticals, and often discard drug candidates prematurely due to weak patent protection.¹³⁷ Prior to the BPCIA, innovators with weak patent protection could rely on regulatory barriers created by the absence of a biosimilar pathway, which effectively provided infinite data protection. However, the introduction of biosimilars pathways that lack substantial data protection periods will make launches of innovative biologics with weak patent protection much more

¹³⁴ Grabowski 2009 at 5.

¹³⁵ Holman at 776.

¹³⁶ *Id.*

¹³⁷ Roin, Benjamin N. *Unpatentable Drugs and the Standards of Patentability*, Texas Law Review, Vol. 87, pp. 503-570 (2009).



unlikely.¹³⁸ Such an approach could have profoundly negative impacts on public health, particularly with respect to neglected diseases.

V. Looking Forward – Requirements for a TPP-Wide Intellectual Property Regime

The existing standards found in agreements between the United States and its trading partners provide a good foundation to build upon, but must be updated to reflect the realities and challenges facing developers of new biological products. In particular, given the challenges of securing broad patent rights that can cover variations of an innovative biological product, and the need to ensure that investors see the potential to secure commercial success of these products, a period of data protection of not less than 12 years of duration is necessary. That was the period that the U.S. Congress found to be the minimum necessary to provide continued incentives to the biotechnology industry, and the investment communities upon which that industry depend, to develop new biological products.

Implementing standards of protection that effectively protect innovation for biological products within the TPP region is of critical importance to BIO and its members. The realities of modern research and development in this industry demonstrate that each TPP member has the potential to participate in the discovery and development of new biological products, or new uses of existing products. The highly leveraged and disseminated nature of the biotechnology industry enables research institutions and small start-up companies in any TPP country to be the seed of this process of discovery, innovation and development. Indeed, there are numerous examples of an individual or small group of scientists, often located in a university or publicly funded research institution, starting a chain of events that make possible discovery and development of a new biological product. There is no reason why a scientist in any one of the TPP countries cannot become that seed of innovation and development.

However, this innovative potential requires an intellectual property infrastructure that is certain and consistent throughout the TPP region. As we move to more tightly integrate the economies of the TPP countries and to promote collaborations throughout this region, discrepancies in the intellectual property infrastructure will become substantial obstacles to collaboration. For this reason, we believe it is imperative that the TPP include a strong set of

¹³⁸ Holman at 767.



intellectual property standards – particularly those governing data protection, patents and trade secret protection – that are relevant to biological products.

Both the United States' Hatch-Waxman Act and biosimilar regimes illustrate the importance of transparency in any regulatory scheme. Both innovator and generic companies need as much certainty as possible to allow them to make sound business decisions, often years in advance of product commercialization. The Hatch-Waxman Act's requirement that generic companies notify innovator companies of intent to challenge patents and encouragement of early patent suits promote both transparency (through notification) and certainty (through encouraging finality of patent issues). Similarly, the BPCIA requires notification of intent to challenge patents or intent to launch biosimilar products by follow-on companies, and provides mechanisms for early resolution of any patent suits that arise.¹³⁹ While the exact details differ from the Hatch-Waxman Act, the BPCIA also promotes transparency and certainty.

Transparency and certainty are beneficial to investment, and indeed necessary for long-term commitments such as those required in biotechnology. As NVCA reported to Congress during debates on a biosimilars pathway, venture capitalists "must have some certainty that the innovation they are backing will be protected."¹⁴⁰

We believe the recent experience of the United States, particularly the deliberations leading to the enactment of the BPCIA, provide insight into the necessary intellectual property infrastructure required to encourage discovery and development of new biological products. That infrastructure must:

- provide a minimum of 12 years of data protection for new biological products;

¹³⁹ PHS § 351(k), (l).

¹⁴⁰ Letter of Mark G. Heesen, NVCA, to Congresswoman Anna Eshoo & Congressman Joe Barton (May 16, 2008) at 1-2. As also noted, inadequate "data exclusivity for innovator products . . . would deter investment and undermine incentives for the development of innovative, new biotechnology drugs, impeding patient access to these lifesaving therapies." *Id.* at 2. NVCA also stressed the importance of "[t]imely resolution of patent disputes" and "notice requirements and exchanges of information" involving biosimilar products. *Id.* It was explained that "[s]uch mechanisms will serve to protect the intellectual property rights of innovative biotech companies and other third parties, including academic institutions, while providing certainty to the [follow-on biologics] manufacturer and avoiding patient confusion." *Id.*



- enable patent owners to identify infringement and assert patents relating to biological products, their uses, and their manufacture before regulatory approval is granted to market biosimilar products;
- provide adjustments to the term of patents covering biological products and their use and manufacture to compensate patent owners for delays in securing those patent rights, and to compensate them fairly for time lost during the regulatory approval process of biological products;
- grant patents on the full range of biotechnology innovation, whether in the form of new protein or nucleic acid sequences, host cells used to make proteins, or uses of the biological product to treat human disease; and
- ensure that trade secret information provided to a government authority to secure approval of a biological or biosimilar product is protected from disclosure to the public, and not improperly used by the regulatory authority to approve competitor applications.

BIO and its members believe a successful TPP Agreement will create an environment that promotes collaboration and innovation throughout the trans-Pacific region.