BIOLOGICS AND BIOSIMILARS: BALANCING INCENTIVES FOR INNOVATION

HEARING

BEFORE THE

SUBCOMMITTEE ON COURTS AND COMPETITION POLICY

OF THE

COMMITTEE ON THE JUDICIARY
HOUSE OF REPRESENTATIVES

ONE HUNDRED ELEVENTH CONGRESS

FIRST SESSION

JULY 14, 2009

Serial No. 111–73

Printed for the use of the Committee on the Judiciary

Available via the World Wide Web: http://judiciary.house.gov

U.S. GOVERNMENT PRINTING OFFICE

51–014 PDF WASHINGTON : 2010

For sale by the Superintendent of Documents, U.S. Government Printing Office
Internet: bookstore.gpo.gov Phone: toll free (866) 512–1800; DC area (202) 512–1800
Fax: (202) 512–2104 Mail: Stop IDCC, Washington, DC 20402–0001

COMMITTEE ON THE JUDICIARY

JOHN CONYERS, JR., Michigan, *Chairman*

HOWARD L. BERMAN, California
RICK BOUCHER, Virginia
JERROLD NADLER, New York
ROBERT C. "BOBBY" SCOTT, Virginia
MELVIN L. WATT, North Carolina
ZOE LOFGREN, California
SHEILA JACKSON LEE, Texas
MAXINE WATERS, California
WILLIAM D. DELAHUNT, Massachusetts
ROBERT WEXLER, Florida
STEVE COHEN, Tennessee
HENRY C. "HANK" JOHNSON, JR., Georgia
PEDRO PIERLUISI, Puerto Rico
MIKE QUIGLEY, Illinois
LUIS V. GUTIERREZ, Illinois
BRAD SHERMAN, California
TAMMY BALDWIN, Wisconsin
CHARLES A. GONZALEZ, Texas
ANTHONY D. WEINER, New York
ADAM B. SCHIFF, California
LINDA T. SANCHEZ, California
DEBBIE WASSERMAN SCHULTZ, Florida
DANIEL MAFFEI, New York

LAMAR SMITH, Texas
F. JAMES SENSENBRENNER, JR., Wisconsin
HOWARD COBLE, North Carolina
ELTON GALLEGLY, California
BOB GOODLATTE, Virginia
DANIEL E. LUNGREN, California
DARRELL E. ISSA, California
J. RANDY FORBES, Virginia
STEVE KING, Iowa
TRENT FRANKS, Arizona
LOUIE GOHMERT, Texas
JIM JORDAN, Ohio
TED POE, Texas
JASON CHAFFETZ, Utah
TOM ROONEY, Florida
GREGG HARPER, Mississippi

PERRY APELBAUM, *Majority Staff Director and Chief Counsel*
SEAN MCLAUGHLIN, *Minority Chief of Staff and General Counsel*

SUBCOMMITTEE ON COURTS AND COMPETITION POLICY

HENRY C. "HANK" JOHNSON, JR., Georgia, *Chairman*

JOHN CONYERS, JR., Michigan
RICK BOUCHER, Virginia
ROBERT WEXLER, Florida
CHARLES A. GONZALEZ, Texas
SHEILA JACKSON LEE, Texas
MELVIN L. WATT, North Carolina
BRAD SHERMAN, California
MIKE QUIGLEY, Illinois

HOWARD COBLE, North Carolina
JASON CHAFFETZ, Utah
BOB GOODLATTE, Virginia
F. JAMES SENSENBRENNER, JR., Wisconsin
DARRELL ISSA, California
GREGG HARPER, Mississippi

CHRISTAL SHEPPARD, *Chief Counsel*
BLAINE MERRITT, *Minority Counsel*

CONTENTS

JULY 14, 2009

Page

OPENING STATEMENTS

The Honorable Henry C. "Hank" Johnson, Jr., a Representative in Congress from the State of Georgia, and Chairman, Subcommittee on Courts and Competition Policy 1
The Honorable Howard Coble, a Representative in Congress from the State of North Carolina, and Ranking Member, Subcommittee on Courts and Competition Policy 2

WITNESSES

The Honorable Anna G. Eshoo, a Representative in Congress from the State of California
Oral Testimony 7
Prepared Statement 10
Mr. Bruce A. Leicher, Senior Vice President and General Counsel, Momenta Pharmaceuticals, Inc., Cambridge, MA
Oral Testimony 14
Prepared Statement 16
Mr. Jeffrey P. Kushan, on behalf of the Biotechnology Industry Organization (BIO), Woodrow Wilson School of Public and International Affairs, Princeton, NJ
Oral Testimony 38
Prepared Statement 40
Mr. Alex M. Brill, Research Fellow, American Enterprise Institute (AEI), Washington, DC
Oral Testimony 173
Prepared Statement 175
Mr. Jack W. Lasersohn, General Partner, Verticle Group, on behalf of National Venture Capital Association (NVCA), Arlington, VA
Oral Testimony 181
Prepared Statement 184
Mr. Larry McNeely, Healthcare Reform Advocate, U.S. Public Interest Research Groups (USPIRG), Washington, DC
Oral Testimony 189
Prepared Statement 191
Ms. Teresa Stanek Rea, President, American Intellectual Property Law Association (AIPLA), Washington, DC
Oral Testimony 196
Prepared Statement 198

LETTERS, STATEMENTS, ETC., SUBMITTED FOR THE HEARING

Prepared Statement of the Honorable Howard Coble, a Representative in Congress from the State of North Carolina, and Ranking Member, Subcommittee on Courts and Competition Policy 4
Prepared Statement of the California Healthcare Institute (CHI) submitted by the Honorable Darrell Issa, a Representative in Congress from the State of California, and Member, Subcommittee on Courts and Competition Policy 224

Page

Bloomberg Article submitted by the Honorable Darrell Issa, a Representative in Congress from the State of California, and Member, Subcommittee on Courts and Competition Policy 233

Bloomberg Article submitted by the Honorable Brad Sherman, a Representative in Congress from the State of California, and Member, Subcommittee on Courts and Competition Policy 239

APPENDIX

Material Submitted for the Hearing Record

Response to Post-Hearing Questions from Bruce A. Leicher, Senior Vice President and General Counsel, Momenta Pharmaceuticals, Inc., Cambridge, MA 244

Response to Post-Hearing Questions from Alex M. Brill, Research Fellow, American Enterprise Institute (AEI), Washington, DC 252

BIOLOGICS AND BIOSIMILARS: BALANCING INCENTIVES FOR INNOVATION

TUESDAY, JULY 14, 2009

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON COURTS AND
COMPETITION POLICY
COMMITTEE ON THE JUDICIARY,
Washington, DC.

The Subcommittee met, pursuant to notice, at 2:20 p.m., in room 2141, Rayburn House Office Building, the Honorable Henry C. "Hank" Johnson, Jr. (Chairman of the Subcommittee) presiding.

Present: Representatives Johnson, Gonzalez, Jackson Lee, Watt, Sherman, Issa, Goodlatte, and Coble.

Staff Present: (Majority) Christal Sheppard, Subcommittee Chief Counsel; Eric Garduno, Counsel; Rosalind Jackson, Professional Staff Member; (Minority) and Blaine Merritt, Counsel.

Mr. JOHNSON. This hearing of the Subcommittee on Courts and Competition Policy will now come to order.

Without objection, the Chair will be authorized to declare a recess of the hearing.

Under current law, generic versions of the chemical pharmaceutical products may be introduced through an expedited pathway that allows generic makers to rely on the safety and efficacy test data of an original Food-and-Drug-Administration-approved drug. This dramatically reduces the cost of entry for generics, which has translated into substantial savings to customers. The Congressional Budget Office has estimated that consumers save $8 billion to $10 billion a year, thanks to the price competition from generics.

There is, however, no equivalent statutory pathway for generic versions of biological pharmaceutical products, otherwise known as biosimilars. Congress has explored the creation of a generic pathway for biosimilars for some time, but it wasn't until this Congress that real momentum has built behind such a legislative endeavor. This is in large part due to the effort by Congress and the Obama administration to pass comprehensive health care reform. Many believe that establishing a pathway for biosimilars will contribute to our efforts to reduce the cost of health care.

Creation of a pathway for biosimilars has been a contentious issue. Much of the debate concerning such a pathway revolves around whether the science is perfected enough to determine if a biosimilar that relies on an innovator's test data will have the same health benefits as the innovator drug without additional health risks. Additional concerns center on the intellectual property

protections afforded drug innovators and how the nature of those protections will impact competition, future biotechnology industry investment and the cost of biological pharmaceutical products.

It is, without a doubt, that the development of new biologics is an expensive endeavor. Estimates put average development costs as much as $1.37 billion. It is also without a doubt that the cost of pharmaceutical products, and in particular biologics, is huge. In 2007, pharmaceutical expenditures accounted for $231.3 billion in health care costs, and biologics represented $40.3 billion of this total.

The question before us today is how to frame the intellectual property protections in a pathway for biosimilars that incentivizes the extraordinary investment required to develop new biologics but does not discourage biosimilar introduction.

I look forward to our hearing with the distinguished witnesses that we have on board who will comment on whether there should be a long data exclusivity period that significantly delays biosimilar competition, whether biotechnology patents are broad enough to apply to biosimilar products and processes, and the extent to which other factors provide market-entry barriers that will limit biosimilar entry and thereby protect innovators.

I now recognize my colleague, Mr. Howard Coble, the distinguished Ranking Member of the Subcommittee on Courts and Competition Policy for his opening remarks.

Mr. COBLE. Thank you, Mr. Chairman, and I thank you for having called the hearing which addresses an important health care issue and directly affects subject matter that is a portion of the Judiciary Committee's jurisdiction.

Mr. Chairman, I will try not to be too verbose, but this subject is very detailed and very complex; perhaps not so detailed and complex to the scientifically adept, but I belong to the scientifically inept group, and to me, it is very complex.

The Hatch-Waxman Act, which is almost a quarter century old, gave birth to the generic chemical drug industry, as we all know. By most accounts, it has worked well by balancing the interests of brand manufacturers, generic companies, and patients. It has generated greater price competition in the pharmaceutical industry without destroying the incentive for brands to conduct further research and roll out new products that benefit patients worldwide.

In recent years, Mr. Chairman, legislators and other health care experts have contemplated the creation of a similar legislative pathway for a generic biologics industry. This discussion not only resurrects some of the same issues confronting Congress during consideration of Hatch-Waxman, it also invites debate over the wisdom of using Hatch-Waxman as an appropriate template for biosimilars.

As I said at the outset, I am no expert in the fields of biology, chemistry, or recombinant DNA, but I do understand the basic difference between chemical pharmaceuticals and biologics.

Chemical drugs are usually produced in pill form. They are chemically synthesized and comprised of small molecules. Compared to biologics, chemical pharmaceuticals are far easier to manufacture and replicate.

Biologics are made, as we know, from living organisms. They are normally comprised of protein and are increasingly a part of recombinant DNA research and production. Their characteristic properties include a high molecular weight, varying levels of hard-to-remove biological impurities, and a high degree of sensitivity to environmental conditions. The manufacturing process is therefore critical to the final product. This complexity means one cannot guarantee that reproduction of a biological drug results in an exact duplicate.

This is not the case for chemical pharmaceuticals regulated under Hatch-Waxman since it is chemically identical to the innovator drug. That is why the term generic biologic is technically inaccurate, it seems to me. Biosimilar or follow-on biologic would be preferred.

In our quest to develop a legislative pathway for biosimilars, we must keep these differences in mind. While the Judiciary Committee's jurisdiction does not include public health and related safety issues, all Members, whatever their Committee assignments, cannot discharge the importance of protecting patients. Any bill we end up supporting cannot sacrifice public safety on the alter of potential cost savings.

I have some more to say, Mr. Chairman, but in the interest of time, I would ask unanimous consent to have my entire statement put into the record, and we hope that we will have a balanced and talented roster of witnesses, which we will have, who will add to our understanding of this complex subject.

I look forward to participating and thank you again, Mr. Chairman, for having called the hearing.

Mr. JOHNSON. Without objection, that will be done, Mr. Coble.

I thank the gentleman for his statement.

[The prepared statement of Mr. Coble follows:]

PREPARED STATEMENT OF THE HONORABLE HOWARD COBLE, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NORTH CAROLINA, AND RANKING MEMBER, SUBCOMMITTEE ON COURTS AND COMPETITION POLICY

HEARING STATEMENT OF THE HONORABLE HOWARD COBLE SUBCOMMITTEE ON COURTS AND COMPETITION POLICY "BIOLOGICS AND BIOSIMILARS: BALANCING INCENTIVES FOR INNOVATORS" JULY 14, 2009

Thank you Mr. Chairman. I appreciate your calling this hearing today, which addresses an important healthcare issue and directly affects subject matter that is part of the Judiciary Committee's jurisdiction.

The Hatch-Waxman Act, which is almost a quarter-century old, gave birth to the generic chemical drug industry. By most accounts, it has worked well by balancing the interests of brand manufacturers, generic companies, and patients. It has generated greater price competition in the pharmaceutical industry without destroying the incentive for brands to conduct further research and roll-out new products that benefit patients worldwide.

In recent years, legislators and other healthcare experts have contemplated the creation of a similar legislative pathway for a "generic" biologics industry. This discussion not only resurrects some of the same issues confronting Congress during consideration of Hatch-Waxman, it also invites debate over the wisdom of using Hatch-Waxman as an appropriate template for biosimilars.

Mr. Chairman, law school was created for non-scientists such as yours truly. And while I am no expert in the fields of biology, chemistry, or recombinant DNA, I understand the basic difference between chemical pharmaceuticals and biologics. Chemical drugs are usually produced in pill form. They are chemically-synthesized and comprised of small molecules. Compared to biologics, chemical pharmaceuticals are far easier to manufacture and replicate.

Biologics are made from living organisms. They are normally composed of protein, and are increasingly a part of recombinant DNA research and production. Their characteristic properties include a high molecular weight, varying levels of hard-to-remove biological impurities, and a high degree of sensitivity to environmental conditions. The manufacturing process is therefore critical to the final product.

This complexity means one cannot guarantee that reproduction of a biological drug results in an exact duplicate. This isn't the case for a chemical pharmaceutical regulated under Hatch-Waxman, since it is chemically identical to the innovator drug. That's why the term "generic" biologic is technically inaccurate; "biosimilar" or "follow-on biologic" is preferred.

In our quest to develop a legislative pathway for biosimilars, we must keep these differences in mind. While the Judiciary Committee's jurisdiction does not include public health and related safety issues, all Members – whatever their Committee assignments – cannot disregard the importance of protecting patients. Any bill we end up supporting cannot sacrifice public safety on the altar of potential cost savings.

Nor can we disregard the importance of creating and maintaining appropriate incentives for innovator companies to do their jobs. As much as it costs a chemical pharmaceutical company to bring a state-of-the-art drug to market – about $800 million, give or take – it costs even more for a biotech firm to do the same – in excess of a billion dollars.

Our Committee retains jurisdiction over the Patent Act, which provides the greatest incentive available for pharmaceutical companies to raise capital, immerse themselves in R&D, and produce drugs – chemical and biological – that enable patients to enjoy longer and healthier lives. It is imperative that any legislation creating a biosimilar pathway contain reasonable patent and exclusivity protections. Without these incentives, the core research and development won't get done. This would cripple the industry and produce an even worse outcome for patients awaiting the next generation of biological therapeutics.

That concludes my statement, Mr. Chairman. We have a balanced and talented roster of witnesses who will add to our understanding of this complex subject. I look forward to participating, and thank you again for calling the hearing.

###

Mr. JOHNSON. Without objection, other Members' opening statements as well will be included in the record.

I am now pleased to introduce the witness for the first panel of today's hearing. Our first panel will feature Congresswoman Anna Eshoo.

Representative Eshoo, you are the top dog on this panel, there is no question about it.

Ms. ESHOO. Wait until I tell my children.

Mr. JOHNSON. You may want to put this in the new book that you are coming out with also.

Representative Eshoo has served in Congress since 1993 and represents California's 14th Congressional District, which includes large portions of Silicon Valley. She serves on the House Energy and Commerce Committee and on the House Permanent Select Committee on Intelligence. In addition, Representative Eshoo co-chairs the Congressional High-Tech Caucus and the House Medical Technology Caucus and serves as Vice Chair of the 21st Century Health Care Caucus.

Representative Eshoo, please proceed with your testimony.

TESTIMONY OF THE HONORABLE ANNA G. ESHOO, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CALIFORNIA

Ms. ESHOO. Good afternoon, Mr. Chairman, and thank you very much for allowing me to be here today to give testimony on the issue of biosimilars before this distinguished Subcommittee.

Ranking Member, Mr. Coble, a good and long-time friend, to my friends Congressman Gonzales and Congressman Watt, thank you for being here.

This is a very important, yet complex, discussion, to develop a regulatory pathway for biosimilars that, as Mr. Coble and others have said, protects patients—protects patients, that must be our number one goal—while balancing incentives for innovation.

The field of biotechnology is the future of medicine. We are just beginning to scratch the service of the potential to harness the extraordinary power of biology and the astounding natural processes which occur in the human body, in animals, and in other living organisms to advance breakthrough medical discoveries and treatments.

This vital future, in my view and I am sure yours, must advance. But the cost of biologic treatments are very expensive, and I think the time has come to develop a pathway, as the Congress did many years ago and was mentioned by the Ranking Member, to develop a pathway for biosimilar products in our country the way we did for pharmaceutical compounds.

Now, what exactly do I mean when I say develop a pathway for biosimilars? In 1984, the Drug Price Competition and Patent Term Restoration Act, better known as the Hatch-Waxman Act, ushered in a new era of competition and cheaper drugs for traditional pharmaceuticals, called compounds. It is now appropriate for us to create a pathway for follow-on versions of biologics.

But biologics and traditional drugs are fundamentally different, and they require different legal and scientific frameworks. First,

we need to understand the differences between biologics and traditional drugs.

Many of us take a prescription or an over-the-counter drug frequently. Each time we reach for a pill, we expect the same safety and efficacy, whether we are using a brand name or a generic drug.

Small molecule chemical compounds of traditional drugs are ideal for replication as generics. These products have well-defined structures that can be thoroughly characterized and copied, and generic drugs are chemically identical, chemically identical, to the brand name products they copy. Doctors and patients can expect the generics will have the same properties, the same efficacy and the same safety characteristics as the product that they copied.

Biological products are fundamentally different. A biologic is a large complex molecule which is grown in living cells, in living systems, such as a microorganism, a plant, or an animal cell. The resulting protein is unique to the cell lines and the specific processes that are used to produce it, and even slight differences, even the slightest differences, in the manufacturing of a biologic can alter its nature. And that will have an effect on the patient.

As a result, biologics are difficult and sometimes impossible to characterize, and laboratory analysis of the finished product is insufficient to ensure its safety and efficacy.

I brought a chart. They say a picture is worth a thousand words. You see on the stand here the chart. These are both breast cancer treatments. The top is Tamoxifen. That is a small-molecule compound. You can see its simplicity. The picture says it all.

Below it is Herceptin, and that is a biologic. Look at the complexity of that biologic.

Even if a biosimilar is proven to be safe and effective, it will likely still have different properties than the original innovative product. There may be differences in dosing, different side effects or safety profiles, and differences in effectiveness for certain diseases or for different patient groups.

Biologics are expensive, and they are risky to develop. A recently released study sponsored by the National Venture Capital Association analyzed the relative cost for investors in biotechnology and found that the cost of capital for startup biotech companies is more than double the costs that other companies must pay. These costs stem from long developmental timelines of typically 10 years or more and extraordinary levels of risk.

Fewer than 1 percent of biologics make it to the market. Imagine that. Fewer than 1 percent. And the large amounts of capital required to support this development are at the other end of the scale.

So, to preserve the existing incentives for investment and innovation, the Pathway for Biosimilars Act provides a data-exclusivity period equivalent to patent protections for small molecules. The Congressional Budget Office has determined that 11.5 years is the average length of time that drugs are marketed under patent. In other words, innovative drugs and biologics typically stay on the market for about 12 years before facing competition. My legislation maintains this level of protection for biologics.

Now, today innovators are assured that the costly clinical trial results and data that they develop during their approval process

cannot be used by competitors to secure approval and enter the market even if their patents do not prevent entry. In effect, innovators today have infinite data protection, which allows for competition but doesn't permit free-riding on their data.

I am proposing to allow competitors access to their data and a shortcut into the market, but we preserve through the legislation the existing incentives for innovators by maintaining a 12-year period of exclusivity of concurrent data protection as a backstop to existing patent protections.

In order to protect the rights of all parties and ensure that all patent disputes involving a biosimilar are resolved before, and I emphasis the word before, the expiration of the data-exclusivity period, H.R. 1548 also establishes a simple, streamlined patent resolution process.

This process would take place within a short window of time, roughly 6 to 8 months after the biosimilar application has been filed with the FDA. It will help ensure that litigation surrounding relevant patents will be resolved expeditiously and prior to the launch of the biosimilar product, providing certainty to the applicant, the reference product manufacturer, and the public at large.

Unlike any other proposal, our legislation also preserves the ability of third-party patent holders, such as universities and medical centers, to defend their patents.

Once a biosimilar application is accepted by the FDA, the agency will publish a notice identifying the reference product and a designated agent for the biosimilar applicant. After an exchange of information to identify the relevant patents at issue, the applicant can decide to challenge any patents' validity or applicability. All information exchanged as part of this procedure will be maintained in strict confidence and used solely for the purpose of identifying patents relevant to the biosimilar product. The patent owner will then have 2 months to decide whether to enforce the patent, and if the patent owner's case is successful in court, the final approval of the application will be deferred until the patent expires.

So this legislation I think sets forth a straightforward, scientifically-based process for an expedited approval of new biologics based on innovative products already on the market, with patient safety coming first. This new pathway will promote competition and lower prices and, most importantly again, protect patients and give them the safe and the effective treatments and I might say the hope that this represents to really conquer the most dreaded diseases that still plague humankind, and all through the scrutiny and testing by the FDA.

The legislation enjoys today 130 bipartisan cosponsors, many on this Committee, the House Judiciary Committee, and it is known as the Kennedy Bill in the Senate. Last evening, the Health Subcommittee in the Senate voted the bill out 16-7, which I think is really quite a victory for the legislation. After all, it is complicated and enormously complex, as well as enormously important.

I also want to note that the bill is endorsed by the Association of American Universities, the National Venture Capital Association, the Biotechnology Industry Organization, the Governors of four States, and a wide array of patient and industry groups.

Mr. Chairman and distinguished Members of the Subcommittee, I appreciate being welcomed here today. It is an honor to testify before my House colleagues.

I thank you, and I stand willing to answer questions, should you have any.

[The prepared statement of Ms. Eshoo follows:]

PREPARED STATEMENT OF THE HONORABLE ANNA G. ESHOO, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CALIFORNIA

Statement of Congresswoman Anna G. Eshoo
House Committee on the Judiciary
Subcommittee on Courts and Competition Policy
Hearing on "Biologics and Biosimilars: Balancing Incentives for Innovation
July 14, 2009

Thank you Mr. Chairman. I'm pleased to be here today to discuss this important issue – developing a regulatory pathway for biosimilars that protects patients while balancing incentives for innovation.

The field of biotechnology is the future of medicine – we're just beginning to scratch the surface of the potential to harness the extraordinary power of biology and the astounding natural processes which occur in the human body, in animals, and in other living organisms to advance breakthrough medical discoveries and treatments.

This vital future must advance, but the costs of biologic treatments are very high and I believe the time has come to develop a pathway for biosimilar products in our country.

What, exactly, do I mean when I say "develop a pathway" for biosimilars?

In 1984 the *Drug Price Competition and Patent Term Restoration Act*, otherwise known as 'Hatch-Waxman,' ushered in a new era of competition and cheaper drugs for traditional pharmaceuticals – compounds.

It's now appropriate to create a pathway for follow-on versions of biologics. However, biologics and traditional drugs are fundamentally different and require different legal and scientific frameworks.

First, we need to understand the differences between biologics and traditional drugs.

Many of us take a prescription or over-the-counter drug frequently. Each time we reach for a pill, we expect the same safety and effectiveness, whether using a brand name or generic drug.

Small-molecule chemical compounds of traditional drugs are ideal for replication as generics. These products have well-defined structures that can be thoroughly characterized and copied, and generic drugs are chemically identical to the reference products they copy. Doctors and patients can expect that generics will have the same properties, the same efficacy, and the same safety characteristics as the innovative product they copy.

Biological products are fundamentally different. A biologic is a large, complex molecule, which is 'grown' in living systems such as a microorganism, a plant or animal cell. The resulting protein is unique to the cell lines and the specific process used to produce it, and even slight differences in the manufacturing of a biologic can alter its nature. As a result,

biologics are difficult, sometimes impossible to characterize, and laboratory analysis of the finished product is insufficient to ensure its safety and efficacy. *[SEE DISPLAY]*

Even if a biosimilar is proven to be safe and effective, it will likely still have different properties than the original innovative product. There may be differences in dosing, different side effects or safety profiles, and differences in effectiveness for certain diseases or patient groups.

Biologics are expensive and risky to develop. A recently released study sponsored by the National Venture Capital Association analyzed the relative costs for investors in biotechnology and found that the 'cost of capital' for start-up biotech companies is more than double the costs that other companies must pay. These costs stem from long developmental timelines of typically 10 years or more, extraordinary levels of risk (fewer than 1% of biologics make it to market), and the large amounts of capital required to support development.

To preserve existing incentives for investment and innovation the *Pathway for Biosimilars Act* provides a data exclusivity period equivalent to patent protections for small molecules. The Congressional Budget Office has determined that 11.5 years is the average length of time that drugs are marketed under patent. In other words, innovative drugs and biologics typically stay on the market for about 12 years before facing competition. My legislation maintains this level of protection for biologics.

Today innovators are assured that the costly clinical trial results and data that they develop during their approval process cannot be used by competitors to secure approval and enter the market, even if their patents do not prevent entry. In effect innovators now have 'infinite' data protection, which allows for competition but doesn't permit 'free riding' on their data.

I'm proposing to allow competitors access to their data and a shortcut into the market, but also preserving the existing incentives for innovators by maintaining a 12-year period of concurrent data protection as a 'backstop' to existing patent protections.

In order to protect the rights of all parties and ensure that all patent disputes involving a biosimilar are resolved before the expiration of the data exclusivity period, H.R. 1548 also establishes a simple, streamlined patent resolution process.

This process would take place within a short window of time – roughly 6-8 months after the biosimilar application has been filed with the FDA. It will help ensure that litigation surrounding relevant patents will be resolved expeditiously and prior to the launch of the biosimilar product, providing certainty to the applicant, the reference product manufacturer, and the public at large.

Unlike any other proposal, our legislation also preserves the ability of third-party patent holders such as universities and medical centers to defend their patents.

Once a biosimilar application is accepted by the FDA, the agency will publish a notice identifying the reference product and a designated agent for the biosimilar applicant. After an exchange of information to identify the relevant patents at issue, the applicant can decide to challenge any patent's validity or applicability. All information exchanged as part of this procedure must be maintained in strict confidence and used solely for the purpose of identifying patents relevant to the biosimilar product.

The patent owner will then have two months to decide whether to enforce the patent. If the patent owner's case is successful in court, the final approval of the application will be deferred until the patent expires.

The *Pathway for Biosimilars Act* sets forth a straightforward, scientifically based process for expedited approval of new biologics based on innovative products already on the market. This new biosimilars approval pathway will promote competition and lower prices, but also ensure that patients are given safe and effective treatments that have been subjected to thorough scrutiny and testing by the FDA.

I'm pleased that Congressmen Inslee, Barton and I have been joined by a diverse group of 125 bipartisan cosponsors in the House.

I also want to note that my bill is the only legislation endorsed by the Association of American Universities, the National Venture Capital Association, the Biotechnology Industry Organization, the governors of 4 states, and a wide array of patient and industry groups.

This broad support is extremely encouraging, and I look forward to working finally addressing this critical issue in the 111th Congress.

Thank you again for inviting me to testify today.

Mr. JOHNSON. Thank you, Madam Congresswoman. It is our pleasure to host you today.

Without objection, your written statement will be placed into the record.

I now call for the second panel to take their seats. Thank you.

I might add here also that Representative Waxman has introduced a similar bill, and he was offered the opportunity to come

today, but he is very much tied up with the health care issue, so he could not make it.

Ladies and gentleman, our second panel will begin with Bruce Leicher. Mr. Leicher is senior vice president and general counsel at Momenta Pharmaceuticals, which is an innovative biotechnology company engaged the development of novel and follow-on biologics. Prior to joining Momenta, Mr. Leicher served in leadership capacities in a number of other biotechnology companies.

Mr. Leicher also served as a law clerk to the Honorable Thomas F. Hogan in the United States District Court for the District of Columbia.

Welcome, sir.

Next will be Jeffrey Kushan, who is a partner with Sidley Austin and serves as the Chair of the firm's D.C. Patent Group. Mr. Kushan specializes in Hatch-Waxman and biotechnology patent litigation, patent appeals, and complex patent administrative proceedings. He represents several biotechnology clients including, Genentech. Today he is representing the Biotechnology Industry Organization.

Welcome, sir.

Following will be Mr. Alex Brill, who is a research fellow at the American Enterprise Institute and CEO of the consulting firm Matrix Global Advisers. He is former chief economist and senior adviser to the House Committee on Ways and Means, and has served on the staff of the White House Council of Economic Advisers. His expertise lies in U.S. Federal tax policy, budget, trade and health care policy.

Welcome, sir.

Mr. Jack Lasersohn will be our next witness, who is a founding general partner of the Verticle Group, one of the Nation's oldest and most successful venture capital firms, which focuses on health care venture capital investments. Mr. Lasersohn has served on the board of directors of 40 public and private companies and currently serves on the board of directors of the National Venture Capital Association, which he is representing today. He is also the named inventor on six U.S. patents.

Welcome, sir.

Next will be Mr. Larry McNeely, who is a health care advocate for the United States Public Interest Research Groups, otherwise known as USPIRG. Mr. McNeely advocates for legislation that will tame rising health care costs and offer consumers better choices in the health care marketplace. Prior to joining USPIRG, Mr. McNeely dedicated nearly a decade of his life to working as a community activist, political organizer, and union representative.

Welcome, sir.

Last will be Ms. Teresa Rea, who is a partner in the Washington, D.C., office of Crowell and Moring and is a member of the firm's Intellectual Property Section. Her work there focuses on complex patent litigation, prosecution and procurement. Ms. Rea is also a registered pharmacist in the State of Michigan and worked for years as a hospital pharmacist. Ms. Rea is president of the American Intellectual Property Law Association and is representing the association today.

Welcome, ma'am.

Thank you all for your willingness to participate in today's hearing. Without objection, your statements will be placed into the record, and we will ask that you limit your oral remarks to 5 minutes.

You will note that we have a lighting system that starts with a green light. At 4 minutes, it turns yellow, and then red at 5. After each witness has presented his or her testimony, Subcommittee Members will be permitted to ask questions subject to the 5-minute rule.

Mr. Leicher, would you please commence with your testimony, sir.

TESTIMONY OF BRUCE A. LEICHER, SENIOR VICE PRESIDENT AND GENERAL COUNSEL, MOMENTA PHARMACEUTICALS, INC., CAMBRIDGE, MA

Mr. LEICHER. Thank you, Mr. Chairman.

Good afternoon, Mr. Chairman, and Members of the Committee. Thank you for the opportunity to participate today. I am Bruce Leicher, senior vice president and general counsel at Momenta Pharmaceuticals. I believe I offer a unique perspective.

Serving as counsel to biotech companies for almost 20 years, I have worked on the development and launch of some of the earliest breakthrough products, including EPO, recombinant factor VIII and IX, and many others. I have participated in numerous financings and collaborative research deals between biotech and large pharma. I have served on product development committees that seek to balance risk versus reward. I have experienced the joy of meeting parents whose children's lives have been transformed by biologics. I have also participated in many of the seminal biotech patent cases that determined market exclusivity and biologic patent strength. I understand biotechnology's potential to save lives.

Momenta also offers a unique perspective in this debate. We are a biotech company that develops both generic and novel therapeutics. We use innovative technology to characterize or better understand the picture that Congresswoman Eshoo presented earlier, and we use this technology to control the manufacture of complex drugs and potentially biologics. We are seeking a balanced approach. We believe Waxman-Deal offers that approach, and I will explain why Eshoo-Barton does not.

I would like to address three key points. First, the law should let science drive both brand and biogeneric innovation so that we can develop breakthrough therapies and affordable biologics to patients. Second, we must not use data exclusivity and other barriers to reward inefficient and non-innovative R&D.

Third, thee patent clearance process should promote health care reform through timely access to affordable products. It must be transparent, efficient and respectful of both brand and biogeneric intellectual property. Each of these objectives we believe are best served by the Waxman-Deal bill.

Patents drive innovation. They drive speed to market and already favor biologics. A complex web of patent rights provides substantial protection for each biologic, its genetic code, its biologic pathway, the technology it uses, its manufacture and formulation. While some argue that individual patent claims may be somewhat

less certain, the aggregate of this web provides many multiple defenses.

Notably, biologics generally have more market exclusivity during their brand life than drugs. Add to this 5 years of patent extension, and I have to ask, why should biologics need more data exclusivity than drugs to recoup investment?

Beyond that, brand innovation and competitiveness are motivated by limited data exclusivity as well. Extended data exclusivity will attract capital, but the wrong kind. It will promote low-risk, non-innovative development, and make biotech in the long run far less competitive. Biotech funding should be directed to innovative, patentable new cures. Or is our goal to offer brand exclusivity profit for me-too products?

Biogeneric innovation and safer biologics also need limited data exclusivity to attract capital. Momenta's first project was to characterize low molecular weight Heparin, a biologic-like drug. Having an ANDA pathway available made it possible to finance Momenta and develop its innovative technology.

We thoroughly characterized Heparin, including its potential for immunogenicity. Notably brand companies assert that this is not possible, yet continue to market the products. This matters today and tomorrow.

We are applying these tools to develop the first biogenerics and to enhance patient safety. Last year, Momenta used these tools to assist MIT and other academic centers, in collaboration with the FDA, to identify the contaminant in Chinese-sourced Heparin. Because of the ANDA incentive and limited data exclusivity, we were able to do the work and knew what should and should not be in the Heparin product.

So let me sum up. The wisdom of Hatch-Waxman was that it did not dictate investment decisions. Rather it put guardrails and incentives in place that reward innovation and assured affordability at a time when products matured. Breakthrough innovation was aligned with return on investment, and biotech flourished in the 1980's and 1990's, creating high-paying jobs and critical new cures.

As the first generation of breakthrough biologics emerges from patent protection, will we learn from this experience?

Will we support legislation like Waxman-Deal that uses the competitive incentive of biogenerics to promote long-term competitive advantage, global leadership and job growth? Or will we ignore this wisdom and allow R&D investment to veer off track?

Will we create a fertile environment for biologics companies to invest in the hard science, to understand and make biologics safer and better, and will we let the patent system drive efficiency and high rewards for breakthrough biologics as biogenerics provide affordable access to mature products?

As I see it, this is exactly what health care reform is all about.

Thank you for this opportunity, and I would be pleased to answer any questions.

[The prepared statement of Mr. Leicher follows:]

STATEMENT
OF

BRUCE A. LEICHER

SR. VICE PRESIDENT AND GENERAL COUNSEL

MOMENTA PHARMACEUTICALS, INC.

BEFORE THE HOUSE OF REPRESENTATIVES

SUBCOMMITTEE ON THE COURTS AND COMPETITION POLICY

OF THE

COMMITTEE OF THE JUDICIARY

HEARING: BIOLOGICS AND BIOSIMILARS: BALANCING INCENTIVES FOR INNOVATION

JULY 14, 2009

Good afternoon Mr. Chairman and Members of the Committee. Thank you for the opportunity to participate today. I am Bruce Leicher, Senior Vice President and General Counsel at Momenta Pharmaceuticals, a biotechnology company with a breakthrough technology platform for characterizing complex therapeutics and biologics. [1] Momenta's unique capabilities apply to both generic and novel biologics, which means our scientists are exploring both follow-on and novel development by thoroughly characterizing and determining the structure-function relationship of biologics so that their side effects and efficacy can be better understood, controlled and improved.

I am pleased to discuss the important intellectual property issues facing biogeneric and biosimilar products[2]. The differences between the Waxman-Deal (H.R. 1427) and Eshoo-Barton (H.R. 1548) bills[3] are critical, and the choices we make today will drive the long-term competitiveness, growth, and health of our biotechnology industry for many years to come. I believe I can offer a unique perspective with respect to both the need for and the protection of intellectual property as it relates to biological products. Serving as counsel to biotech companies for almost 20 years, I have been involved in the development and commercial launch of some of the earliest breakthrough products, including EPO, recombinant factor VIII and IX, Interleukin-11 and 12 and other biologics. I also have participated in numerous

---

[1] A brief summary of Momenta Pharmaceuticals is attached as Exhibit A.

[2] We use "biogenerics" to refer to interchangeable generic biologics that have been sufficiently characterized or studied to be interchangeable and substitutable, and "biosimilars" refer to follow-on biologics that are similar but not interchangeable and substitutable.

[3] Although not the subject of this hearing, we note that the Waxman-Deal bill as well as the companion Schumer-Vitter-Brown-Collins (S. 726) bill in the Senate contain scientific and regulatory provisions that will promote the development of safe, pure and potent biogenerics and biosimilars while incentivizing innovation by brands and biogenerics alike. While the Kennedy HELP (S. 1695 2007) bill has excessive data exclusivity in our view, its regulatory, scientific and patent clearance provisions would also create the right incentives by allowing the FDA to consider applications based on real data from the date of enactment. It, like Waxman-Deal, lets science drive the process. Additional challenges to innovation with the Eshoo-Barton bill are that it mandates clinical trials, establishes mandatory guidance document requirements, and imposes lengthy waiting periods for filing an abbreviated application. These hurdles would discourage investment in biogeneric enabling technology because one could not obtain approval within a period of time that would warrant the cost of the capital investment.

financings and collaborative research deals between emerging biotechnology companies and large pharmaceutical companies. I have served on product development committees that seek to balance risk vs. reward. I have experienced the joy of meeting parents whose children's lives have been transformed by these products. I have also participated in many of the seminal biotech patent cases that determined marketing exclusivity and the strength biologics patents offer. Last fall, I participated in the FTC Roundtable: "Emerging Health Care and Competition and Consumer Issues" that resulted in the June 2009 FTC Report on follow-on biologic drug competition.[4] All of these activities imprinted me with a strong sense of biotechnology's contribution to society, how challenging R&D can be, and how rewarding the breakthroughs can be. Our goal should always be to bring safe, effective, and potentially life-saving products to patients and to prime the pump for future discoveries and innovation. And fundamental to achieving and sustaining this mission is the need to provide timely access to affordable medicines, for even the best of medicines are of no value if their high cost puts them out of reach for patients who need them.

I would like to briefly mention three key points that I believe must be addressed in any biogeneric legislation to make it workable and to ensure that it provides the means of achieving the desired goal.

1. The law should include intellectual property features that drive <u>both</u> brand innovation and biogeneric innovation to assure future growth, global leadership and long term biotech competitiveness.

2. The law should avoid needless intellectual property features that erect barriers to generic competition – a proven driver of new drug innovation -- and thereby create an undesired incentive for inefficient and non-innovative R&D spending.

---

[4] A copy of Momenta's comments to the FTC is attached as Exhibit B.

3. The law should promote timely access to affordable biogenerics and biosimilars by implementing a patent clearance process that is transparent, efficient and respects the intellectual property rights of both brand and biogeneric companies alike.

These three tenets are critical to establishing a biogeneric approval process that maintains a balance between innovation and access. Because Momenta is both a novel therapeutics company and a biogeneric company, we can attest to the need for such a balance. Moreover, we believe this balance can only be achieved by enacting legislation that takes the Waxman-Deal approach to intellectual property and market exclusivity.

1. Patents are a proven force for driving innovation and speed to market. But more importantly, patents provide at least as much if not more market exclusivity to biologics than drugs and an opportunity to earn a return on investment. Biologics also have far less brand to brand competition during brand life than small molecule drugs. As noted by the FTC, biotechnology products benefit from a complex web of patent rights, including, but not limited to, covering the product, its genetic code, methods to regulate the biologic pathway in which the product is involved, the technology on which it is based, the manufacturing and formulation approach used, and the use of patentable biomarkers for dosing. While some will argue that individual patent claims may be somewhat less certain, the aggregate complexity provides a strong defense in the marketplace. This has been the experience in brand to brand competition and should be expected to continue as biogenerics emerge. Current regulations under Hatch-Waxman already provide patent term extension for up to 5 years to compensate for regulatory approval delays, and this applies to both chemical and biologic drugs. So if aggregate patent protection provides greater market exclusivity, then why should we be considering significantly longer data exclusivity periods for biologics than those for small molecules under Hatch-Waxman?

2. Aside from robust patent protection, there is a far more important reason to appropriately limit data exclusivity: to incentivize innovation and future competitiveness. Consider the effect of extended data exclusivity on R&D

investment decisions. The issue is not whether data exclusivity will trigger substantial R&D investment, but rather what kind of R&D it will promote. Will funding be directed to innovative, patentable discovery of new cures -- the hallmark of biotechnology companies in the 1980s and 1990s? Or, will it instead reward de-risking of product development portfolios by offering exclusivity for the development of non-innovative or "me too" products? From an investment perspective, financial investors are agnostic to the degree of medical need and will certainly drive us toward the lower risk, higher reward development that have extended data exclusivity. By extending exclusivity beyond patent life, we put truly new innovative R&D further at risk, which will delay urgently needed efforts to discover cures for so many unmet needs.

3. Now let's discuss biogeneric innovation and safety. Consider Momenta's experience. Without a biogeneric pathway, Momenta's first application of its technology was to characterize low molecular weight heparin, a biologic-like drug that is regulated under the ANDA pathway. Having an ANDA pathway available made it possible for Momenta to obtain financing and develop its innovative technology to thoroughly characterize the structure and better understand structure-function relationships of heparin, including its potential for immunogenicity. Notably, brand companies assert that this degree of product characterization and understanding is not possible, while continuing to market these products. Having developed the tools for understanding heparin, we are now able to use our technology to understand biologics and develop biogenerics as well. But perhaps most importantly, our technology platform has already contributed to the safety of heparin. Last year, Momenta used its tools to assist MIT and other academic centers in collaboration with the FDA to identify the contaminant in Chinese heparin precisely because it had thoroughly characterized heparin for an ANDA and knew what should and should not be in the product. Thus, biogeneric innovation can play a key role in improving quality control and assuring patient safety. If we and others are barred by data exclusivity or other barriers in the legislation from using our technology, then our opportunity to finance this kind of innovation will be put at risk.

Innovation on the brand and generic side, not just affordability, was the wisdom of the original Hatch-Waxman legislation. Despite claims that Hatch-Waxman would end pharmaceutical innovation, the opposite unfolded, as the biotech industry was launched, as noted by the FTC. As generic products replace mature brands, brand companies are incented to invest in innovative, patentable programs to fill their pipelines. In the absence of generic products, brand companies may find it move economically attractive to de-risk their portfolios because they will not have to compete with generic priced products.

Our concern with Eshoo-Barton bill is that it would do exactly that— namely that it would deter true new drug innovation. Ironically, this would be the complete opposite effect than what supporters of the bill hope to achieve.

1. For starters, Eshoo-Barton creates a complex, lengthy patent clearance process that only begins 3 years before the end of a lengthy data exclusivity period. Because this would not provide sufficient time to complete litigation, it would extend biologic entry well beyond the 12-14 years data exclusivity period in the bill.

2. Unlike Waxman-Deal, Eshoo-Barton includes the entire complex web of biologic patent rights in the clearance process, even if they are not controlled by the brand company. This could double the time and expense for the litigation, including for the courts, and unnecessarily increase the cost of biologics. Waxman-Deal properly limits the litigation to the patents controlled by the brand company. More importantly, patent clearance can be initiated when the abbreviated application is filed by the FDA, providing ample time for litigation before the expiration of the patent rights or data exclusivity.

3. Finally, Eshoo-Barton mandates disclosure of critical confidential information that is not related to proving infringement in the patent clearance process. Just as a brand company is not obligated to disclose its confidential information at the FDA, neither should a biogenerics company, lest we discourage biogeneric

innovation. Hatch-Waxman limited disclosure of confidential information to that needed to determine infringement which properly balanced these interests.

Mr. Chairman, as you and the Committee deliberate over the important issue of establishing a pathway for the approval of biogenerics and biosimilars, you will hear that biologics are complex and generics cannot be safely manufactured. Our experience teaches otherwise.

The wisdom of Hatch-Waxman was that it did not dictate investment decisions; rather it put guardrails or incentives in place that rewarded innovation and assured affordability when products matured. Investment in breakthrough research and the biotechnology industry flourished at that time creating high-paying jobs and critical new cures. As the first generation of breakthrough biologics emerges from patent protection, will we learn from this experience? Will we support legislation like Waxman-Deal that uses the competitive incentive of biogenerics to promote long term competitive advantage, global leadership and job growth? Or, will we ignore this wisdom and allow R&D investment to veer off track?

The bottom line is this: Will we create a fair and reasonable system that balances incentives to innovate with the need for access to affordable medicines, or will we accept a process that entrenches pharmaceutics profits for less innovative brand research, and do so at the expense of patients in need of less-costly medicines. Will we create a fertile environment for biogeneric companies to invest in the hard science to understand and make biologics and biogenerics safer and better? Will we let the patent system drive efficiency and high rewards for breakthrough biologics as biogenerics provide affordable access to mature products?

As I see it, this is exactly what health care reform is all about.

Thank you for this opportunity. I would be pleased to answer any questions.

Exhibit A

MOMENTA

Momenta Company Overview

Momenta is a biotechnology company, founded in 2001 based on a technology platform initially developed and licensed from Massachusetts Institute of Technology. We currently employ approximately 175 employees at our offices in Cambridge, Massachusetts. We are applying our innovative technology for the detailed structural analysis of complex mixture drugs to the discovery and development of both novel and complex generic biopharmaceuticals. We leverage this platform to study the *structure* (i.e., thorough characterization of chemical components), *structure-process* (i.e., design and control of manufacturing process), and *structure-activity* (i.e., relating structure to biological and clinical activity) of complex mixture drugs. The development product candidates and research programs from our generic and novel portfolios are outlined below.

Momenta Pharmaceuticals—Product and R&D Pipeline

	Complex Mixture Generic and Follow on Biologic Drugs	Novel Drugs
Development Product Candidates	M-Enoxaparin[1] (Generic Lovenox®) M356 (Generic Copaxone®) M178[1] (Follow-on Biologic)	M118 (Anticoagulant)
Research Programs	Follow-on Biologics (FOBs)	M402 (Oncology)

[1] In collaboration with Sandoz/Novartis Pharmaceuticals

Complex Mixture Generics Portfolio

Our complex mixture generics and follow-on biologics effort is focused on building a thorough understanding of the *structure-process-activity* of complex mixture drugs to develop generic and follow-on versions of marketed products. While tailored specifically for each specific product candidate, we utilize a similar analytical and development approach across all of our product candidates. Our first objective is to apply our core analytical technology to thoroughly characterize the *structure* of the marketed product. By defining the chemical composition of multiple batches of a marketed product, we are able to develop an "equivalence window" which captures the inherent variability of the innovator's manufacturing process. Using this information we then build an extensive and robust understanding of the *structure-process* relationship, to design and control our manufacturing process to manufacture reproducibly an equivalent version of the marketed product. Where necessary, and as required by FDA, we will supplement our application with additional supportive *structure-activity* data (e.g., immunogenicity, pharmacodynamics). Our goal is to obtain FDA approval for and commercialize generic or follow-on versions of complex mixture products, thereby providing high quality, effective, safe and affordable medicines to patients in need.

Our most advanced product candidate, **M-Enoxaparin**, is designed to be a technology-enabled generic version of Lovenox® (enoxaparin sodium injection), a low molecular weight heparin, or LMWH, used to prevent and treat deep vein thrombosis, or DVT, and to support the treatment of acute coronary syndromes, or ACS. This drug is a complex mixture of polysaccharide chains derived from naturally sourced heparin. An Abbreviated New Drug Application (ANDA) for M-Enoxaparin, submitted in August, 2005, is currently under FDA review. Our second major generic product candidate is **M356,** a technology-enabled generic version of Copaxone® (glatiramer acetate injection), a drug that is indicated for the reduction of the frequency of relapses in patients with Relapse-Remitting Multiple Sclerosis, or RRMS. Copaxone® consists of a complex mixture of polypeptide chains. With M356, we have extended our core characterization capabilities from the characterization of complex polysaccharide mixtures to include the characterization of complex polypeptide mixtures. An ANDA for M356, submitted in December, 2007, is currently under FDA review.

MOMENTA

In addition to our two complex generic product candidates, we have further extended our analytical and development platform to pursue generic or follow-on versions of biologic drugs. Our collaborative efforts on **M178**, as well as our ongoing internal **Glycoprotein Research Program**, are focused on developing generic or follow-on versions of marketed therapeutic proteins, which are derived from natural or cell based manufacturing processes. By thoroughly characterizing these biologic molecules, we seek to gain a deeper understanding of the relationship between their manufacturing processes and final product compositions. Our goal is to replicate our development approach with M-Enoxaparin and M356 and pursue the development and commercialization of multiple generic or follow-on versions of marketed therapeutics.

Novel Drugs Portfolio

Our complex mixture novel drug research and development efforts leverage our analytical technology platform and *structure-process* knowledge to develop novel drugs by studying the *structure-activity* of complex mixtures and develop novel drugs. With our capabilities to thoroughly characterize complex mixtures, we are targeting our efforts to understand the relationship between structure and the biological and therapeutic activity of various complex mixture drugs. Our goal is to capitalize on the structural diversity and multi-targeting potential of these complex mixtures to engineer novel drugs that we believe will meet key unmet medical needs in various diseases. While we believe that our capabilities to engineer improved and novel complex mixture drugs can be applied across several product categories with significant therapeutic potential, such as polysaccharides, polypeptides and glycoproteins, our initial focus has been in the area of complex polysaccharide mixtures.

Our lead novel drug candidate, **M118**, is a LMWH that has been engineered to possess what we believe will be an improved therapeutic profile (compared with other currently marketed products) to support the treatment of ACS. We are currently completing a Phase IIa study in patients undergoing percutaneaous coronary intervention, or PCI. **M402**, our second novel drug candidate, entered early development this year as a potential inhibitor of angiogenesis and tumor metastasis. We also are seeking to discover and develop novel therapeutics by applying our technology to better understand the function of these polysaccharide mixtures in multiple biological processes, with an initial focus in oncology.

Momenta Technology

Our integrated technology platform for the study of complex mixtures utilizes three different types of analytical tools. First, we have accumulated a comprehensive library of enzymes that we use to break down the components of a complex mixture into smaller, measurable units. Second, we apply proprietary improvements to established analytical techniques (such as Matrix Assisted Laser Desorption Ionization-Mass Spectrometry, or MALDI-MS, nuclear magnetic resonance, or NMR, and capillary electrophoresis, or CE, among others), to gather and analyze information regarding the components, structure and arrangement of the chemical building blocks of the complex mixture. Third, we apply proprietary mathematical methods that integrate the disparate information obtained from these analytical techniques to arrive at a specific, numerically-derived solution that describes the complete composition of a specific complex mixture. It is the combination of these tools that enables us to characterize complex polysaccharide, polypeptide and glycoprotein mixtures.

While a similar integrated analytical approach is applied across different product categories, we develop a unique characterization toolkit for each specific complex mixture. Once the chemical components of the complex mixture are known (*structure*), we (1) further employ these methods and data sets in the design and control of our manufacturing process (*structure-process*) to produce generic versions of marketed drugs, and (2) relate structure to biological and clinical activity (*structure-activity*) to engineer novel drugs which meet key unmet medical needs in various diseases.

Company Contact Information

Our principal executive offices are located at 675 West Kendall Street, Cambridge, Massachusetts 02142, and our telephone number is (617) 491-9700. Our Internet address is *www.momentapharma.com*.

Exhibit B

Submitted in Electronic Form

December 22, 2008

Federal Trade Commission
Office of the Secretary
Room H-135 (Annex F)
600 Pennsylvania Ave, NW
Washington, DC 20580

Re: Emerging Health Care and Competition and Consumer Issues – Comment, Project No. P083901

Momenta Pharmaceuticals, Inc. ("Momenta") was very pleased to participate in the November 21, 2008 Roundtable on Follow-On Biologic Drugs (the "Roundtable") at the Federal Trade Commission (the "FTC"). We support the FTC's initiative to seek public comment and participation, and welcome this opportunity for open dialogue.

There are very important immediate and long term pro-competitive advantages that will result from the creation of an abbreviated regulatory approval pathway for follow-on biologics. We believe that any legislation must provide the FDA with the full authority to approve both Biosimilars and Biogenerics (as defined below) or these benefits will not be fully realized.[1] We also believe the maintenance of the status quo creates an economic environment that discourages innovation and investment in the next generation of quality by design technology. In other words, the absence of an abbreviated pathway for Biogenerics and Biosimilars under current law establishes a legislative barrier to scientific innovation. We are also very concerned that even if legislation is adopted, that several of the procedures and features in the proposed legislation could have the same anti-competitive impact on follow-on biologics as the absence of an abbreviated pathway.

We appreciate your request for supplemental comments and the opportunity to spell out our views as expressed at the Roundtable. Our comments are focused on three key points:

---

1 A review of the comments submitted prior to the Roundtable as well as the questions and comments raised at the Roundtable, suggests that many of the articulated positions of the pharmaceutical and biotechnology industry are based on the assumption that follow-on biologics will by definition be Biosimilars and not Biogenerics. While we recognize that many product definitions are used when discussing follow-on biologic products, we believe, as the FTC suggested at the Roundtable, that it is appropriate to use two terms "Biogeneric" and "Biosimilar" in an effort to more accurately understand the impact of Biogenerics and Biosimilar products in the marketplace -- Biogeneric products being those follow-on biologic products that are approved and designated interchangeable to the innovator product, with Biosimilar products being those follow-on biologic products approved but not designated by FDA as interchangeable to the innovator product (e.g., Omnitrope®).

ENDALL STREET CAMBRIDGE, MA 02142 T: 617.491.9700 F: 617.621.0431 WWW.MOMENTAPHARM

- An abbreviated pathway for both Biosimilars and Biogenerics will create an immediate pro-competitive impact by spurring investment in innovative research and development, promoting quality improvement, and creating the opportunity to control costs for payors while improving access for patients to brand and follow-on products alike.

- The proposals to extend data exclusivity periods for brand biologics should be carefully examined to preserve innovation and encourage investment in basic research, cures and unmet medical needs. A careful examination will reveal that the existing patent regime and patent term extension rules are as protective and in many respects more protective of reference brand biologic products than the protections afforded reference brand small molecule products, making the need for greater exclusivity open to question; and

- It is essential to ensure that the patent resolution process is transparent, efficient and does not create anti-competitive barriers to market entry.

1. There are Immediate Important Pro-Competitive Market Impacts that will result from the adoption of a Biogeneric and Biosimilar Regulatory Pathway.

a. Momenta offers a case study of how research and development of follow-on biologics will spur innovation and create an immediate pro-competitive impact that will facilitate quality improvements, price competition and investment in research and development of therapeutics for unmet medical needs.

Momenta was formed to develop the next generation of characterization technology and overcome the technical barriers that impeded the scientific understanding of complex molecules and proteins. Our initial goal was to unravel and thoroughly characterize the chemical structures of these important complex molecules to gain insights into their biological activity and the process for manufacturing them. Over the past 6 years, Momenta pursued these goals, and expanded its capabilities for understanding of complex polysaccharide, polypeptide and protein drugs.

Our initial work was to develop technology and analytic tools to develop generic versions of complex products that can be filed as traditional abbreviated new drug applications or ANDAs. A second area involves applying our understanding of chemical structures to unlock the biology of complex mixtures and engineer novel new drugs. Our third area of research and development is applying our innovative analytical technology to the development of follow-on biologic products. Our complex generics pipeline includes M-Enoxaparin and M356, which are partnered with Sandoz, a division of Novartis. M-Enoxaparin, a generic version of Lovenox® (ANDA filed in August, 2005), and M356, a generic version of Copaxone® (ANDA filed in December, 2007), are currently both under review at the FDA. These complex mixtures were once thought to be impossible to characterize thoroughly and manufacture reproducibly. Our investment in characterization and analytical tools has resulted in two ANDA filings to date, and each program represents an example of the kind of innovative research and investment that could

be further encouraged with the creation of an abbreviated regulatory pathway for follow-on biologics. Had the Hatch-Waxman pathway not been available for the review and approval of these kinds of products, Momenta would have been unable to raise the capital to undertake these programs and enter into a collaborative partnership to finance the research and development to substantially improve the quality of complex mixture and protein products, and gain more knowledge and insights into these complex molecules.

The results of this work have already led to important short term benefits. In the past year, we collaborated with FDA and other academic institutions in helping to resolve the global heparin contamination crisis. Through the use of our innovative analytic approach, we aided the FDA in identifying the nature and the source of the contaminants in the heparin imports, and through our expertise in disease biology we helped to establish the biological plausibility linking the contaminant to the observed adverse event profile. See Gerrini et al.,"Oversulfated chondroitin sulfate is a contaminant in heparin associated with adverse clinical events," Nat Biotechnol. 2008 Jun;26(6):669-75. Epub 2008 Apr 23 and Kishimoto et. al., "Contaminated Heparin Associated with Adverse Clinical Events and Activation of the Contact System," N Engl J Med. 2008 Jun 5;358(23):2457-67. Epub 2008 Apr 23.

With this in mind, we have also invested heavily in adapting our technology and our tools to characterize proteins with the intent of creating follow-on biologic, or protein products. Our investment in this area enables the potential to characterize thoroughly protein products. Historically, due to the lack of more advanced analytical tools, proteins have not been fully characterized and are defined in large part by their manufacturing process. These new tools can enable thorough characterization and offer the very real potential to develop equivalent, substitutable versions of protein products.

These tools also offer the opportunity to significantly add value and cost savings to the innovator drug development process. As the technology is developed to allow for thoroughly characterized proteins, brand manufacturers will have an incentive to use these technologies to enhance the quality of their products by more precisely controlling variability of a number of attributes in the final drug product. They would also be able to apply the technology to the qualification of new manufacturing facilities and product enhancements, and reduce the need for very costly, potentially unnecessary clinical trials. Today, brand biologic products undergo very expensive clinical testing to evaluate safety and efficacy, but clinical trials are not necessarily the most useful, effective or ethical means for identifying low frequency risks such as immunogenicity or the risks of product contamination. As the features and complex differences in complex drugs and protein products are characterized, the risks that are associated with immunogenicity can be avoided by design, contaminants detected, and the cost of unnecessary clinical trials avoided. These are real and significant quality improvements and cost savings. To the extent that new technology will more thoroughly characterize follow-on biologics and allow for the establishment of equivalence and interchangeability, then it would be unethical to run clinical trials because of the needless delay in bringing these products to market. The net result of a delay in approval is to preserve the existing monopoly for the branded product and further impede access to these more affordable and potentially life-saving medications. Instead, the

potential for follow-on biologic competition would shift investment bias at brand companies more in favor of products addressing new unmet needs and discovery research into new cures.

Consider the emergence of the biotechnology industry. In the early 1980s, there were calls for restrictions on the use of recombinant DNA technology in the development of therapeutic proteins. Claims of safety risks and uncertainty about cloning were made, but reason prevailed and restrictive legislation was not adopted to stifle these important scientific advances. Had these voices prevailed, the industry would not have attracted the necessary investment capital to develop the first generation of recombinant therapeutic proteins. Just as legislation at that time restricting such research and development or the ability of the FDA to regulate and approve recombinant proteins was unwarranted, today, as the first generation of therapeutic proteins approach the end of their patent terms, legislation should not block or inhibit the development of characterization technology and quality improvements that make it possible to develop safe and effective Biogenerics and Biosimilars.

Consider the state of the pharmaceutical industry prior to the adoption of Hatch-Waxman. It was focused on assuring quality and innovation, for sure, but its investments and resources in the 1970s and early 1980s may have focused less on higher risk discovery of new therapeutics, and perhaps more on lower risk development of two, three or four competing therapeutics in a class as well as on product life-cycle management strategies. Hatch-Waxman created a transformation in the pharmaceutical sector. By facilitating the pro-competitive launch of generics, the profit associated with multiple drugs in a class or in life extension strategies was reduced as products approached the expiration of their patent life, and the *relative* profit associated with the development of innovative new therapeutics increased. The biotechnology industry emerged, and the pharmaceutical industry invested heavily in the 1980s and the 1990s in biotechnology, in biology as a basis for screening small molecule libraries of compounds and in the field of rational drug design. We believe that Hatch-Waxman played a significant role in this transformation of research and development in the pharmaceutical sector (i.e. that the reality of fair and appropriate generic competition contributed to this change in behavior).

The enactment of an abbreviated pathway for approval of Biosimilars and Biogenerics offers a similar opportunity for transformative change. Today, biotechnology and biopharmaceutical companies focus their investment in characterization technology for quality assurance purposes, but limit their research and development into thorough characterization of biologics. This leads to the belief that biologics cannot be thoroughly characterized, that Biogenerics are not feasible and that Biosimilars will offer limited competitive advantages. Aside from their vested interest in this view, we believe that the history of Hatch-Waxman proves the contrary. We believe that once the pathways are in place, there will be an immediate competitive impact on research and development at biotechnology and biopharmaceutical companies who will see the competitive advantages of product quality improvement. We also note with interest the fact that many large pharmaceutical companies such as Merck and Lilly have recently announced their intention to pursue the development of follow-on biologics. Federal policy should support this competitive change.

The absence of an abbreviated pathway for FDA approval of Biosimilars and Biogenerics is also the key challenge facing us, and innovator companies like us. While we believe our work with M-Enoxaparin and M356 has demonstrated the power of our technology to make abbreviated pathways possible for complex mixture based drugs, and that our on-going work on proteins indicates that the same should be possible with follow-on biologics, the absence of unambiguous legislation authorizing the FDA to implement an abbreviated pathway may be the rate limiting factor restricting availability of investment capital for us and companies like us.

The enactment of an abbreviated pathway is thus essential to open the doors for competition and encourage innovation by Momenta, companies like Momenta, and brand biotechnology companies alike. As the technology develops, we believe it will significantly reduce the cost of drug development and ultimately result in improved patient access to high quality, safe, effective, and potentially life-saving medications at a more affordable price. We also believe that the FDA is fully qualified to evaluate the emerging product and process characterization technology and must have the discretion to review each follow-on biologic application based on the science presented. This will facilitate the entry of generic biologic competition while assuring the highest standards of product quality to ensure patient safety. We consider ourselves to be an innovator company and are concerned that some of the more traditional innovator companies are seeking to erect legislative, regulatory, and market barriers to legitimate, technology based competition. Opening the door to such innovative analytical science, will also improve the quality of both innovative and generic drugs in the future.

b. Biogenerics, in particular, offer a significant pro-competitive opportunity, and it is essential that any legislation provides the FDA with discretion for approval of Biogenerics as well as Biosimilars to ensure these benefits accrue to patients.

If one only anticipates the development of Biosimilar products, then it is conceivable that absent interchangeability, there will be higher development costs than those incurred in the traditional generic drug marketplace, and thus, less cost savings. Similarly, if one relies on clinical trials to demonstrate "similarity" rather than "sameness" to obtain approval of a Biosimilar, then one would not expect there to be a significant incentive to develop improved characterization technology that would allow for incorporation of quality by design into the product. In addition, one would continue to expect significant continued spending on sales and marketing activities to promote Biosimilars because they would not be interchangeable.

On the other hand, if one anticipates the development of Biogenerics and grants the FDA discretionary approval authority, the analysis presented in the comments of many of the biotechnology companies and pharmaceutical companies warrants further scrutiny. First, and perhaps foremost, as noted above, the mere potential for Biogenerics will stimulate significant investment in innovation. This investment will lead not only to the cost saving benefits of Biogenerics themselves, but to significant advancement in the technology used by the pharmaceutical and biotechnology industry to characterize and develop all biologics. Previously unknown contaminants and features of complex molecules will begin to be better understood, and engineered out of final products during the development process. The need to rely on

clinical trials to establish comparable efficacy and safety as well as to avoid the risks of immunogenicity could be reduced and potentially avoided. As noted above, Momenta has begun to demonstrate these innovations in the field of complex generics where the ANDA pathway is available and has enabled Momenta to raise investment capital and apply these new skills. The authorization of the FDA to approve Biogenerics, based on its scientific discretion, will, we believe, stimulate brand and generic companies alike to develop the necessary tools and technology to create the opportunity for Biogenerics in the future.

In the mid-term, we also anticipate that these new tools and technology will accelerate development of Biosimilar products. As the technology advances, the extent of clinical testing may vary based on a company's characterization capabilities. In addition, brand companies seeking to expand or improve manufacturing capacity (and patients in turn) will benefit from cost reduction to the extent characterization similarly reduces the need for clinical trials.

In the longer term, when Biogenerics are approved and interchangeable, the benefits of the price reductions associated with avoiding unnecessary clinical development costs and a generic marketing and pricing model will offer the greatest economic benefit to payors and patients. We do agree however that because of the complexity of demonstrating "sameness" for interchangeability, fewer Biogenerics will enter the market than in the traditional generic drug marketplace, and that price reductions for Biosimilars and Biogenerics may not be to the same degree as for small molecule generics. Ultimately, the greater the incentive offered by the pathway, the greater the likelihood more companies will invest in Biogenerics. The more companies that invest in Biogenerics, the more competitive products will emerge. To suggest as some participants at the Roundtable did, that pricing would decline by only 10% seems to be well below what we would expect. We believe that one could assume at least 30-40% discount and as the technology develops and the number of market participants increase, and as the number of competitive products increase, discounts may further increase.

In summary, we see immediate, mid-term and long-term advantages to the creation of an abbreviated approval pathway for Biogenerics and Biosimilars. While Biosimilars are more likely to emerge in the next 0-5 years, and Biogenerics in the next 5-10 years, the immediate approval of a Biogenerics pathway will spur real time investment in new quality-enhancing, cost-saving technology that will benefit patients and enhance the development of innovator products and Biosimilar products alike.

2. Data Exclusivity Should be Carefully Prescribed to Avoid Stifling Innovation.

We believe a balanced discussion of data exclusivity at the Roundtable may have been impaired by the separation of the discussion across multiple panels. One needs to consider data exclusivity in relation to the investment decision of brand companies, the relative patent strength of the innovator products as compared to brand drugs, and the existence of the right to challenge the patent rights during the exclusivity period. In addition, by examining these points separately, important distinguishing factors between Biosimilars and Biogenerics may have been overlooked that are important to this analysis.

First, we believe that Professor Brill identified a critical issue for consideration by the FTC and the Congress in his review of Professor Grabowski's analysis of breakeven periods for biologics. The fact that Professor Grabowski's analysis assumes that sales of the innovator brand product essentially end upon expiration of data exclusivity is not a reasonable assumption. We agree with most panelists that anticipated market share for Biosimilars and for Biogenerics will not interfere with continuing and robust innovator brand sales after the expiration of a data exclusivity period -- particularly during the first few years following expiration. Consequently, the breakeven point will be significantly earlier than 12.9 to 16.2 years posited by Professor Grabowski. We agree with Professor Brill that appropriately accounting for these continuing sales suggests that a data exclusivity period of 7 years is sufficient to provide a return on investment. This is because he estimates they will have at least 10 years of revenue (3 years beyond a 7 year data exclusivity period) which is a much more realistic assumption. It is important to note that "breakeven" is not the point at which profits begin to be earned. Rather it is the point at which the expected rate of return (i.e., profit) from an investment along with return of principal is recovered. Moreover, this is only the breakeven point, and we believe that sales of the innovator brand product will continue well beyond this 10 year period as well.

Second, a principal assertion made by several companies filing comments and by the panelists at the Roundtable was that a longer period of data exclusivity is warranted for follow-on biologics than for generic drugs under Hatch-Waxman because biologic patent rights are somehow weaker than small molecule drug patent rights. This claim is made despite the record of broadly issued patent rights on biologics that even the panelists admit, for the first generation of protein therapeutics and antibodies are broader and more complex than small molecule patent rights. The patent filings relating to the biology in which a biologic product acts include, but are not limited to claims drawn to:

- The target receptor or biologic pathway
- DNA encoding the receptor or the ligand to the receptor
- The cloned protein itself
- A Monoclonal antibody which binds to the receptor and regulates the receptor or biologic pathway
- Generic therapeutic claims for treatment of a disorder resulting from regulation of the receptor or pathway

In other words, the discovery and understanding of the biology of a pathway often allows for patent protection that not only covers the therapeutic protein or antibody itself, but offers the potential to claim coverage of other therapeutic proteins and antibodies that regulate the biological landscape in which the biologic acts.

In addition to this broader range of patent coverage for biologic products, there are frequently technology platform patents and manufacturing patents that result from biological understanding that may be essential to using the biologic. These might include patents covering the process for production of antibodies or proteins in general; processes for controlling the

shape or structure of proteins or antibodies to reduce the risk of side effects, or patents for increasing the efficiency of production or the purification of the protein or antibody. Unlike small molecule drugs, these patents often provide a level of market protection because the biological origin of their discovery makes them necessary for production of a product.

Contrast this patent landscape with those for small molecule drugs. In most cases the small molecule is discovered by screening against a target or receptor in a pathway and the patent rights are generally limited to the composition of matter of the molecule, its method of manufacture and its method of use. Thus, while the patent may be strong in terms of its validity, its coverage would not generally block another small molecule that is screened that regulates the same target or has the same therapeutic effect. This is a key point frequently omitted in the discussion. That is why there are multiple small molecule brand products while there are rarely, absent a license agreement or collaboration, multiple brand biologics (e.g, contrast statins with EPO or G-CSF). This means that brand biologics, unlike brand small molecule products, have less competition during the period of exclusivity, and thus a much greater potential to earn a profit in a shorter period of time. Finally, because many biologics emerge from early stage research at Universities and biotechnology companies before they are launched by a fully-integrated biopharmaceutical company, one still may have to obtain licenses for some of the non-product specific patent rights to launch a follow-on biologic.

The result is that follow-on biologics face a much more complex, and broader array of patent rights than one typically faces with respect to launching a small molecule generic.[2] Given this set of circumstances, it is not clear why there should be a data exclusivity period for follow-on biologics that exceeds the exclusivity period provided for under Hatch-Waxman. This is particularly true given that the innovator companies have been able to take full advantage of the existing patent term extension provisions in the law that permit extensions of up to 5 years (not to exceed 14 years from approval) for delays in the regulatory approval process.[3] The patent term extension provisions were added to the patent laws as part of Hatch-Waxman for *both* small molecule and biologic products. The right to challenge patents prior to submission of an ANDA was only added to the patent laws for small molecules, not biologics. Thus, not only is there an

[2] Several panelists that asserted the "weaker position" of biologic patent rights, conceded at the Roundtable that the first generation of biologic product may have very strong and broad coverage and that could account for many of the products having successfully prevented new entrants for periods exceeding 18 years (E.g. EPO, G-CSF). They noted that the Court of Appeals for the Federal Circuit has restricted the ability of innovators to seek the full breadth of coverage afforded the first generation of recombinant proteins and antibodies. That said, the opportunity to obtain a broad array of patent rights covering a biological pathway is still available for novel inventions, and the fact that the courts have curtailed over-expansive patent claims does not mean that the rights are weaker than those afforded small molecule products. For example, the screening of a small molecule in a pathway may not afford coverage over all small molecules that regulate that pathway today, but the invention of a protein or antibody that is integral to the biology of a receptor pathway might still result in claims covering all proteins or antibodies with similar sequences that regulate the receptor pathway.

[3] At the Roundtable, Hospira noted that brand companies are continuing to prosecute so-called "submarine" patent applications on many first generation brand products that are timed to issue on expiration of the core brand product patent estates resulting in 20 years or more of market exclusivity for these products and that this has impacted several of their follow-on biologic programs.

opportunity to obtain stronger patent rights today for biologics, but there is no opportunity for an early challenge to those rights by a developer of a follow-on biologic. The absence of a timely right to challenge questionable patent rights tilts the playing field and restricts competition.

Several panelists took the position at the Roundtable that the European model of 8+2+1 had worked effectively and should be considered as support for a 12-year data exclusivity period. A key difference in Europe, however, is that a follow-on biologic developer is able to file an opposition to the patents and clear the path at any time after the patent issues for publication. Early publication of patent applications providing notice to third parties was the historical practice pre-GATT in Europe. This right to challenge early in the life cycle of a product (and before a filing for approval) adds balance to the European approach. Moreover, in Europe, the regulations and guidance do not contemplate the approval of Biogenerics, only Biosimilars. To the extent that a product is different than the brand product, the differences may take it outside the scope of the patent rights for the brand product and thus affords less patent coverage. This would not be the case with a Biogeneric. In theory, valid, enforceable patent composition of matter biologic patent rights should be as strong as any small molecule rights, because, by definition, it will be the same product. The choice of a regime which affords 8+2+1 years of data exclusivity was predicated on the early stage right to challenge the patents and the potential for less patent coverage on a Biosimilar.

Stepping back, we believe that Hatch-Waxman has demonstrated a reasonable period for Biogeneric product data exclusivity as long as there is a reasonable period for bringing a patent challenge prior to approval. We also believe that taking into account Professor Brill's analysis; it appears that data exclusivity for Biosimilars of up to 7 years may be warranted to accommodate the rate of return on investment. The proposals for 12-14 years of exclusivity, however, in light of the significant patent protection available to biologic products, is unwarranted are not needed to encourage new product innovation. A 12-14 year data exclusivity period would serve instead to extend the time for launch of competitive Biosimilar or Biogeneric products and would create a significant disincentive to investment and defer the economic benefits of follow-on biologic competition, and in particularly, the timely market entry of more affordable and potentially life-saving follow-on products.

Finally, we believe it is also essential, and there appeared to be general consensus on the panel, that regardless of the data exclusivity period, a minimum of a four (4) year period is needed in advance of expiration of any data exclusivity period to allow for legal clearance through litigation. The complexity of the biologic patent rights, and the experience with prior litigation of biologic patent rights means that a shorter period would likely lead to a delay in launch for a follow-on biologic beyond the exclusivity period.

3. **It is Essential to Ensure that the Patent Resolution Process is Transparent, Efficient and does not Create Anti-Competitive Barriers to Market Entry.**

An early and clear resolution of patent disputes is essential to encourage investment in follow-on biologics. The process established under the current Hatch-Waxman procedures

balances the need for investment with the need to protect innovator patent rights.[4] Under the current process, a generic ANDA filer must certify to the non-infringement or invalidity of publicly disclosed patent rights. The reference brand product owner must then either file suit in response to the filing or the FDA can proceed with the review and approval of the application. This avoids putting the FDA in the position of determining patent rights – an expertise beyond its traditional area of experience. If suit is filed, a 30 month stay issues that sets the time period for litigating the case. The stay is lifted if the suit is resolved sooner and the FDA can then proceed. If the suit continues after the stay expires and the ANDA is approved, then the generic applicant can decide to launch "at risk" or await the outcome of litigation before launching.

While we do not object to the use of an Orange Book process for follow-on biologics, we do not see the need to entangle the FDA in the process and we recognize that it may create a number of unintended, undesirable consequences. For this reason, if an alternative process can be enacted for follow-on biologics that is transparent, efficient and is de-coupled from the FDA review process we would support the alternative approach as well. Our primary concern, however, is that by developing an alternative process, proposals will be made that are designed to use the legislative process to enact procedural barriers that could delay entry of follow-on biologics and undermine their pro-competitive effect. In the end, any approach must assure that upon expiration or termination of the reference biologic patent rights, or an acceptable data exclusivity period, the follow-on biologic is not further delayed, but launched. Invalid or unenforceable patent rights must not be able to delay competition beyond a pro-competitive exclusivity period.

A key question raised at the Roundtable was whether the complexity of the patent rights warranted additional procedural protections to assure that the patent clearance process respects the patent rights of reference brand biologics while assuring the pro-competitive advantages of a timely launch of a follow-on biologics. We agree with the panelists that biologic patent rights are often more complex and often cover patents methods of use and production that involve platform technology and biological pathways. We also agree that frequently the patent rights covering a biologic are in-licensed by the brand manufacturer and are owned by a biotechnology company, a University or the U.S. Government, and that multiple players are involved. While this adds some complexity we believe this can be addressed in the legislation in the first instance

[4] One should note that when the pharmaceutical industry submitted to the FTC its White Paper on "The Intersection of Intellectual Property and Antitrust Law" (April 22, 2002), a principal theme asserted was that the Hatch Waxman regime provides the essential balance and opportunity to challenge brand patent rights, and thus makes the strong intellectual property rights pro-competitive under the antitrust laws. Now that a similar regime is being considered for legal clearance of follow-on biologics, the same arguments should apply to follow-on biologics to assure a balanced approach. For example, in the White Paper, PhRMA notes that the failure to resolve patent issues prior to product approval presents problems for both the brand and generic manufacturer alike. *Id.* At 17. Similarly, the White Paper notes that the interests of competition are served under the antitrust laws because of the remedies available for abusive patent prosecution, including affirmative defenses of non-patentability, inequitable conduct, or fraud on the patent office. *Id.* at 44-46.

by limiting the legal clearance process to patent rights that are owned or controlled[5] by the reference brand biologic manufacturer, and leaving it to follow-on biologic company to clear on its own patent rights that are not owned or controlled by the reference brand manufacturer. We are concerned, however, that if all patent rights have to be cleared in the legislative litigation clearance process, that the number of potential patents involved might make the legal clearance pathway unworkable and create an insurmountable barrier to market entry. Limiting it to the rights owned or controlled by the reference brand biologics manufacturer leaves the follow-on biologic manufacturer freedom to conduct a customary patent search, identify the patent rights filed that may be applicable to its product, its manufacture and launch, and then determine how to best proceed.

A second key question raised is when should an artificial act of infringement be created and how should the legal clearance process work. Hatch-Waxman has a 5-year data exclusivity period and permits the filing of the ANDA up to one year prior to the expiration of data exclusivity. The generic manufacturer then can elect, if the patent rights are questionable, to make a certification that the patents are either not infringed or invalid and initiate litigation or await patent expiration. If the same data exclusivity periods are used, we believe the period should be increased to more than one (1) year prior to the end of data exclusivity to allow for completion of the litigation. If, however, an alternative approach is taken that affords greater periods of data exclusivity, then we believe that it is essential to assure and provide for the artificial act of infringement to occur at least four (4) years prior to expiration of data exclusivity. As proposed at the Roundtable, one would anticipate litigation lasting four (4) years in biologic patent. The brand manufacturer is protected because in the unexpected event that the litigation ends sooner, the data exclusivity period would restrict launch until the end of the four (4) year period.

A third key question raised was how should the legal clearance process operate if the Orange Book is not utilized. First, it is important to note that Hatch-Waxman was designed prior to the adoption of the rules requiring publication of patent rights in the United States. Prior to this rule change, it was possible to maintain pending patent applications for extended periods of time and surprise potential infringers despite conducting a thorough patent search. Today, there is greater transparency. We believe the legislation should assume that a follow-on biologic manufacturer is able to conduct its own patent search and be in a position to initiate the process at the time an abbreviated application is filed. We believe that the following process would

[5] Control generally takes the form of an exclusive license, however, to avoid gaming we believe the concept of control is necessary so that any contractual arrangement, even a non-exclusive license, that restricts access to the patent rights by a third party is covered by the process. Control might take the form of restricting the grant of a license to a third party or the right to sue third parties, or the form of contractual provisions that have economic or commercial terms with the same purpose or effect. If a University, for example, holds a manufacturing related patent right that is available for license to the follow-on biologic manufacturer without any restrictions to the reference brand manufacturer, then a license would generally be available and need not be included in the process. If a reference brand manufacturer controls a University patent right, then the University's patent right should be part of the legal clearance process.

provide a timely, efficient method for legal clearance of patents that are owned or controlled by a brand biologic manufacturer.

- The follow-on biologic applicant, upon filing its abbreviated application with the FDA, sends a notification (a "Notice") to the brand reference biologic manufacturer and either certifies its intention to delay marketing of a Biogeneric or Biosimilar product until patent expiry or any data exclusivity, or if appropriate, a certification of non-infringement or invalidity. The Notice should contain a list of the patent rights of which the follow-on biologic manufacturer is aware that it believes should be the subject of the legal clearance process, and a level of disclosure similar to the existing Hatch-Waxman notification process.
- Within ten (10) days of receipt of the notice, the referenced biologic drug manufacturer should be obligated to identify any other patents it owns or controls that cover the referenced product (and any subsequently issued patents within a reasonable period of time).[6]
- The referenced biologic drug manufacturer must then be obligated to sue or should be estopped from bringing suit on the identified, challenged patents no later than 45 days after receipt of the Notice. Alternatively, the applicant should have an express right to declaratory judgment jurisdiction if the referenced biologic drug manufacturer does not sue with respect to the patents listed in the Notice.
- Third party patent rights should be included only to the extent they are owned or controlled by the reference brand biologic manufacturer.

We believe this process balances the rights of reference brand biologic manufacturers with the precompetitive objectives of follow-on biologics manufacturers. It allows for follow-on biologic companies and their investors to evaluate the patent risk, and in cases where patent rights are weak, proceed with a well-defined process to obtain approval. If a different process were adopted for follow-on biologics, it would create further uncertainty and the opportunity for litigation that could delay new entry of competition and reduce the incentive for investment.

Conclusion

We appreciate the opportunity to submit these additional comments. We welcome further discussion, recognizing that there are multiple positions being offered on these complex issues. We remain committed, however, towards supporting final legislative language that will provide incentives for companies to compete and innovate, meet the appropriate high quality standards as set by FDA, and bring safe, affordable medicines to patients in need.

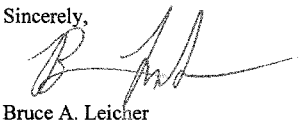
---

[6] Because the brand reference biologic manufacturer is not necessarily aware of the manufacturing process or formulation used by the follow-on biologic manufacturer, it should not be obligated to identify manufacturing patent rights that could not in good faith have been identified from the information provided by the follow-on biologic manufacturer in the Notice. This also avoids a need for disclosure of the follow-on biologic product information or manufacturing process prior to the initiation of or outside the protection of protective orders issued under any resulting litigation. The burden can be placed on the follow-on biologic manufacturer to conduct a freedom to operate search and to include any such patents in its Notice should clearance be needed.

Federal Trade Commission
Office of the Secretary
December 22, 2008
Page 13 of 13

If you have any questions regarding our submission, please feel free to contact me at 617-395-2786 or our Chief Operating Officer, Steve Brugger at 617-395-5105. We would be very interested in meeting with you at your convenience in January to discuss our proposals further with FTC Staff.

Sincerely,



Bruce A. Leicher
Sr. Vice President and General Counsel

Cc: Steve Brugger

Mr. JOHNSON. Thank you, Mr. Leicher.
Mr. Kushan, will you proceed with your testimony now, sir?

TESTIMONY OF JEFFREY P. KUSHAN, ON BEHALF OF THE BIOTECHNOLOGY INDUSTRY ORGANIZATION (BIO), WOODROW WILSON SCHOOL OF PUBLIC AND INTERNATIONAL AFFAIRS, PRINCETON, NJ

Mr. KUSHAN. Thank you, Mr. Chairman and Members of the Committee, for providing BIO with an opportunity to testify today.

BIO supports creation of an abbreviated regulatory pathway for biosimilar products. A viable biosimilar pathway will increase competition and improve access to the remarkable biomedical advances our industry has delivered over the past 20 or 30 years.

A biosimilar pathway will be successful only if it preserves the incentives that exist today in our vibrantly competitive and innovative biotechnology industry. If it does not, fewer new biological products and treatments will ensue to the detriment of patients with unmet medical needs. And given the decade-plus time that it takes to bring a new biological product to market, we simply cannot afford to guess wrong about the proper incentives for this field.

BIO is encouraged to see there is widespread support for several critical elements of any biosimilar regime. First, nearly all stakeholders agree that data exclusivity must be part of an abbreviated biosimilar pathway.

Data exclusivity is a regulatory mechanism that functions by deferring when biosimilar products can be approved on the basis of the innovator's clinical data. The differences of opinion that exist now revolve around how long the data exclusivity period should be and how it should relate to continued clinical development of products.

Currently, as Representative Eshoo pointed out, biological products have an unlimited period of data exclusivity. This is because there is no pathway today that lets another biotech company free-ride on the clinical investments of a first innovator.

Biotech innovation has flourished in this environment. We have seen constant innovations resulting in new protein therapeutics, new ways of exploiting cellular processes to treat diseases, new diagnostic tools, and new manufacturing techniques for making proteins. Indeed, the manufacturing innovations Mr. Leicher just pointed out that his company has developed have been made in this environment where there is unlimited data exclusivity.

Actual experience shows that innovators also do not stop clinically developing their products in this environment, despite being given essentially an unlimited period of data protection. Instead, it shows that innovators continue to invest heavily in new clinical development and research on their approved biological products and have brought hundreds of important new treatments to the market for the benefit of patients.

I think these real-world results are the simplest answer to the various theories we have heard suggesting that excessive data exclusivity will somehow hinder innovation and slow the delivery of new clinical benefits to patients.

The real question is not whether it should be provided; it is, how much should it be shortened by a biosimilar pathway?

Some have suggested that data exclusivity provided today for small-molecule drugs will be adequate for biological production. Several factors explain why this is not true.

Studies have shown that in the small-molecule area, on average, generic competition starts around 12 to 14 years after the innovator product is launched. Patents are why that happens. Patents can do that because any generic drug must be structurally identical to the innovator product.

That means drug innovators do not need broad patent claims to protect their investments. They can protect their innovative drug products with what we call picture claims on the exact molecule. All this means is that a small-molecule drug innovator deciding whether to make the investment and start the 10 to 15 year path to develop and bring a new drug to market today can assume that their patents, if they are upheld, will prevent the marketing of an infringing generic product until those patents expire.

This is not going to be true for biological products. Biosimilar products will invariably have different structures than innovator products. The biosimilar bills we see today all do not require structural identity.

Compounding this problem is the problem that most biotech patents issuing today are narrow. Let me say very clear, these are not weak patents. They are very strong and effective patents. They are just narrow patents. The same uncertain science that makes it difficult to make an exact copy of a biological product is actually why we have narrow patent rights.

Together, these two factors make it impossible for an innovator to predict when it is deciding to invest in development of the product whether its patent estate is going to provide effective protection against a future biosimilar product, and that is why the Hatch-Waxman model as it exists today cannot be directly applied to the biosimilar environment. This patent loophole must be closed by the data exclusivity provisions.

BIO strongly supports the data exclusivity provisions of H.R. 1548, introduced by Representative Eshoo. We believe that provides the appropriate balance. It also incorporates fair and balanced patent review procedures that will precede approval of a biosimilar, and importantly includes regulatory linkage.

Thank you.

[The prepared statement of Mr. Kushan follows:]

PREPARED STATEMENT OF

JEFFREY P. KUSHAN
SIDLEY AUSTIN LLP

ON BEHALF OF

THE
BIOTECHNOLOGY INDUSTRY ORGANIZATION

ON

Biologics and Biosimilars: Balancing Incentives for Innovation

Before the Committee on the Judiciary
Subcommittee on Courts

July 14, 2009

Biotechnology Industry Organization
1201 Maryland Avenue SW, Suite 900
Washington, D.C. 20024
(202) 962-9200
www.bio.org

TABLE OF CONTENTS

I. OVERVIEW 1

II. BACKGROUND ON BIO AND THE BIOTECHNOLOGY INDUSTRY 6

II. KEY CONCEPTS INVOLVED IN BIOSIMILAR LEGISLATION 8

A. Data Exclusivity 8

B. Patent Protection 14

C. Patents Alone Cannot Provide the Incentives Necessary to Encourage Today's Level of Innovation and Clinical Development of Biological Products in a New Biosimilar Approval System 18

III. ADDRESSING ISSUES CONCERNING EFFECTIVE DATA PROTECTION AND PATENT PROTECTION MEASURES IN BIOSIMILAR LEGISLATION 23

A. BIO Positions on Pending Legislation Concerning Biosimilar Approval Procedures 23

1. BIO Strongly Supports the Data Exclusivity and Patent Provisions in H.R. 1548 23

2. BIO Opposes the Data Exclusivity and Patent Provisions in H.R. 1427 26

B. The FTC Has Made Radical Proposals Not Supported by Evidence or 30 Years of Experience of the Biotechnology Industry 28

1. The FTC Has Incorrectly Portrayed the Nature and Effects of Competition between Biosimilar and Innovator Companies 29

2. The FTC Incorrectly Describes the Capacity of Patent Rights Alone to Encourage Initial and Ongoing Clinical Research in a Biosimilar Market 31

3. Preventing Enforcement of Patents until after Marketing of a Biosimilar Product Begins Will Cause Undesirable Confusion in the Market and Undermine Patent Rights 35

4. The FTC Incorrectly Asserts that Data Exclusivity under Hatch-Waxman Is Provided Only for Unpatentable Drugs 41

IV. CONCLUSIONS 43

Attachments

A. September 30, 2008 Response of the Biotechnology Industry Organization to the FTC Request for Comment on Emerging Health Care Competition and Consumer Issues – Project No. P083901 (Federal Register, September 3, 2008, Volume 73, Number 171, pp. 51479-51482, "Notice of Public Workshops and Roundtables and Opportunity for Comment")

B. BIO White Paper: *A Follow-on Biologics Regime without Strong Data Exclusivity Will Stifle the Development of New Medicines* (September 2007)

C. Data Exclusivity Periods for Biologics: Updating Prior Analyses and Responding to Critiques, Duke University Department of Economics Working Paper, No. 2008-10

(December 22, 2008) (available at http://www.econ.duke.edu/Papers/PDF/Data_Exclusivity_Periods_for_Biologics.pdf)

D. BIO Rebuttal to FTC Findings (June 2009)

I. Overview

The Biotechnology Industry Organization (BIO) appreciates the opportunity to provide the views of its members on intellectual property issues implicated by an abbreviated regulatory procedure for the approval of highly similar biological products, or so-called "biosimilars."

BIO supports the creation of an abbreviated pathway for biosimilars to help increase competition among, and access to, the many breakthrough biomedical advancements that have been developed by the biotechnology industry over the past 25 years. In doing so, providing effective intellectual property protection for biological products must remain a central focus of Congressional efforts. Measures that operate to lessen the economic incentives of our current system will translate into fewer new biological products and therapies, to the detriment of patients with currently unmet medical needs.

Patents are an important component of these economic incentives. Patents protect the inventions that are made throughout the process of discovering and developing a new biological product. For example, our members use patents to protect not only the protein that is the heart of a new biological product, but new treatments based on that product, new formulations necessary to make the product viable, and a wide range of techniques and systems used to produce, test, evaluate and use these products. Our companies also rely on trade secrets to protect manufacturing know-how and a range of data generated during the extensive and expensive process of clinical testing of a new biological product or treatment.

The effectiveness of the intellectual property incentives that exist today for encouraging development of new biological products and therapies, however, is inextricably linked to the regulatory system that governs these biological products.

Today, any company wishing to market a biological product must independently prove that its product is safe, pure and potent. This means that each company wishing to bring a new biological product to market must conduct the same scale of clinical testing for its product, and face the same risks, costs and other barriers to market, whether the product is highly similar to an existing product or an entirely new molecule. This level playing field among competitors directly influences decisions an innovator makes to undertake new product development, and continue clinical development of biological products after they have been approved. It also has functioned to blunt the impact of the limits of patent protection available for biotechnology products imposed by current law and strict examination standards used by the U.S. Patent and Trademark Office (PTO).

An abbreviated regulatory pathway for approving biological products will fundamentally change this environment. By its very design, an abbreviated approval process leverages the investments and efforts of the earlier innovator to facilitate approval and market entry of a biosimilar product that will directly compete with the innovator product. By allowing the biosimilar manufacturer to "free-ride" on the clinical data of the innovator, the abbreviated pathway helps the biosimilar manufacturer bring its product to market faster, with far less risk and uncertainty, and at a fraction of the innovator's development costs.

Unquestionably, the business of biotechnology innovation will change once an abbreviated pathway for biosimilar products becomes available. And patent rights, as they exist in today's system, simply will not be sufficient to preserve the incentives for development of new biological products and treatments that exist in today's industry. Measures that offset the impact of these fundamental changes to the nature of competition in today's biotechnology industry must be integrated into any new regulatory approval system for biosimilar products.

With these points in mind, BIO believes three principles must be followed in shaping any new abbreviated biosimilar approval process.

First, a substantial period of data exclusivity must be provided for the companies that conduct the clinical testing necessary to bring a new biological product, or a new use of biological product, to market. The certainty delivered by a lengthy period of data exclusivity is essential to preserve the dynamic economic environment essential to the viability of this industry and to continue to foster its entrepreneurial, innovation-focused and high risk-taking character. It is also necessary to offset the limits of patent protection that are presently mitigated by high barriers to entry facing other innovator products, but which will not be present once an abbreviated pathway for biosimilars is available.

In this regard, BIO strongly supports the data exclusivity provisions in H.R. 1548 introduced by Representative Anna Eshoo (D-CA) and supported by a broad bipartisan coalition of more than 125 Members of the House of Representatives, along with a wide range of stakeholders, including the American Association of Universities, the National Venture Capital Association, and scores of patient advocacy groups. This bill provides a base period of 12 years of protection, with the possibility of up to two and a half more years for conducting additional clinical research for new indications and pediatric populations.

Alternative proposals that provide no or only short periods of data exclusivity – or rely solely on the patent system – ignore the obvious and substantial changes to the biotechnology business model that will occur with the creation of an abbreviated approval pathway. These proposals also ignore the fact that patents will play a very different role in these systems as compared to how they operate today for generic drugs under the Hatch-Waxman Act. Specifically,

under the regulatory system that governs approval of small molecule drugs, innovators do not see competition from generic products for 12 – 14 years after the innovator product was launched, as a result of the combination of innovator patents, patent term restoration and data exclusivity provided for new molecules and new indications of drug products.

The critical distinction that makes this model break down for biological products is that biosimilar products will not be required to have an active ingredient that is the same as the active ingredient in the innovator's product, given the impossibility, with today's science, to make an exact copy of a biologic. Rather, they require differing degrees of "similarity." Indeed, some of the legislative proposals in this area would permit abbreviated approval of a biosimilar with significant differences in molecular structure, mechanism of action, and manufacturing processes. The lack of a "sameness" requirement will create significant questions about whether patents that cover an innovator's product will also cover a potential biosimilar product. The possibility exists that they will enable biosimilar manufacturers to achieve something generic drug manufacturers cannot, namely, avoid the innovator's patent rights but still get the benefit of the innovator's clinical data. A substantially longer period of data exclusivity than that provided to small molecule innovators in today's generic drug approval system is thus needed to preserve the incentives for innovation and clinical development of biological products.

Second, any legislation must include a balanced and fair procedure for identifying and resolving patent disputes implicated by the structure of a biosimilar product and how it is made *before* the biosimilar product is approved and put on the market. Nearly all stakeholders agree that doing so is better for patients, caregivers, and both innovator and biosimilar companies. To be fair and effective,

the system must permit participation by all relevant biotech stakeholders – including the universities and small biotech companies that have a significant role in our industry – and must not artificially skew the way that patent litigation is conducted to favor one party or the other. Indeed, doing so would likely run afoul of our international trade commitments, because they would make use of biotechnology patents less effective and useful compared to patents in other fields of technology.

In this respect, BIO strongly opposes statutory provisions, such as those found in H.R. 1427, the biosimilar legislation introduced by Representative Henry Waxman (D-CA), that would operate to arbitrarily limit the number of relevant patents that could be litigated prior to biosimilar approval, that would give one but not the other party control over whether, where and how litigation is conducted, or that impose onerous sanctions on the patent owner to enforce administrative compliance with the system. Measures that disrupt the well-settled rules of civil procedure and evidence and limit judicial autonomy will invariably make litigation more complex, more unpredictable and produce unfair results – directly contrary to the goals this Committee has had for years in its efforts to enact patent reform. BIO supports the patent notification and litigation procedures in H.R. 1548 because they do not suffer from these problems and will provide a fair and straightforward process for expeditiously identifying and resolving patent issues implicated by a biosimilar product

Third, any legislation should provide regulatory linkage to encourage innovator companies to promptly raise and resolve patent issues. Regulatory linkage, which is integral to the Hatch-Waxman Act, provides that, if a patent owner establishes through litigation that its patent is valid and infringed, the Food and Drug Administration (FDA) will defer granting final approval to the generic

application until the infringed patent expires. BIO believes a similar regulatory linkage must be integrated into any new analog to the Hatch-Waxman system created for biosimilar products to ensure that valid patent rights are respected. In this respect, we support the regulatory linkage provisions of the Eshoo bill, and regret that this measure has been excluded from H.R. 1427.

BIO also wishes to bring to the Subcommittee's attention a number of serious concerns it has with the recent report of the Federal Trade Commission (FTC) on intellectual property issues and biologics. BIO firmly believes the FTC's recommendations on data protection and patents are grounded on a number of serious errors and omissions, and reflects opinions that are contrary to decades of experience within our industry. If adopted, the FTC recommendations would seriously erode the incentives for development of new biological products.

II. Background on BIO and the Biotechnology Industry

BIO represents more than 1,200 companies, universities and research institutions that use biotechnology to research and develop cutting-edge healthcare, agricultural, industrial and environmental products and applications. As of December 31, 2008, there were more than 1,700 biotechnology companies established and doing business in the United States, 371 of which were publicly held, having an aggregate market capitalization of over $340 billion. The biotechnology industry and its contribution to U.S. economic growth has mushroomed since 1992, with U.S. healthcare biotech revenues increasing from $8 billion in 1992 to $70.1 billion in 2008. U.S. employment in the biosciences reached 1.3 million in 2006, and this industry indirectly supports approximately 6.2 million U.S. jobs Biotechnology companies can be found in every State of the Union. Roughly 80 percent of BIO's corporate members are small businesses.

The biotechnology industry is one of the most research-intensive industries in the world. In 2008 alone, biotechnology companies spent more than $30 billion in R&D. Between 2003 and 2007, the biotechnology industry raised more than $100 billion in private investment. These investments are paying off. There are more than 200 new drug products and vaccines on the market and hundreds more in development. These products are now improving, and will continue to improve, the lives of millions of Americans, and offer hope for cures for a wide range of illnesses.

The key to success of the biotechnology industry – across all of its sectors – is a business model that is based on taking significant risks to develop products based on innovation. Specifically, the biotechnology business model is based on making significant investments (often hundreds of millions of dollars) in early stage research and development with the hope that some of these investments and efforts will yield a commercial product. This model has worked despite the fact that it is lengthy (often taking more than a decade) and that the vast majority of biotechnology R&D investments and efforts do not result in a commercial product reaching the market. It is only by pushing boundaries of science and taking these risks that breakthrough inventions are discovered and converted into commercially viable products and services.

The biotechnology business model requires an environment that, as much as possible, reduces unpredictability in the commercial sector. One important factor in this environment is the guarantee of data exclusivity and effective patent protection. Specifically, by ensuring that the products or services that may eventually be marketed can be protected from unauthorized copying and use, companies can justify taking risks and making significant R&D investments. Introducing greater unpredictability by inadequate periods of data exclusivity, or

by limiting the conditions in which patent rights can be asserted, will adversely affect the business environment that is so crucial to supporting innovation in the biotechnology sector. And reducing this uncertainty has, time and again, proven to be critical to the decision-making processes of those providing funding for this research and development, particularly the venture capital community.

II. Key Concepts Involved in Biosimilar Legislation

A. Data Exclusivity

In the ongoing biosimilars debate, what "data exclusivity" is and what its effects will be have been misconstrued and often obfuscated. Misleading terms such as "marketing exclusivity" or "branded exclusivity" have been used interchangeably with this term; indeed, data exclusivity has even been characterized as a "monopoly" right. Given its central importance to the debate, it is important to have a clear understanding of what data exclusivity is, and what it can and cannot do within an abbreviated regulatory approval pathway.

An abbreviated regulatory approval procedure for biosimilar products will be able to provide a substantially faster, more certain and vastly less expensive regulatory approval process by allowing the biosimilar manufacturer to rely, at least in part, on the clinical evidence produced by an innovator and used to support FDA approval of the innovator's product (often called the "reference" product). In this type of an approval system, "data exclusivity" refers to a period of time after the approval of the innovator product during which the FDA is not allowed to rely on the approval of the innovator's product, including data contained in the innovator's Biologics License Application (BLA), to support approval of the

biosimilar product. Data exclusivity will prevent "unfair commercial use" of clinical test data, which often cost hundreds of millions of dollars to generate.[1]

Data exclusivity is provided today under the Federal Food, Drug and Cosmetic Act (FDCA) for small molecule pharmaceutical products.[2] In that system, a certain amount of time must elapse (between five and seven and one half years) before the FDA can approve a marketing application by a drug applicant who, instead of doing its own clinical trials, wants to rely on clinical studies that were done by another for an earlier drug. If the generic applicant does not want to wait until the "data exclusivity" period expires, it can generate and submit its own safety and efficacy data at any time.

This deferral of FDA reliance on the innovator's clinical data plainly is not an innovator "marketing exclusivity" or a "monopoly" right. Any competitor can submit independently generated clinical safety and efficacy data for its product at any time and receive FDA approval. Indeed, data exclusivity gives no innovator the right to monopolize the market for a new drug molecule, and current experiences in the biotechnology industry prove the contrary, as the FTC report

---

[1] Data exclusivity provisions are found in the regulatory systems of most developed countries. Data protection independent of trade secret protection is also required by international agreements, such as the Agreement on Trade Related Aspects of Intellectual Property (TRIPS). *See* TRIPS Agreement, Article 39.3.

[2] Under U.S. law, data exclusivity is also provided for agricultural chemical products. In that system, the producer of a "generic" pesticide must wait at least ten years before it can rely on the EPA's approval of the innovator pesticide. *See* Federal Insecticide Fungal and Rodenticide Act (FIFRA), 7 U.S.C. § 136a(c)(1)(F)(i) and (ii). This ten-year data exclusivity period for pesticides is supplemented by compensation paid by the "generic" manufacturer to the innovator for the five years following the end of the innovator's exclusivity period. *See* 7 U.S.C. § 136a(c)(1)(F)(iii).

amply demonstrates.[3] Terms such as "monopoly" or "marketing exclusivity" simply should be eliminated from the biosimilars debate.

Under the FDCA, the timelines for FDA action also apply regardless of patent status. For example, if an innovator obtains FDA approval of a new molecule, the FDA can accept and approve a competitor's application based on independently generated clinical evidence for the same molecule at any time, regardless of who owns the patent (or regardless of whether the molecule is patented at all). If the competitor wants to rely on the innovator's safety and efficacy data, however, the FDA will not accept an application for a copy of that molecule for four to five years from the innovator's approval date – again, irrespective of who owns the patent, if any.[4] Data exclusivity thus operates independently of patents. Also, unlike patents, data exclusivity is not enforceable by one private party against another, and there is no mechanism under which an innovator can sue a competitor for violating its data exclusivity.

Although data exclusivity does not confer marketing exclusivity or monopoly power, it does play a very important role in incentivizing innovation and in protecting investments – a role also commonly associated with patents. But in doing so, data exclusivity operates in a very different, but complementary, manner to patent exclusivity. For example, a drug applicant that seeks FDA approval based on an earlier drug's clinical safety and efficacy data, but does not infringe any patent could be deemed a free-rider of the innovator's investment in clinical

[3] For example, seven different human growth hormone products have been introduced and compete in the U.S. market. *See* FTC Report at 21-22.

[4] An applicant may submit an abbreviated new drug application ("ANDA") four years after approval of the NDA if it contains a patent certification under § 505(j)(2)(A)(vii)(IV) asserting that one or more patents listed for the drug product are invalid or would not be infringed by the ANDA product. *See* FDCA § 505(c)(3)(E)(ii). If there are no patents listed for the drug, or if the ANDA applicant does not intend to challenge any listed patents, the ANDA may be filed on the date that is five years after the approval of the innovator's NDA.

research, but not a patent infringer. By contrast, a drug applicant that has made large investments in clinical research and seeks FDA approval of a molecule patented by another but on the basis of its independently generated clinical evidence could be deemed a patent infringer, but not a free-rider.

Both scenarios occur regularly today. To avoid patent infringement, the applicant would have to design around the patent and make something other than a copy of the patented molecule. To not "free-ride", the applicant would have to conduct its own clinical research instead of relying on a competitor's clinical research. Data exclusivity thus will prevent free-riding on investments in clinical research that are necessary to secure marketing approval of a biological product, while patents operate to prevent unauthorized use or copying of innovative technology, each for a limited time. And, because copying and free-riding are both toxic to the initial and continued development and clinical testing of innovative biologics and therapies, both of these complementary and independent mechanisms are necessary, especially when one recognizes that the risk of patent avoidance and patent design-arounds will inherently be a much more significant problem for biologics, as explained below, than it is under the Hatch-Waxman Act framework for generic drugs.

Currently, there is no authority for the FDA to rely upon the clinical data a biologics manufacturer has provided to the agency in its BLA to support approval of any other biological product.[5] This means that, today, any company that wishes

[5] As is the case with the abbreviated new drug approval procedures for small molecule drugs under § 505(j) of the Federal Food, Drug and Cosmetic Act, any authority given to the FDA to rely on the innovator's BLA to justify approval of a later biosimilar application would not authorize the FDA to publish or share any confidential, trade secret information contained in the BLA. *See* FDA Response to Citizen Petition Docket Nos. 2001P-0323 *et al.* at fn 14 (Oct. 14, 2003). Instead, like the § 505(j) authority, it would grant FDA a limited authority to "use" that information to support its decision to find the biosimilar product pure, potent and

to obtain approval for a biological product, including one that is highly similar to an innovator product, must independently generate its own clinical data and convince the FDA on the basis of that data that its new product is pure, potent and safe. The average cost of doing this, as has been well-documented, is enormous, exceeding $1.2 billion.[6]

Today's biotechnology development environment thus imposes a substantial economic barrier to entry for new biological products, including those that are the similar to, or function similarly to, existing biological products. Indeed, this feature of the industry is *why* a substantial period of data exclusivity is essential to any future system for approval of biosimilar products. Decisions made by innovator companies today are based not only on the assumption that some degree of patent protection will be available to protect the innovator product in the future, but that every other potential direct competitor will face similar risks of failure, costs of conducting clinical investigations, and the same scientific uncertainties that the innovator faced. These factors have operated, in practice, to encourage not only the extremely high-risk initial development effort, but also the continued clinical research to find new uses for the product once it has been initially approved.

The availability of an abbreviated approval process for biosimilar products will fundamentally change this economic equation for innovators. Data exclusivity, and more specifically the length of data exclusivity, will become critical. As numerous experts have explained, a substantial data exclusivity period will be required to, in essence, "recreate" the dynamic and competitive

---

safe in the absence of independently generated clinical data and reports establishing the safety, potency or purity of the biosimilar product.

[6] *See, e.g.*, Joseph A. DiMasi and Henry G. Grabowski, *The Cost of Biopharmaceutical R&D: Is Biotech Different?* 28 MANAG. DEC. ECON. 469, 470 (2007).

environment that exists today and is so critical to driving initial and continued clinical investigation and development of drugs and new indications.[7]

A substantial data exclusivity period is particularly critical in areas such as cancer research, where initial marketing approval generally focuses on late-stage disease, and where research and development needed for early-stage or adjuvant cancer therapies, which are more difficult and take longer, generally occur later. The substantial exclusivity provided for the original treatment will encourage and support the risky, complex and expensive further development of the product for these additional indications, and will be critical to bring to market the vibrant pipeline of treatments that can allow cancer patients to live longer and better lives.

Importantly, data exclusivity periods will run concurrently (not in addition to) any patent exclusivity that may exist for the innovator's product, which may last up to or beyond 14 years after approval of that product. In one sense, a 14-year data exclusivity period will serve as an insurance policy that provides the innovator with certainty of protection for this period. In the case of patents that cannot be designed around and that have significant amounts of patent term remaining, long data exclusivity will have no impact. On the other hand, a substantial data exclusivity period becomes relevant where the available patent term is short, or where the biosimilar was designed to be different enough to avoid that patent but similar enough for approval. A substantial period of data exclusivity thus is an essential component of a balanced statutory pathway for biosimilars, making possible their introduction and use in the market while appropriately safeguarding incentives for biotechnology innovation.

---

[7] *See, e.g.*, Benjamin N. Roin, *Unpatentable Drugs and the Standards of Patentability*, 87 TEX. L. REV. 503-570.

BIO accordingly supports the data exclusivity provisions found in H.R. 1548. Under H.R. 1548, a new biological product would enjoy a base period of 12 years of data exclusivity, meaning that no biosimilar application could be approved that references the innovator's BLA earlier than 12 years after the BLA was approved. H.R. 1548 provides incentives for encouraging continued clinical research on an innovator biological product by providing that the base period can be extended by two additional years if the product is subsequently approved for a significant new indication. It also encourages pediatric testing of biologics, by providing the possibility of an additional six-month period of exclusivity. These periods are cumulative, so that an innovator product could enjoy a period of up to 14.5 years measured from the original approval of the product.[8] BIO believes both the structure and the periods of data exclusivity provided by H.R. 1548 reflect a fair balance, and will help to preserve the incentives existing under our current system to drive both original research and development of new biological products, and to stimulate continued clinical development of existing products to address new and unmet medical needs.

B. Patent Protection

A patent provides its owner with the right to prevent others from making, using, selling, offering for sale or importing the patented invention.[9] Patents are granted by the PTO following an examination process during which a patent examiner evaluates whether the invention is new, useful, non-obvious and

---

[8] Some have argued that this bill and others like it would permit innovators to make minor changes to their products and receive additional, successive 12-year periods of data exclusivity. This is incorrect. The bill's express language makes clear that the date of "first licensure," which starts the 12-year data exclusivity clock, cannot be extended by changes to a product's dosage, strength, or route of administration, and provides only a single, two-year extension for any new indication approved for the biological product.

[9] 35 U.S.C. § 154.

adequately described and enabled in the patent application.[10] Patent claims – which define the boundaries of protection conferred by the patent – are evaluated, and ordinarily narrowed, during the examination process to correspond to what the PTO believes represents the patentable invention. The exclusive rights under a patent are enforced through litigation in a Federal district court, which is an expensive, resource-intensive and often unpredictable process.

Over the past 15 years, the legal standards governing patentability of biotechnology inventions, and how the PTO applies them, have become significantly more stringent. For example, the utility requirement under 35 U.S.C. §101[11] and the written description requirement under 35 U.S.C. § 112, first paragraph,[12] have been construed by courts and the PTO to require more information about the nature and implications of changes to a protein or nucleic acid structure to justify the grant of patent claims extending beyond the literal protein sequence that has been discovered. *See, e.g., In re Fisher*, 421 F.3d 1365 (Fed. Cir. 2005); *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997), *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988). At the same time, the courts and the PTO have tightened the requirements for a finding of

---

[10] 35 U.S.C. §§ 102, 103, and 112.

[11] In 1995, and again in 2001, the PTO issued guidelines relating to the "utility" standard of 35 U.S.C. §101. *See, e.g., Utility Examination Guidelines,* 66 Fed.Reg. 1092 (Jan. 5, 2001). Under these guidelines, the PTO has demanded applicants identify a specific, substantial and credible utility for their inventions. The PTO has supplemented these guidelines with training materials that illustrate how to apply the standards properly. *See* **http://www.uspto.gov/web/offices/pac/dapp/mpep_examguide.html**.

[12] In 2001, the PTO issued guidelines on application of the "written description" requirement of 35 U.S.C. §112, first paragraph. *See Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, P1, "Written Description" Requirement*, 66 Fed. Reg. 1099 (2001). As applied by the PTO, the guidelines require applicants to provide a comprehensive written description of what they perceive their invention to be as of the filing date of the patent. Again, the PTO followed the guidelines with training materials that provide examples of commonly encountered scenarios, with clear guidance on when to impose rejections. *See* **http://www.uspto.gov/web/offices/pac/dapp/mpep_examguide.html**.

"non-obviousness" of an invention – a measure of whether the pre-existing knowledge in the prior art makes an invention "obvious" or not – under 35 U.S.C. § 103.[13] The effect of these changes in law and examination practice has made it increasingly difficult to emerge from the examination process with claims that grant broad rights beyond the specific protein sequence that was tested and evaluated before the original patent application was filed, or slight variations relative to that sequence.[14]

Biotechnology patents must be pursued promptly after an invention is made. If an inventor waits to file the application, and the research becomes public, it can prevent the patenting of the invention, both within and outside the United States. This pressure to file early, however, creates a tension with the potential commercial value of the patent, as patent rights can only be used, as a practical matter, after FDA approval of the innovator's product or an infringing biological product. In other words, given that the term of a patent runs 20 years from the original filing date of the patent, and that it can take 12 to 15 years to obtain marketing approval for a new biological product, the resulting period of "effective" term remaining after the BLA for the biological product is approved thus can be quite short.

---

[13] *See, e.g.*, *KSR Int'l. Co. v. Teleflex Inc.*, 550 U.S. 398 (2007); *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009); *Leapfrog Enter., Inc. v. Fisher-Price, Inc.*, 485 F.3d 1157 (Fed. Cir. 2007).

[14] Patents claiming proteins or nucleic acids often employ a concept of "homology" relative to a specified sequence. For example, a patent may claim all proteins having an amino acid sequence that is 99% homologous to a specified sequence. The PTO has issued extensive guidance to its examiners and the public regarding evaluation of "homology claims" during the examination process. *See, e.g.*, PTO Written Description Guideline Training Materials, Revision 1 (March 25, 2008), available at **http://www.uspto.gov/web/menu/written.pdf**; PTO Revised Interim Utility Guidelines Training Materials, available at **http://www.uspto.gov/web/offices/pac/utility/utilityguide.pdf**.

Moreover, as part of the Hatch-Waxman Act package in 1984, Congress statutorily exempted from infringement any activities conducted by the developer of a new drug or biological product that are reasonably related to obtaining FDA approval of the product.[15] This means that the owner of a patent covering an infringing drug or biological product cannot stop infringements arising solely from the FDA approval-related activities of a biosimilar manufacturer.

Recognizing both of these factors, Congress, as part of the original Hatch-Waxman package, provided these patent owners with a way to restore lost "effective" patent term caused by the requirement for pre-market regulatory review. The patent term extension provisions permit a patent owner to recover up to five years of effective patent life, subject to several limitations. First, the overall effective patent term after the extension cannot exceed 14 years, regardless of how long the regulatory review of the product took. Second, only the initial approval of a biological product can serve as the basis for restoration. Third, the rights granted by the extension are limited to those that correspond to the approved product. And, finally, only one patent may be extended on the basis of a regulatory review period, and no patent may be extended more than once.[16]

---

[15] Congress exempted from infringement those acts that are reasonably related to obtaining approval of a new drug, biological product or medical device. *See* 35 U.S.C. § 271 (providing that "It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention … solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products."); *see also Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193 (2005).

[16] The limitations of the existing patent term restoration authority under 35 U.S.C. § 156 raise a number of questions concerning biological products. For example, biotech companies often obtain, using special accelerated approval procedures, a first approval of a new biological product for a relatively narrow indication that affects fewer, but desperately ill patients. This first approval, however, by statute, serves as the basis of any restoration period request. Thus, a company that conducts substantially longer, more complex and more expensive clinical investigations for the primary indication of a biological product cannot secure a patent term restoration corresponding to the much longer regulatory review period required

The parameters of the patent term restoration provisions of the Hatch-Waxman Act in 1984 reflect Congress' determination that an effective patent term of 14 years following approval of the product is an appropriate period of patent exclusivity.[17] In enacting these provisions, Congress acknowledged that – unlike most other industries – the pharmaceutical industry rarely benefited from the full length of the standard patent term (then 17 years from grant of the patent) due to the long development and regulatory approval process for drugs. Given that Congress has previously concluded that 14 years of patent protection is appropriate for drugs and biological products, any statutory formula that allows for biosimilars should at least guarantee that same degree of effective market protection – and, for the reasons discussed above, that protection can be accomplished most predictably through data exclusivity.

C. Patents Alone Cannot Provide the Incentives Necessary to Encourage Today's Level of Innovation and Clinical Development of Biological Products in a New Biosimilar Approval System

Reliance on the patent system alone in a future system including a biosimilar pathway will prove insufficient to stimulate the scale of continued innovation and clinical development of biologic products that exists in today's system. A "patents only" approach also ignores past and ongoing changes in patent law and the

---

for that primary indication. Patent term restoration rights are also limited to the rights in the "product." Some have questioned whether the patent term restoration rights would cover a biosimilar product that has a different molecular structure relative to the innovator product. Revisions to these provisions of 35 U.S.C. § 156 to preserve the intended functioning of the patent term restoration authority, or to permit greater latitude for biotech companies to select the basis of the extension, may be warranted incidental to review of a new follow-on biologics ("FOB") approval system.

[17] Extension is calculated by taking: ½ of the time spent diligently from the investigational new drug application effective date to new drug application ("NDA") submission; and the full NDA review period; patents cannot be extended by more than five years. The patent extension also cannot result in a patent that has a term of more than 14 years post-NDA approval.

fundamental changes to the biotechnology business model that would be implemented by an abbreviated approval pathway, and that patents and regulatory standards will interplay very differently under a biosimilar pathway compared to how they operate today under the Hatch-Waxman framework for generic small molecule drugs.

Under the 1984 Hatch-Waxman Amendments to the Federal Food, Drug and Cosmetic Act, a generic version of a small molecule drug may be approved for marketing only if its active ingredient is the "same" as the innovator product.[18] Thus, any patents that cover the innovator's drug molecule necessarily apply to the duplicate, generic version, and a generic may not enter the market until the innovator's patent expires. Indeed, the manufacturer of a generic drug may not have it both ways – it camot gain FDA approval of its product by demonstrating that the active ingredient is the same as the innovator product and then turn around and claim in the patent context that it is different.

Overall, the robust framework of patents, data exclusivity, and stringent generic drug approval standards under the Hatch-Waxman Act has resulted in a dynamic, innovation-driven and highly competitive market for small molecule drugs. In this market, through this combination of measures, innovator small molecule drugs enjoy substantial periods before generic competition commences. The Congressional Budget Office found that the average period of time for marketing of a drug product with patent protection before generic competition begins is 11.5 years,[19] and new molecular entities, on average, are marketed in the U.S. for 13.5 years before the entry of generic competition.[20]

---

[18] FDCA § 505(j); FDA, Critical Path Opportunities for Generic Drugs (May 2007)

[19] Congressional Budget Office, A CBO Study: How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry, July 1998, Chapter

Under the statutory framework being considered for biosimilars, the same array of measures will not consistently produce equivalent periods for innovator biological products. Unlike a small molecule generic drug, a biosimilar will not be required to be the "same" as the innovator product. Instead, it will only have to be "similar" or "highly similar" to the innovator product. While the meaning of this standard may vary between legislative proposals, there is no question that it falls short of the degree of sameness required of generic drugs relative to their pioneer reference products. In fact, under some current legislative proposals, the requirements for similarity are defined in a way that would allow for approval of biosimilars with significantly different structures or other differences relative to the innovator product.

As a result, under these proposed approval schemes, a biosimilar product will frequently achieve what has been expressly prevented by the design of the Hatch-Waxman Act; namely, a finding that the biosimilar product is "sufficiently similar" to the innovator biologic to justify reliance on the safety and effectiveness of the innovator's clinical evidence (and thereby secure expedited approval of the biosimilar product), yet sufficiently "different" to avoid patent infringement. This paradox will permit a biosimilar product to bypass the mechanisms that Congress has designed to encourage innovation and investments in clinical development of the innovator product, and to thereby get on the market well in advance of innovator patent expiration at a fraction of the innovator's development costs.

Four, "The Effects of the Hatch-Waxman Act on the Returns from Innovation." A more recent study found that this period is actually closer to 13 years. *See* Charles Clift, *The value of patent term extensions to the pharmaceutical industry in the USA*, 5 J. GEN. MED. 201 (2008).

[20] Henry G. Grabowski and Margaret Kyle, *Generic Competition and Market Exclusivity Periods in Pharmaceuticals*, MANAGERIAL AND DECISION ECONOMICS (*forthcoming*).

The impact of a less stringent "similarity" approval standard is compounded by the fact that patent claims on biologics must often be narrowly drawn to the specific innovative aspect (*e.g.*, a specific protein or nucleotide sequence) to be allowable. The unpredictability inherent in the biological products, in particular, leads to stringent applications of the patent law standards of utility, written description and enablement.[21] In turn, this prevents issuance of broad "genus" claims that cover a wide range of structural variations to the particular protein sequence discovered and tested by the innovator.[22] By contrast, a group of structurally related bioactive molecules (a so-called genus) that are the basis of most NDA drugs can often be covered by a single patent claim.[23]

Due to a series of court decisions, the patent law is leading inexorably to even narrower patent claims. While this trend impacts all inventions, it has especially significant consequences for protecting innovator biologics in a new biosimilar regime. Developments that lead to narrower patent claims for biological products and how they are made will create wider gaps that may enable a biosimilar to exploit the innovator's investments in clinical development and

---

[21] *See, e.g.*, *Elan Pharm., Inc. v. Mayo Found. for Med. Educ. and Research*, 346 F.3d 1051 (Fed. Cir. 2003); *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

[22] The "utility," "written description," and "enablement" requirements of the Patent Act are interpreted more stringently for biotechnology inventions than for most other technologies. Moreover, patents cannot claim something that occurs naturally. Because many biotech products are "artificial" (recombinant) versions of naturally occurring proteins, the patent claims must be narrowly crafted (*i.e.*, limited to specific isolated and purified DNA sequences, proteins, or clonal cell lines) in order to avoid encompassing naturally produced molecules. In contrast, most of the small medicinal molecules are synthetic, and because they these molecules were not pre-existing in nature, broader claims can be secured covering a range of structurally similar molecules.

[23] The active ingredient identity requirements in the FDCA approval procedures for generic drugs also lessens the necessity of broad "genus" patent protection in conflicts between an innovator and a generic drug manufacturer.

thereby receive regulatory approval while still eluding the innovator's patents.[24] Furthermore, the sheer size of biologic products – often several hundred- or thousand-fold larger than small molecule drugs – increases the number of possible ways of altering the product such that it would be similar enough to the original product to qualify as "biosimilar" but different enough to be outside the scope of the patents on the original product. Disputes over patent claim coverage that are likely to arise from this situation would lead to an increase in litigation expenses and add to the uncertainty that biotechnology companies face.

Because of differences in available patent protection and less stringent biosimilar approval standards, the mix of robust patents and data exclusivity periods currently provided to small molecule drugs will prove incapable of preserving the incentives necessary for discovery and clinical development of biologic products that exist today in the biotechnology industry. Instead, significantly longer data exclusivity periods are needed to offset this patent uncertainty and preserve the balance that Congress found necessary to stimulate innovation in the small molecule pharmaceutical industry.

In crafting a biosimilars regime, it is especially important to err on the side of incentivizing innovation due to the unique elements of the biotechnology industry, which is largely comprised of small, unprofitable, privately-funded start-up companies without reliable revenue streams. These companies are heavily dependent on private capital to support their research and development activities. They must bear not only the enormous costs and high degree of uncertainty of their product development, but must make the case that they should be given, over and

---

[24] Bruce S. Manheim, Patricia Granahan, and Kenneth J. Dow. *'Follow-On Biologics': Ensuring Continued Innovation in the Biotechnology Industry*, HEALTH AFFAIRS (March/April 2006).

over again, additional investments of private capital they need to continue their innovative research and development work. Thus, compared to the broader pharmaceutical industry, biotechnology companies are more vulnerable to factors that make securing investments more difficult, particularly those that could result from a poorly-crafted biosimilars regime.

III. Addressing Issues Concerning Effective Data Protection and Patent Protection Measures in Biosimilar Legislation

BIO supports the establishment of an appropriately balanced system for approval of biosimilar products. Of course, the devil is in the details. Intellectual property issues that must be resolved include the duration and structure of data exclusivity provisions, and the availability and nature of measures to resolve patent disputes prior to approval of the biosimilar product.

A. BIO Positions on Pending Legislation Concerning Biosimilar Approval Procedures

The two bills pending before the House (H.R. 1548 and H.R. 1427) reflect highly divergent perspectives on data protection and procedures for addressing patent conflicts.

1. BIO Strongly Supports the Data Exclusivity and Patent Provisions in H.R. 1548

As noted earlier, the data exclusivity measures in H.R. 1548 will provide an effective structure for and duration of data exclusivity for innovators. BIO strongly supports both the structure and duration of data exclusivity that would be provided under H.R. 1548 for innovator biological products. BIO believes those provisions will provide strong incentives to conduct both the original development of a new biological product, and to continue clinical research to extend use of the biological product to address additional unmet medical needs of patients.

H.R. 1548 also would establish balanced and inclusive measures concerning patents implicated by a biosimilar product. Significant features of this system, which BIO supports, include:

- A procedure that enables the BLA holder and third-party patent owners to identify relevant patents based on information provided by the biosimilar applicant under appropriate conditions of confidentiality.[25] This structure will permit small biotech companies and universities to participate in pre-marketing patent identification procedures, and will not require these entities to have their interests represented exclusively by the BLA holder. This makes sense, given that in many instances patents implicated by the biosimilar product will not be assigned to or subject to the control of the BLA holder.

- A requirement for the biosimilar applicant to take a position, as is done in the Hatch-Waxman Act, on each patent that has been identified which expires after the end of the data exclusivity period for the innovator's product. The biosimilar applicant must either request the FDA to defer grant of final approval until the expiration of a particular relevant patent, or assert that the patent is invalid or not infringed. Like the Hatch-Waxman Act, doing this creates the artificial act of infringement necessary to provide standing for suit, in light of the §271(e) exemption, which exempts activity done to generate information for FDA review from infringement.

- A requirement that a patent owner commence suit within 60 days of receiving a certification adverse to the patent by the biosimilar. It also preserves the ability of a biosimilar applicant to commence a declaratory judgment action at an appropriate time during this process

[25] The FTC incorrectly suggests that requirement is unprecedented, and could lead to anticompetitive conduct. *See* Fed. Trade Comm'n, EMERGING HEALTH CARE ISSUES: FOLLOW-ON BIOLOGIC DRUG COMPETITION (June 2009) at p. 57-59, *available at* www.ftc.gov/os/2009/06/P083901biologicsreport.pdf. In reality, patent owners routinely obtain this type of information from patent defendants in litigation, subject to the terms of a protective order issued by a court. Moreover, current law already provides analogous procedures. Under the Hatch-Waxman Act, a generic drug applicant may make an offer of confidential access of its ANDA to the NDA holder during the 45-day period where the NDA holder must commence suit under any listed patents that the generic has challenged. *See, e.g.*, FDCA § 505(j)(5)(C)(i)(III). The provisions of H.R. 1548 simply parallel these routine practices followed in litigation and under the Hatch-Waxman Act.

to resolve questions about any patents, which the patent owner has not asserted but in respect of which the biosimilar applicant made a certification.

- A regulatory linkage provision directing the FDA to defer approval of the biosimilar application until the date a patent found to be valid and infringed expires, provided that the district court does so prior to the date that the data exclusivity in the product has ended.

Notably, H.R. 1548 does not include a provision imposing an administrative deferral of approval of a biosimilar application during the pendency of the patent litigation, as is done in the Hatch-Waxman Act. Instead, it provides a powerful incentive for patent owners to conclude the litigation as rapidly as possible. This incentive provides regulatory linkage for those entities that obtain a district court ruling on the patent prior to the expiration of the data exclusivity period. The structure of this provision will encourage the parties, particularly the patent owner, to promptly conclude the litigation. In addition, the structure of these provisions, which provides that the FDA will be able to grant final approval to the biosimilar application at the expiration of the data exclusivity period of the innovator, will ensure that ongoing patent litigation will not affect the timing of FDA final action on biosimilar applications.

H.R. 1548 also does not contain measures that unfairly sanction patent owners who do not comply with administrative procedures relating to patent notification, or that unfairly tilt the litigation process in favor of one party at the expense of the other. Instead, under the structure of the bill, a patent owner that does not accurately identify patents or timely participate in the notification process concerning identified patents will not be able to secure regulatory linkage for those patents. The bill thus preserves the autonomy of the courts to manage litigation, and does not attempt to change well-established rules governing civil procedure, evidence and venue.

2. BIO Opposes the Data Exclusivity and Patent Provisions in H.R. 1427

The data protection provisions in H.R. 1427, in contrast to those in H.R. 1548, are extremely limited in duration and subject to conditional eligibility and post-approval developments. These measures will not provide effective incentives for initial development and approval of a new biological product or for the continued development of new indications of biological products. Indeed, under the bill's provisions, only those products that are "not similar" to existing products could receive any period of data exclusivity. Plainly, these provisions will not provide the certainty and clarity that biological innovators require *before* they commence the risky, expensive and difficult process of discovering and clinically developing a new biological product or treatment.

The patent provisions in H.R. 1427 are similarly unbalanced and will prove ineffective in achieving the goal of identifying and promptly resolving patent disputes prior to approval and launch of a biosimilar product. These provisions would inappropriately limit and distort the standards governing venue and standing in patent disputes, and impose harsh punitive sanctions on patent owners – including on patents expressly excluded from the patent notification procedures – to enforce compliance with administrative measures governing notice about patents. These administrative sanctions, would statutorily limit the exclusive rights conferred by the patent in unprecedented ways in American patent law. For example, a patent owner who attempted to timely comply with the administrative notification process, but failed, would be foreclosed from obtaining injunctive relief and would have its patent remedies limited to recovery of a reasonable royalty regardless of the actual harm caused by the infringement. The sanctions for administrative errors that would lead to a failure to identify a relevant patent –

whether owned by the BLA holder or not – would result in a sanction that would entirely foreclose use of the patent against any infringer.[26]

These curtailments of the patent property right are unprecedented in American patent law and reflect an overt bias against the use of legitimate, constitutionally mandated patent rights. They also will operate to make biotechnology patents less effective in preventing the unauthorized use of the inventions that these patents are supposed to protect, which will run afoul of U.S. commitments under the WTO Agreement on Trade Related Aspects of Intellectual Property (TRIPS). In particular, Article 27.1 of TRIPS prohibits discrimination in the availability and enjoyment of patents rights based on the field of technology of the invention. If these measures pass, they would single out biotechnology patents only for limitations that undoubtedly alter the capacity of these patents to prevent unauthorized use of the protected technology, and thus run afoul of this important international standard.

H.R. 1427 also provides no incentives for patent owners to participate in the scheme that has been designed, including, critically, no regulatory linkage for the successful assertion of a patent against a biosimilar applicant. Instead, the bill expressly provides that the FDA is to approve the biosimilar application regardless of whether patent litigation has been commenced or concluded. Designing a process, which, on the one hand, acknowledges that valid patents may be infringed by a biosimilar product, yet, on the other hand, actually makes it harder to enforce or use those patent rights, provides no incentive for patent owners to expeditiously

[26] H.R. 1427 takes the unprecedented step of entirely nullifying the patent property right to enforce the administrative notification provisions of the bill. Specifically, the bill proposes to add to the patent statute new §271(e)(6)(C), which would provide that "the owner or licensee of a patent that should have been disclosed [under the notification process of the bill] but that was not timely disclosed … may not bring an action under this title for infringement of the patent."

conclude litigation, nor does it remove uncertainty over the status of the biosimilar product in light of these valid patents.

B. The FTC Has Made Radical Proposals Not Supported by Evidence or 30 Years of Experience of the Biotechnology Industry

The FTC, in its recent report on intellectual property issues in biologics, has missed an opportunity to constructively advance the legislative discussions about intellectual property issues in a new biosimilar approval pathway. Instead, it has staked out radical positions that ignore the substantial experience of industry and the extensive economic evidence about development of biological products that was provided to the Commission. In addition, several of its critical assumptions rest on serious errors about the nature of biotech patent rights and the operation of data exclusivity provisions.

The FTC reached two conclusions following its solicitation of public input: (i) no period of data exclusivity can be justified by the FTC's understanding of the economics of the biotechnology industry, and (ii) no procedure should be provided to permit early resolution of patent conflicts before the actual commercial launch of a biosimilar product. In essence, the FTC takes the position that the nature of competition between innovator and biosimilar manufacturers in the future will be identical in character and effect as that which exists today between innovative biological producers. As a result, the FTC concludes that no changes are needed to accommodate what nearly all commentators recognized will be a fundamentally different competitive landscape in the biotechnology industry.

BIO believes adopting legislation based on the FTC's flawed and unsound theories will fundamentally erode the incentives for developing new biological

products, for conducting clinical research to bring these products to market, and expanding their use to new indications.

1. The FTC Has Incorrectly Portrayed the Nature and Effects of Competition between Biosimilar and Innovator Companies

BIO recognizes that the nature of competition between an innovator and biosimilar producer in the future will not be the same as that which exists today between small molecule pioneer drug manufacturers and generic drug companies. For example, the requirement that the biosimilar producer conduct some amount of clinical investigations on its product, the higher overall costs and greater complexity of producing biological products, and critically, the lack of a current scientific basis for treating the biosimilar product as being interchangeable with the pioneer biologic, all will contribute to greater barriers to market entry for biosimilar manufacturers than those faced by generic drug manufacturers. Biosimilar manufacturers also will likely have to engage in some amount of marketing and promotion of their products, in addition to leveraging the lower costs of producing them, to achieve significant market penetration relative to generic drug products.[27]

The FTC, however, flips this point on its head, concluding that, because the nature of competition between innovator and biosimilar manufacturers will not be the same as that between innovator and generic drug manufacturers, somehow this means there will be no economic impact of an abbreviated biosimilar pathway

[27] Once patent and data exclusivity expires in a pioneer small molecule drug, conversion of the market to generic versions of the drug is essentially automatic. *See, e.g.*, http://energycommerce.house.gov/Press_110/110-ltr.050208.respto040308.FTC.pdf (observing that as a result of the policies of public and private health plans and state substitution laws, generic manufacturers typically capture anywhere from 44 to 80 percent of branded sales within the first full year after launch of lower-priced generic products).

sufficient to justify creating any new incentive measures for biotech innovator companies. The FTC makes several fundamental errors in reaching this conclusion.

The first, critical error the FTC makes is to equate the nature of future competition between biosimilar and innovator manufacturers with the competition that exists today between only innovator companies. In reality, there will be a fundamentally different type of competition in the future when a biosimilar pathway is established. Indeed, to conclude otherwise, the FTC must assume the central objective of creating a biosimilar pathway (*i.e.*, to substantially decrease the costs, risks and uncertainty of bringing a competing biological product to market) will fail. In other words, despite acknowledging that a biosimilar pathway will create an entirely new form of competition within the biotechnology industry, and will undoubtedly have a negative impact on the market of innovator companies, the FTC somehow concludes that no new incentives of any kind should be included in the new regime to preserve today's incentives for biotechnology innovators.

The FTC also incorrectly assumes that patents alone are the means by which innovator companies justify their decisions to develop new biological products and treatments. They are not. Central to the decision of a biotech company to undertake development of a new biological product, or to continue clinical development of an existing product, is assessing the risk of a competitor developing a competing product. That risk today is defined in terms of an environment where every company faces the same level of risks and costs of development. Patents cannot today, and will not in the future, provide certainty regarding competition with these products.

Simply put, the picture created by the economic risks that first innovators see in today's market from competition from other innovators has no relevance to the picture they will see when a biosimilar approval pathway exists. Indeed, virtually no industry outside of pharmaceuticals does the government permit wholesale "free riding" on the investments of the first innovator to market, much less encourages it to promote price competition. How the FTC concludes that that there will be no impact on innovation from this fundamental change to the nature of competition within the biotechnology industry is simply baffling.

The FTC also phrases its question in a way that is destined to lead to the wrong answer. The question is not whether Congress should enact provisions that delay entry and restrict competition – of course, Congress should not. The proper question is what measures must Congress include in a system designed to facilitate creation of a fundamentally new type of competition in the biotechnology industry (*i.e.*, between biosimilar and innovator biologics manufacturers) without substantially diminishing today's incentives for innovators to invent, develop and bring new biological products and treatments to market, for the benefit of patients. The answer, provided by rigorous, peer reviewed economic research, is a substantial period of 12 to 14 years of data exclusivity. Nothing other than conjecture supports the FTC's unfounded assertions.

2. The FTC Incorrectly Describes the Capacity of Patent Rights Alone to Encourage Initial and Ongoing Clinical Research in a Biosimilar Market

As noted above, while patent rights can be secured to protect biotechnology products, these patent rights tend to be narrow and centered on the specific product and features of the innovator biological product. A biotech company, or an investor considering supporting that company, evaluates the risk that these narrow

patents will not block competition by structurally similar biological products by assuming that few, if any, of those products will reach the market, and they will do so only after the first product has enjoyed a substantial period of commercial success. The considerable market barriers in today's *innovator-only* market thus operate to offset the risks created by these narrow or uncertain patent rights. If substantial data exclusivity provisions are not included in a future biosimilar approval system, there will be no "offset" to these patent risks.

There is no question that biotechnology companies assert their patents against competitors today to prevent the unauthorized use of the protected technology, and will do so in the future against biosimilar manufacturers. However, the capacity of these patents to prevent unauthorized use of the innovator's technology is uncertain. And it is this uncertainty, coupled with a fundamentally different form of competition that a biosimilar approval pathway will create, that demands additional measures to incentivize innovation, particularly data exclusivity. The FTC's conclusions to the contrary are based on its incorrect assumptions about the scope and effectiveness of biotechnology patents.

First, the FTC asserts that patent claims can be secured today that cover proteins or nucleic acid sequences that vary up to 30% relative to the innovator's product, asserting that "an FOB drug product's molecule could differ by up to 30 percent and still infringe the patent protecting the pioneer product."[28] In patent claim terms, this is a claim that would cover a polypeptide or nucleic acid sequence that is "70% homologous" to a reference sequence.

[28] *See* FTC Report at 36-37, citing Chris Holman, 17 ALB. J.SCI & TECH, 1, 44 (2007).

The FTC is simply wrong in asserting that the PTO routinely grants patent claims conferring this breadth of protection. Importantly, the FTC does not provide any analysis from its sister agency, the PTO, about the PTO's actual practices in granting patents on protein or nucleic acid sequences to support these assertions. It also undertook no independent analysis of issued patents, whether historical or under current practices, and elected to ignore the extensive evidence provided by patent practitioners about their current experiences with PTO practices concerning "sequence homology" claims. This is surprising, given how important the FTC's assumption of effective patent protection being available is to its conclusion that no new measures will be needed to preserve incentives for biotechnology innovation once a biosimilar pathway has been established.[29]

What the evidence shows is that the PTO historically has taken a very conservative stance on "homology" claim breadth. Indeed, the PTO, particularly after adoption of more stringent written description and utility standards in 2000, demands extensive evidence from applicants to justify protein or nucleic acid "genus" claims. Under these examination practices, claims are usually limited to the specific protein or nucleic acid sequence discovered by the inventor, or at best cover a narrow range of variants – usually proteins or nucleic acids that are 95% to 98% identical to the reference sequence.

This description of actual experiences before the PTO was clearly communicated by nearly every patent practitioner who participated in the FTC's hearings and public notice process. Inexplicably, the FTC not only chose to ignore this evidence, but relied on it being incorrect to justify a central assumption of its

[29] The PTO maintains a special office, the Patent Technology Monitoring Team (PTMT), to assist other agencies and the public in obtaining information on patenting trends and practices. The PTMT conducts analysis and publishes reports on patents, and patenting trends; *See* http://www.uspto.gov/web/offices/ac/ido/oeip/taf/tafp.html.

paper; namely, that broad patent protection is available now, will be available in the future, and will enable innovators to prevent the unauthorized marketing of biosimilar products for decades to come.

The FTC similarly dismissed arguments from experienced patent litigators who identified challenges in using protein or nucleic acid sequence claims to prevent unauthorized marketing of biosimilar proteins. Instead, the FTC reviewed outcomes from litigation involving patents issued in the late 1980s and early 1990s, which did not employ "homology" limitations, and generally did not involve relevant (if any) questions of infringement.[30] Somehow it concluded "biotechnology drug product claims have been construed so that accused products have been found to infringe even when they have varied from the patentee's corresponding product."

Actual experience in litigating protein or nucleic acid patent claims refutes this central assumption of the FTC, and shows that substantial challenges do exist to proving infringement of a sequence claim even where the changes of the infringing product are relative minor.[31] The FTC thus compounded its errors about the nature of claims being issued *today* – which will be the only patents relevant in

---

[30] FTC Report at 37. Examples of cases the FTC cites to support its assertion include *Genentech, Inc. v. Chiron*, 112 F.3d 495 (Fed. Cir. 1997), which did not involve a question of infringement, but concerned the scope of claims involved in an interference proceeding; *Amgen v. Chugai* 927 F.2d 1200 (Fed. Cir. 1991), concerning a patent issued in 1987 (*i.e.*, long before current written description and utility standards) and in which infringement was not a central issue.

[31] *See Hormone Res. Found., Inc. v. Genentech, Inc.*, 904 F.2d 1558 (Fed. Cir. 1990); *Novo Nordisk of North America, Inc. v. Genentech, Inc.*, 77 F.3d 1364 (Fed. Cir. 1996); *Genentech, Inc. v. Wellcome Found. Ltd.*, 29 F.3d 1555 (Fed. Cir. 1994); *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313 (Fed. Cir. 2003); *Biogen, Inc. v. Berlex Labs., Inc.*, 318 F.3d 1132 (Fed. Cir. 2003); *Genzyme Corp. v. Transkaryotic Therapies, Inc.*, 346 F.3d 1094 (Fed. Cir. 2003). These cases illustrate that courts have indeed sometimes taken a very a narrow view of biotechnology patent claims, under which even very 'close' products were determined not to infringe a valid patent.

future patent litigation concerning biosimilar products – by citing irrelevant cases and ignoring numerous decisions that illustrate the challenges and uncertainty of proving infringement of proteins having even minor variations relative to a claimed protein or nucleic acid sequence.[32] Current PTO practices and experiences from past litigation thus show, contrary to this critical FTC assumption about patent certainty and effectiveness, that substantial challenges will be encountered by innovators attempting to use homology patent claims to prevent market entry by structurally distinct biosimilar products.

3. Preventing Enforcement of Patents until after Marketing of a Biosimilar Product Begins Will Cause Undesirable Confusion in the Market and Undermine Patent Rights

Nearly all stakeholders in the biosimilar debates support inclusion of procedures to identify and resolve patent issues before a biosimilar is approved and placed on the market. The reasons are simple; patent litigation commenced only after the biosimilar product is launched will lead to a longer period of uncertainty about patents and will cause greater market disruptions concerning the biosimilar product. Providing a way to start patent litigation before the biosimilar product is on the market (*i.e.*, during the data exclusivity period of the innovator and while the biosimilar product cannot be marketed because it is undergoing review by the FDA) will benefit patients, physicians, insurers, follow-on manufacturers and innovators alike. Indeed, without such a mechanism, follow-on products will enter the market under a cloud of patent uncertainty, and, once on the market, patent

[32] The FTC also entirely ignored the challenges of proving infringement under the "doctrine of equivalents" under current law, where a claim amendment made before the PTO to narrow a homology claim will create substantial obstacles to securing relief against a protein or nucleic acid sequence that lies outside the literal scope of the patent claim. *See, e.g.*, *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722 (2002).

disputes over such products will not allow patients, physicians, and insurers to assume there will be long-term availability of the biosimilar product.

Congress has recognized the benefits of starting litigation to resolve patent disputes before generic drugs enter the market. In 1984, as part of the Hatch-Waxman Act, it created special procedures for starting patent litigation before generic small molecule drugs are approved. Under this system, patent owners identify patents that are relevant to its drug. Due to the "sameness" requirement integral to generic drug approval, those patents will be relevant to any generic version of the innovator's drug. Generic drug applicants then must take a position on those "listed" patents; either wait until they expire, or identify specific reasons why the patents are invalid or would not be infringed by the generic product. If the generic applicant challenges a listed patent, the patent owner may promptly commence suit, and litigate the patent. While this litigation is ongoing, the FDA will not grant final approval to the generic drug application, provided that litigation is concluded within 30 months of the generic drug providing notice about the patents. If the patent owner ultimately prevails, demonstrating its patent is valid and infringed by the generic drug, the FDA will defer the final approval of the generic drug application until the expiration of the infringed patent.

The patent resolution provisions established by the Hatch-Waxman Act have generally served their intended purpose of reducing uncertainty for innovators and generics alike, which helps explain why there is broad support among stakeholders for inclusion of similar procedures in a future abbreviated biosimilar approval system. Despite this broad support, the FTC argues that a pre-marketing approval patent litigation procedure should not be provided in a future biosimilar approval system. Like its other recommendations, this recommendation is based on flawed assumptions about patent litigation and the broader public interest.

One justification the FTC provides for its position is its conclusion that the rapid market erosion following generic drug entry with small molecule drugs will not occur following the launch of a biosimilar product.[33] The Commission relies on this assumption of slow market erosion to assert, in essence, that patent owners will have plenty of time to litigate their patents while the biosimilar product is on the market before significant economic harm is caused to the innovator. This argument ignores the impact of patent uncertainty around the continued marketing and availability of the biosimilar product, the principle justification that has led most stakeholders to call for a pre-launch patent procedure. It also rests on shaky economic and market behavior assumptions that only the FTC has advanced.[34]

The FTC also somehow manages to conclude that patent owners will be able to effectively enforce their patents without any new procedures, attempting to analogize innovator-biosimilar patent disputes to those between biotech innovator companies, or between patent owners and infringers in other industries. The Agency's attempt to analogize biosimilar-innovator litigation to past litigation between biotech innovator companies is based on a flawed understanding of the circumstances of those cases,[35] and ignores the economic symmetry that existed

---

[33] *See* FTC Report at 52-53.

[34] The FTC data minimizes the potential market impact, based on early information from biosimilar experiences and the 10-year scoring window used by most studies. The FTC uses this same argument to support the notion that patent design arounds, even if they occur, will not harm innovators sufficiently to support the need for data exclusivity. For the same reasons, that analysis is likewise flawed.

[35] The FTC mischaracterizes past cases involving biotech innovators, incorrectly suggesting that this litigation occurs only after the infringing product has been approved by the FDA. *See* FTC Report at 54 ("By contrast, if litigation were to begin post-approval, the way in which branded biologic competitors resolve patent issues currently, …"). In reality, most of the cases cited by the FTC involved situations where the product accused of infringement had not been approved at the time of the litigation. *See, e.g.*, *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200 (Fed. Cir. 1991) (neither Amgen nor Chugai product approved at time of litigation); *Amgen Inc. v. Hoffmann-LaRoche Ltd.*, 2008 U.S. Dist. LEXIS 77343 (D. Mass 2008) (accused product not approved at time of litigation).

between these innovator litigants, which will not exist in litigation between innovator and biosimilar manufacturers. The FTC also ignores the high frequency of patent settlements in biotech cases, which reveals the value innovator companies place on patent certainty after having made significant investments in product development. And, critically, the FTC fails to acknowledge that forcing patent disputes to commence only after a biosimilar has been placed on the market will undermine the value of patent exclusivity, because it will raise the prospect that a court will not enforce the exclusive rights of the patent by issuing an injunction preventing the continued marketing of the biosimilar, even if the patent is found valid and infringed.

The FTC's attempt to analogize innovator-biosimilar litigation to experiences of patent owners in other industries is similarly based on flawed understandings. Two significant factors differentiate innovator-biosimilar litigation from litigation in other industries. First, the Bolar exemption prevents many innovator and biosimilar manufacturers from litigating patent disputes where the biosimilar's pre-approval activities are reasonably related to securing FDA approval for the biosimilar product, and thus are exempt from patent infringement. No such restraint is placed on patent owners in other industries, meaning that a patent owner can commence litigation to enforce its patent rights as soon as a patent owner becomes aware of the infringer's plans to commence marketing an infringing product. Second, other industries do not operate within a statutory scheme that is designed to encourage copying of the innovator's product and free-riding on the innovator's immense pre-market investments. And, the market disruption following removal of an infringing feature from a non-medicinal product, such as a consumer electronics product, cannot be compared to removal from the market of a biosimilar product.

The FTC also claims that a pre-approval patent notice and litigation procedure will be unlikely to succeed in providing patent certainty, citing a variety of theories.

- It asserts that innovators with "vulnerable" patents will benefit from a system where these patents will only have to be litigated after the biosimilar is approved, reasoning, in essence, that these "vulnerable" patents would not be invalidated or held not infringed as early as they would under a pre-approval challenge process.[36] What this hypothetical actually demonstrates is that biotech innovators need a substantial period of data exclusivity to offset risks of inadequate patent estates.

- The FTC appears to believe that a patent owner will have different incentives in pre- vs. post-approval patent litigation, suggesting that only in the latter will patent owners assert their "strongest" patents.[37] In reality, biotech companies will have equal incentives in both situations to select those patents that will deliver the best outcome in the litigation.

- The FTC observes that an early start to patent litigation "does not guarantee that patent issues will be resolved earlier…" citing the possibility that new patents will issue after the litigation starts or even after the biosimilar is approved.[38] The FTC is wrong in a very important respect. An earlier commencement of litigation will help resolve disputes sooner over the patents the innovator held *before the biosimilar application was filed* – which are the patents the FTC believes, in the absence of any data exclusivity for innovator biologicals, innovators will base their investment decisions upon and encourage biotech companies to make the investments necessary to bring the innovator biological product to market.

- The FTC asserts that the availability of a pre-approval opportunity to assert patents will encourage biosimilar companies to challenge more patents held by the innovator.[39] In reality, the biosimilar manufacturer

[36] FTC Report at 54.
[37] FTC Report at 54-55.
[38] FTC Report at 55.
[39] *Id.*

> will have to deal with all of the patents that it infringes if it elects to infringe those patents. Otherwise, the incentives that the patent system is supposed to provide innovators, and, again, which the FTC has placed such a heavy reliance upon, will not be realized by biotechnology innovators.

Other comments in this section of the FTC Report reinforce the Commission's confusion about patent litigation realities. One significant concern raised is over the provision of the biosimilar application or information about the manufacturing of a biosimilar product to the BLA holder or other patent owners in order to enable the identification of relevant patents.[40] The FTC fails to appreciate that these interactions between patent owners and potential infringers occur in every industry, and are integral to the process of deciding whether to commence an action for patent infringement. The FTC's misplaced concerns over confidentiality and inappropriate use of information provided by a biosimilar manufacturer also are simply and routinely addressed today using standard confidentiality provisions that restrict access to and use of the information to prevent the very type of harm that the FTC envisions. Indeed, current law expressly calls for the pre-suit review of an ANDA by the NDA holder incidental to the ANDA patent notification and litigation procedures of the Hatch-Waxman Act.[41]

The FTC also criticizes the capacity of this type of process to identify and resolve all relevant patents before the biosimilar product enters the market. Of course, perfection is rarely achieved in patent litigation. The question is not whether a system can be devised that will resolve with 100% certainty every possible patent dispute. Instead, it is to create a way for motivated patent owners and biosimilar applicants to identify the patents each believes is most critical, and then to begin the process of resolving disputes over those patents as early as

---

[40] FTC Report at 58.
[41] *See, e.g.*, FDCA § 505(j)(5)(C)(i)(III).

possible. The FTC's position, peculiarly, would maintain patent uncertainty for a much longer period, which somehow the FTC concludes would be beneficial to competition and consumers.

Finally, many of the FTC's competition-related concerns over a pre-approval patent litigation procedure are actually addressed in H.R. 1548. As explained above, this bill adapts the Hatch-Waxman procedures to fit the unique aspects of the biosimilar approval process (*e.g.*, the lack of a requirement for identity between the innovator and biosimilar products, the larger array of entities holding relevant patents). This bill also addresses the FTC's historical apprehension over certain features of the Hatch-Waxman system – concerns that have been largely resolved through legislative and regulatory reforms over the past decade. For example, H.R. 1548 would not impose an administrative stay of approval of the biosimilar application to permit resolution of the patent litigation. Instead, it incentivizes patent owners to expeditiously resolve litigation over key patents, providing regulatory linkage only if the patent owner prevails in the district court before the data exclusivity period for the innovator's product expires. It also preserves the ability of the biosimilar applicant to seek declaratory judgment actions to resolve concerns over patents that have not been asserted. And, critically, it permits direct participation by any patent owner, rather than attempting to funnel all potential patent disputes through the BLA holder.

4. The FTC Incorrectly Asserts that Data Exclusivity under Hatch-Waxman Is Provided Only for Unpatentable Drugs

The FTC asserts that data exclusivity provisions were implemented in the Hatch-Waxman Act to stimulate the development of new drugs when the drug molecule is not patentable, and that a longer data exclusivity period for biologics

would depart sharply from this basic trade-off because the biologic has already been incentivized through patent protection and market-based pricing.[42]

Initially, there is nothing in the legislative history of the Hatch-Waxman Act, or the statutory language of the FDCA, to support the FTC's creative re-interpretation of the Hatch-Waxman data exclusivity provisions. None of the data exclusivity provisions of the FDCA are made contingent on the absence of patent protection for a drug. In fact, the very design of the system of approval – which expressly incorporates patent resolution procedures – shows that Congress was fully aware that most drugs given data exclusivity protections will also be subject to patent rights. For example, the Act provides for early filing of an ANDA that references an NDA drug that is subject to listed patents and in which the ANDA applicant makes assertions that the listed patents are invalid or not infringed.[43] If only "unpatentable" drugs were supposed to enjoy data exclusivity protection, why would the FDCA provide for early filing of ANDA's that contain adverse patent certifications?

The FTC's confusion about the role and purpose of existing data exclusivity provisions in the FDCA reveals how fundamentally flawed its conclusions are about data exclusivity for biological products. Exclusivity provisions are available for small molecule drugs in addition to patent protection and market-based pricing, regardless of whether the drug molecule is patentable or not.[44] They do not restrict

---

[42] FTC Report at 44 ("Congress has implemented exclusivity periods to encourage the development of new and innovative drug product when the drug molecule is in the public domain, and therefore not patentable.")

[43] *See, e.g.*, FDCA § 505(c)(3)(E)(ii).

[44] Notably, the FTC report only cites BIO and Harvard Professor Roin as the sources for its contrary assertion that data exclusivity is only necessary for unpatentable drugs. Both BIO and Professor Roin, however, were making the argument that the 5 years of data exclusivity provided by the Hatch-Waxman Act was *insufficient* to ensure the development of drugs with limited or questionable patent protection, and that over-reliance on the patent system

competition except in cases where the competitor seeks to free-ride on the innovator's investment in clinical research. And, substantial, peer-reviewed economic analysis shows that a substantial period of data exclusivity will be necessary to preserve the strong incentives that exist in today's system to invest in clinical trials and continue clinical development of biological products. Simply put, a substantial data exclusivity period for biologics will ensure that the best biologics will continue to be developed – not just the biologics with the best patents.

IV. Conclusions

BIO deeply appreciates the opportunity to present its views on intellectual property issues implicated by creation of a follow-on biological pathway. BIO believes that a strong case has been made that a substantial period of data exclusivity will be necessary to preserve the incentives that exist in today's biotechnology industry to bring new biological products to market, and to continue clinical development of those products after they reach the market. BIO also supports inclusion of procedures within any new abbreviated approval procedure for biologics to permit identification and enforcement of patents, and to ensure that where valid patents are found infringed by a district court, regulatory linkage will ensure that the biosimilar product is not approved and placed on the market until that valid and infringed patent expires.

(particularly under a biosimilars regime) could create suboptimal public policy outcomes under which valuable drugs might not ever get developed due to unclear patent protection. *See* Roin, *supra* at n. 8, at p. 44 ("This gap in the patent system for drugs has created a pervasive problem in the pharmaceutical industry, causing firms to regularly screen their drugs during the research-and-development process and discard ones with weak patent protection. The harm to the public from the loss of these drugs is potentially quite significant. Congress can easily avoid this problem by ensuring that the successful completion of the FDA's rigorous clinical-trial process is rewarded with a lengthy exclusivity period enforced by the FDA.).

BIO believes H.R. 1548 provides the soundest approach for implementing the incentives that are necessary to preserve continued innovation and development of biological products, and strongly encourages the Committee to support this legislation.

ATTACHMENT A

1201 Maryland Avenue SW, Suite 900, Washington, DC 20024
202-962-9200, www.bio.org

September 30, 2008

Federal Trade Commission
Office of the Secretary
Room H-135 (Annex F)
600 Pennsylvania Avenue, NW
Washington, DC 20580
[submitted at http://secure.commentworks.com/ftc-healthcarecompetition]

Re: Emerging Health Care Competition and Consumer Issues – Comment, Project No. P083901 (Federal Register, September 3, 2008, Volume 73, Number 171, pp. 51479-51482, "Notice of Public Workshops and Roundtables and Opportunity for Comment")

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) thanks the Federal Trade Commission (FTC) for the opportunity to respond to FTC's questions regarding competition provided by developing a regulatory approval pathway for follow-on biologic (FOB) drugs. BIO represents more than 1,200 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology products, thereby expanding the boundaries of science to benefit humanity by providing better healthcare, enhanced agriculture, renewable sources of energy, and a cleaner and safer environment.

A. Regulatory Exclusivities and Follow-on Biologic Drug Competition

A1. What is the likely competitive effect of the market entry of a follow-on biologic competitor? Are there empirical models that predict the nature of this competition based on existing biologic drug product competition? How has competition developed between referenced and follow-on products in European markets? Would referenced product manufacturers lower their prices, offer discounts, and/or engage in enhanced marketing activities?

The Congressional Budget Office (CBO) has estimated the savings to the federal government of S. 1695, the Biologics Price and Competition and Innovation Act of 2007, to be $5.9 billion over

the 10-year scoring window. The findings of the study confirm many of the points made below in further response to this question. The CBO score can be found at: http://www.cbo.gov/ftpdocs/94xx/doc9496/s1695.pdf.

While BIO has not, itself, analyzed what the competitive nature of a follow-on biologics market may look like, we believe that a framework developed by Henry Grabowski and the Analysis Group can help to inform this question.[1]

This paper explains that the competitive effect of the market entry of follow-on biologic competitors will reflect the impact of an expedited approval process on both prices and utilization of each affected reference biologic product. While there is considerable heterogeneity among these innovator biologics, the paper identifies a number of critical factors that will drive these market outcomes:

- The timing of patent expiry for these products and the nature of their intellectual property protection
- The time required to develop a United States (U.S.) Food and Drug Administration (FDA) regulatory scheme, testing requirements, and any product-class guidelines following passage of any legislation
- The time required for FOB manufacturers to obtain regulatory approval (three to five years for pre-clinical and clinical testing, and one-and-a-half to two years for FDA review and approval) and to bring manufacturing capacity on-line (four to six years, likely developed concurrently with product development schedule)
- The evolution of utilization of currently approved biologics, driven by:
    - Demographics, disease incidence, medical practice, and regulatory and reimbursement practice
    - The pace and extent of uptake of next generation patent-protected products in markets where follow-on biologics have entered (limiting longer-term uptake of follow-on biologics in markets with unmet medical need)
- The nature of the competitive model in markets for biologics that experience entry by follow-on biologics (likely to be driven by the marketing of branded, proprietary products rather than the "commodity" competition based on price alone seen among generic small molecule generic drugs), and its effect on:
    - The pace and extent of uptake of follow-on products for currently marketed branded products (likely slower and less extensive than for many small-molecule drugs, or 10% to 45% follow-on product share)
    - The price impact of entry by follow-on products (limited discounts of 10% to 30% off brand, due to fewer likely market entrants than in generic drug market[2], among other factors)

[1] Grabowski, Henry, *et al.* "The Effect on Federal Spending of Legislation Creating a Regulatory Framework for Follow-on Biologics: Key Issues and Assumptions," White Paper, August 2007. See URL: http://bio.org/healthcare/followonbkg/Federal_Spending_of_followonbkg200709.pdf

[2] Due to the higher expected development costs for a FOB product versus a generic drug, fewer market entrants are expected in the FOB market than in the generic drug market. The higher development costs associated with the development of a FOB product include, but are not limited to, manufacturing costs, costs associated with clinical trials and potentially post-marketing surveillance. For a more detailed description, please see Grabowski, Henry, *et*

The paper concludes that, with respect to cost savings in the federal budget, the magnitude of such savings is highly uncertain and very sensitive not only to the specific legislative language that emerges, but also to a range of critical assumptions about scientific, regulatory, and clinical issues, the nature of competition in markets for specific biologics, as well as future intellectual property protection, and related litigation and the development of case law.

For more detailed information, the study can be found at:
http://bio.org/healthcare/followonbkg/Federal_Spending_of_followonbkg200709.pdf.

In addition, BIO has critiqued two studies (PCMA and Express Scripts) that claimed large cost savings from a follow-on biologics pathway. The studies overestimated the savings due to, among other factors:

- Misguided estimates of the timing when savings would begin to accrue
- Unreasonable assumptions on interchangeability
- Mathematical errors

BIO's critique may be found at: http://www.bio.org/healthcare/followon/20070222.pdf.

A more recent study by Sonecon, which also suggested large savings, suffers from many of the same issues as the studies by PCMA and Express Scripts. Further, it contains a methodological error that results in an overestimate of savings of at least 110%.

The discussion above focuses on the short term. In the long run, the savings estimates are more difficult to make and depend on a number of factors, including scientific advancement.

Concerning, *"How has competition developed between referenced and follow-on products in European markets,"* the European experience to date may be of only limited value in informing what the U.S. experience will be due to the fact that very little time has elapsed since the introduction of the first biosimilar in Europe and the different ways that reimbursement occurs in Europe versus the U.S.

Concerning the final part of the question, "*Would referenced product manufacturers lower their prices, offer discounts, and/or engage in enhanced marketing activities?,*" as a trade association BIO cannot and does not discuss the strategic marketing and pricing decisions that individual member companies may or may not make.

A2. What is the likely impact of a follow-on biologic product being designated "interchangeable" (i.e., receiving an approval that would permit pharmacists, without physician authorization, to fill a prescription for the referenced product with the follow-on product)? What are the prospects for the use of "authorized follow-on biologics" in these

---

al. "The Effect on Federal Spending of Legislation Creating a Regulatory Framework for Follow-on Biologics: Key Issues and Assumptions," White Paper, August 2007. See URL:
http://bio.org/healthcare/followonbkg/Federal_Spending_of_followonbkg200709.pdf.

circumstances? Do the answers to these questions differ based on the type of biologic product involved?

The degree of competition and potential cost savings arising from a follow-on biologics approval pathway is likely to be dependent on numerous factors, including product quality, cost of production, price discounting, market penetration, number of market entrants, potential market size for any given product, etc. For more detail, please see our answer in response to Question # 1 above.

With respect to designations of interchangeability, it is BIO's position that patients and their physicians should decide the proper course of treatment, including which medicine to take. All biologics should be dispensed as written and prescribed by brand name. We are urging Congress to ensure this approach in any legislation. Indeed, FDA recently stated:

> With protein products, as of today, the FDA has not determined how interchangeability can be established for complex proteins.[3]

The complex nature of biological manufacturing methods means that the manufacturing process used by a follow-on manufacturer will be different from the manufacturing process of the innovator. Because a follow-on manufacturer can never exactly duplicate the innovator's process, differences in process may result in differences in the protein product and, significantly, different effects in the clinic. In fact, even when innovator companies make changes in their *own* manufacturing processes, unanticipated changes in the product can and have occurred. For specific examples of such situations, please see our comments to the European Medicines Agency (EMEA) and FDA, available at http://www.bio.org/healthcare/followon/ (e.g., BIO Comments to 2004N-0355, "Scientific Considerations," December 13, 2004, pp. 18-37). Based on the experience of innovators, BIO agrees with FDA that it has not been determined how interchangeability can be established for complex proteins made by separate manufacturers.

If pharmacists were able, without physician authorization, to substitute the follow-on product for the reference product, patients might not only be dispensed a follow-on biologic rather than the prescribed biologic, but they might be switched back-and-forth among several products over time. Although switching among the innovator small-molecule drug and its generic versions normally raises few concerns, switching among biologics that are "similar" – rather than the same – involves particular risks. As FDA notes:

> For many follow-on protein products – and in particular, the more complex proteins – there is a significant potential for repeated switches between products to have a negative impact on the safety and/or effectiveness. Therefore, the ability to make determinations of substitutability for follow-on protein products may be limited.[4]

---

[3] http://www.fda.gov/cder/news/biosimilars.htm, Possible International Non-proprietary Name (INN) Policies for Biosimilars, September 1, 2006

[4] http://www.fda.gov/ola/2007/protein32607.html, Statement of Janet Woodcock, M.D., before House Committee on Oversight and Government Reform, March 26, 2007

EMEA and certain member states of the European Union likewise have recognized the fundamental differences between drugs and biologics with respect to substitutability. Recently, EMEA issued a statement that "[s]ince biosimilar and biological reference medicines are similar but not identical, the decision to treat a patient with a reference or a biosimilar medicine should be taken following the opinion of a qualified healthcare professional." BIO believes that, consistent with the policies of EMEA and many European countries, patients should receive the product expressly prescribed by a physician.

It is important to note that substitution has been a problem for certain small molecule generics. For example, levothyroxine, the generic form of certain medications treating hypothyroidism, is only safe and effective at a very narrowly defined dose. The American Thyroid Association has issued a public statement noting that patients should be alerted by their physicians or pharmacists that their levothyroxine preparation might be switched at the pharmacy, that patients should ask to remain on their current levothyroxine preparation, and that they should inform their physicians if their thyroid hormone is changed to a generic preparation because, following such a switch, thyroid function should be re-checked. This concern is even more relevant for biologics, which are often hundreds or thousands of times larger and more complex than traditional chemical drugs. The kinds and sizes of studies that would have to be done to address doubts about substitutability – including the risks of switching – would be so large that the dataset presented for approval would likely be larger than that required to be presented by an innovator.

As Secretary Leavitt noted in a letter to Senator Kennedy:

> [I]n light of the current scientific limitations on the ability to make determinations for interchangeability, and because it is critical to protect patient safety, the Administration believes that patients should not be switched from the innovator biological product to a follow-on biological product (or vice versa) without the express consent and advice of the patient's physician, and legislation should not allow for determinations of interchangeability at this time.[5]

Finally, we caution that the term "interchangeability" is not defined by FDA and has no settled legal or regulatory meaning at this time. We note that some use this word to describe products that are not "substitutable" or "therapeutically equivalent," but which, under a physician's supervision, could be used to treat the same disease or condition in the same patient.

Concerning the question, *"What are the prospects for the use of 'authorized follow-on biologics' in these circumstances?,"* as a trade association, BIO cannot and does not discuss the strategic marketing and pricing decisions that individual member companies may or may not make.

A4. How would the prospect of competition from follow-on biologic drugs influence research and development for new biologic drugs, improvements to existing biologic drugs, and the timing and rollout of new and/or improved biologic drugs? Does the market experience with non-biologic generic pharmaceutical drug products provide insights into these issues?

[5] Letter from HHS Secretary Michael O. Leavitt to Senator Edward M Kennedy, June 26, 2007

When discussing future innovation, it is helpful to understand what biotechnological innovation has accomplished to date. Biotechnology has created hundreds of new therapies and vaccines, including products to treat cancer, diabetes, HIV/AIDS and autoimmune disorders, and many other rare and unmet medical conditions. In fact, between 1995 and 2005, 160 different medicines were approved to treat rare diseases that affect 200,000 or fewer patients. Biotechnology also is responsible for hundreds of medical diagnostic tests that keep the blood supply safe and detect other conditions early enough to be successfully treated.

This spectacular innovation depends on an environment where companies can attract the capital needed to continue massive research and development (R&D) investment. Over the past 25 years, the average R&D intensity (R&D spending to total firm assets) for biotechnology was 38%. By comparison, the average R&D intensity for all industries was only about 3%.[6] According to Ernst and Young, "Global Year in Review 2006," the biotechnology industry has increased the amount of money it devotes to R&D by more than 120% since 1994.[7] Biotechnology is one of the most research-intensive industries in the world. The U.S. biotech industry spent $19.8 billion on research and development in 2005 alone.

In this regard, it bears emphasis that the biotechnology industry in the U.S. is still relatively nascent and largely unprofitable: the companies that comprise it are primarily small, private start-ups heavily reliant on venture capital and years away from product commercialization. It is these small companies – many of which will never see a product come to market or turn a profit – that are undertaking the bulk of early development gambles, challenging the boundaries of current medical knowledge toward new and exciting mechanisms of disease treatment amid overwhelming odds. *In fact, small biotechnology companies (all biotechnology companies but the top 10) account for two-thirds of the industry's future clinical pipeline.*[8]

This enormous reservoir of biotech innovation is critically important to the future of healthcare, the U.S. economy, the biotechnology industry, and, of course, patients. Thus, in crafting a follow-on biologics approval pathway, it is important to err on the side of incentivizing innovation, particularly in light of the unique elements of the biotechnology industry. These companies already bear enormous costs and a very high degree of uncertainty, not only in product development and manufacturing, but also in raising the necessary capital to fund innovative research – which is particularly difficult in the current economic environment. Thus, as compared to the broader pharmaceutical industry, biotechnology companies are more vulnerable to the type of changes in investment incentives that could result from a poorly-crafted follow-on biologics regime.

The statistics speak to the challenges this emerging industry faces. Biologics research and development is a high-risk endeavor, with higher capital costs, higher material costs, greater

---

[6] Golec, Joseph H. and John A. Vernon. "Financial Risk in the Biotechnology Industry," NBER Working Paper 13604.

[7] Ernst & Young LLP, annual biotechnology industry reports, 1993–2006. Financial data based primarily on fiscal-year financial statements of publicly-traded companies; constant 2005 dollars.

[8] The Boston Consulting Group: Rising to the Productivity Challenge, July 2004.

manufacturing costs and uncertainties, longer development times, and lower late-stage success rates than compared to small molecule drugs. In fact, from 2001–2005, the success rate of a Phase III trial for the average biotechnology product was just slightly more than 50%.[9] These failures occur at the last stage of product development – after years of research and hundreds of millions of dollars may have been spent.

The industry's heavy reliance on private equity also is notable. In 2005, there were 1,415 biotechnology companies in the U.S., but only 329 were publicly traded. In aggregate, even the publicly traded companies have not yet turned a profit:[10,11]

Year	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Net Loss ($B)	3.6	4.1	4.6	4.5	4.1	4.4	5.6	4.6	9.4	5.4	6.8	1.4	3.5

This situation is very much *unlike* the situation involving the traditional small molecule pharmaceutical market at the time that the Hatch-Waxman Act created a generic drug pathway in 1984 – a market that was dominated by mature and profitable companies with substantial revenues to reinvest in pharmaceutical R&D. Thus, the risk of driving research investment out of the industry, and quite possibly out of the U.S., is substantial if a follow-on biologics approval pathway does not contain sufficient incentives for continued innovation.

Given these unique challenges, patent protection alone (even including patent term restoration under current law) is not sufficient to ensure such adequate incentives under a follow-on biologics regime. Under a statutory framework allowing for follow-on biologics, there is a very real potential that the manufacturer of a follow-on product may be able to secure regulatory approval based at least in part on the innovator's prior approval, and, at the same time, avoid infringing patents that protect the innovator's product. That likelihood exists because of the confluence of critical factors not present in the Hatch-Waxman Act construct for generic small molecule drugs. Unlike a generic drug which must be the same as an innovator product, a follow-on biologic will only be required to be "comparable," "similar' or "highly similar" to the corresponding innovator product. Compared to generic drugs, the emerging follow-on biologics framework thus provides applicants with significantly more leeway to design around the patents that claim the reference product and make products that are sufficiently different to avoid patent infringement, but sufficiently similar to get abbreviated regulatory approval.

---

[9] Parexel's Bio/Pharmaceutical R&D Statistical Sourcebook 2006/2007.

[10] Ernst and Young LLP, annual biotechnology industry reports, 1995 – 2007. Financial data based primarily on fiscal-year financial statements of publicly-traded companies.

[11] Only about 20 biotech companies are currently profitable: Parexel's Bio/Pharmaceutical Statistical Sourcebook 2006/2007, pg. 39.

In light of this increased risk due to the scientific and regulatory facts related to biologics, data exclusivity must be substantially longer than the five years currently afforded to small molecule drugs under the Hatch-Waxman Act. Failure to provide substantial data exclusivity would fundamentally alter the ability of biotechnology companies to continue to innovate because these companies, in order to secure the necessary resources from venture capital firms and other funding sources, must have some certainty that they can prevent free-riding on their investment in the development of new breakthrough therapies for a substantial period of time. Without sufficient data protection, companies and investors will have a great deal of uncertainty as to whether they will be able to recoup the – on average – $1.2 billion in research and development costs that are necessary to bring a biologic to market.[12] This large amount of uncertainty will cause companies and investors to direct their investments to other areas where there is a higher degree of certainty that they will obtain a fair return on their investment.

This decrease in biotechnology R&D investment will be detrimental not just to biotechnology companies, but also to American universities, as less of their cutting-edge research and fewer of their technologies will be licensed because companies will not be able to recoup the R&D investment necessary to take a licensed technology from the laboratory to the marketplace. Investors will turn to other less risky ventures, and cutting-edge research (including the substantial public investment in basic research through the National Institutes of Health) will sit on laboratory shelves, as it often did prior to the Bayh-Dole Act and the Hatch-Waxman Act patent term restoration provisions.

If this occurs, society as a whole will suffer. New treatments in the pipeline hold the promise of continued progress against our most pressing medical challenges. At present, more than 400 biotechnology medicines and vaccines are in development, targeting more than 200 diseases, including various cancers, Alzheimer's disease, heart disease, diabetes, multiple sclerosis, AIDS, and arthritis. Specifically, there are:

- 210 for cancer and related conditions
- 22 for cardiovascular disease
- 15 for diabetes and related conditions

These innovative treatments include:

- Monoclonal antibodies to treat asthma, Crohn's disease, and lupus
- Therapeutic vaccines for AIDS
- Recombinant proteins to treat autoimmune disorders

Without adequate incentives these – and many other – breakthrough cures and therapies for cancer, Alzheimer's, Parkinson's, AIDS and many rare or unmet medical conditions may either take longer to come to fruition or not come to be realized at all.

[12] DiMasi, Joseph and Henry Grabowski. "The cost of biopharmaceutical R&D: is biotech different?" Managerial and Decision Economics 28(4-5), pages: 469-479 (2007).

A properly developed follow-on biologic pathway will ensure that the incentives needed to encourage research and development of new, innovative therapies remain in place. BIO believes that, to accomplish this result, the best data available support a 14-year period of data exclusivity for biologics under a follow-on biologics regime. We emphasize that data exclusivity does not interfere with the existing competition among biologic innovators today, and we are not seeking "marketing exclusivity" to prevent such competition. Rather, data exclusivity only prevents, during this time period, a follow-on manufacturer from short-circuiting the normal FDA approval process by basing its FDA application on the safety and efficacy of the innovator product rather than its own full application.

Several independent factors support BIO's position on the appropriate data exclusivity period. First, we know that the breakeven point for return on investment in a biologic occurs after it has been on the market between 12.9 and 16.2 years,[13] and thus competition from follow-on biologics prior to that time period would clearly undermine incentives for such investment in the first place. Second, in 1984, Congress enacted patent term restoration provisions to provide pharmaceuticals with up to 14 years of patent protection following marketing approval. This time period was selected so that "research intensive companies will have the necessary incentive to increase their research and development activities."[14] As a result, the average period of time for marketing a drug product with patent protection now is 11.5 years,[15] and new molecular entities are, on average, marketed in the U.S. for 13.5 years before the entry of generic competition.[16] A similar length of protection should be available for biologics. For a fuller discussion of these data and the justification for 14 years of data exclusivity, please visit the following URL:

- http://bio.org/healthcare/followonbkg/FOBSMarket_exclusivity_20070926.pdf

In addition, a follow-on biologics pathway must maintain incentives for the development of second-generation products.[17] A second-generation product must go through the same rigorous FDA approval process as a first generation product. It requires development and submission of full clinical safety and efficacy data to support FDA review and approval of the complete marketing application (Biologics License Application (BLA) or New Drug Application (NDA)). Accordingly, FDA approval of a second-generation product should be rewarded with full data

---

[13] Grabowski, Henry. "Data Exclusivity for New Biological Entities," Duke University Department of Economics Working Paper. June 2007.

[14] H.R. Rep. No. 98-857, at 41 (1984).

[15] Congressional Budget Office, A CBO Study: How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry, July 1998, Chapter Four, "The Effects of the Hatch-Waxman Act on the Returns from Innovation."

[16] Grabowski, Henry and Margaret Kyle. "Generic Competition and Market Exclusivity Periods in Pharmaceuticals," Managerial and Decision Economics 28(4-5), pages: 491-502 (2007).

[17] "... second-generation products – those with structural differences designed to improve performance while maintaining the same mechanism of action as the original product – are not conventionally considered as follow-on products." Woodcock, J., "The FDA's Assessment of Follow-on Protein Products: A Historical Perspective," Nature Reviews Drug Discovery 6: 437-442, June 2007.

exclusivity as well. Such exclusivity is necessary to enable manufacturers to invest in the development of such innovative second-generation products and to enable patients to benefit from these treatment advances. Simply put, without sufficient data exclusivity of their own, second generation products will not be developed if a follow-on biologics pathway is enacted. Such a result would be a "lose-lose-lose" situation. A loss for innovators who would not pursue product improvements, a loss for follow-on manufacturers who would not have second-generation products to select from, and most important, a loss for patients who would not have the benefit of improved products.

For new indications, there should be an additional data exclusivity period for the original innovative product (e.g., 2 additional years) as an incentive for innovators to invest in such advances. Data exclusivity for new indications is critical in areas such as cancer research, where initial marketing approval generally focuses on late-stage disease, and research and development activities for early-stage or adjuvant therapies most often occur much later in time. Without this additional exclusivity, there would be little incentive to research and obtain approval for these new indications.

BIO notes that data protection for a second-generation product will in no way affect the ability of a follow-on biologic to enter the market based on the original innovative product. The success of the second-generation product will depend on its benefits for patients and price compared to the follow-on and other competitive marketed products. If the second-generation product's benefit is minor in comparison to existing products, then it is unlikely – particularly in today's price-sensitive payer market – that granting data exclusivity to the second-generation product will impact the marketplace in any meaningful way. However, without any separate data exclusivity for second-generation products, major advances will be stymied.

A6. How are the patent portfolios claiming biologic drugs similar or dissimilar to the patent portfolios that claim small molecule (nonbiologic) drugs approved under the federal Food, Drug, and Cosmetic Act (FDCA)?

There is less public information available about patent portfolios for biologics than for small molecule drugs. However, certain inferences about such patent portfolios can be drawn from current biotechnology patent practice, and from biotechnology patents known to cover existing FDA approved biologics.

Like small molecule drugs, biologics are protected by different classes of patent claims, but there are critical distinctions:

(a) Compound claims. Claims to the active molecule, such as a specific peptide or antibody, exist for biologics, as they do for small molecule drugs. The way in which these active molecules are claimed, however, is often significantly different. For example, unlike small molecules, biologics are often claimed with reference to specific amino acid and/or nucleic acid sequences, and more often include functional claim limitations.[18]

[18] For example, an antibody claim that includes a sequence limitation in addition to multiple functional limitations could be drafted in the following form:

(b) Claims to methods of treatment (use of the compound in a specific indication; dose, route, or schedule of administration, etc.) exist, as they do for small molecule drugs.[19]

(c) Drug product claims (formulation, dosage form) exist, as they do for small molecule drugs.[20]

(d) Product by process claims are more prevalent and important in biotechnology than in small molecule medicinal chemistry. In a biotechnology product-by-process claim, the claimed molecule is defined not (or not solely) by its molecular structure or by its function, but as the product resulting from following the steps of a biotechnological process. Such claims are useful in cases where important characteristics of the claimed molecule depend on the process by which it was made (see below), but where it may not be possible or feasible to otherwise describe all such characteristics in structural and functional terms. This is sometimes the case for inventions that comprise complex mixtures of different compounds (e.g., a vaccine).[21]

(e) Claims that protect manufacturing technology: Process claims. Claims to manufacturing processes are more important in biotechnology than they are in the small molecule space.[22] The

---

"An isolated human antibody, or an antigen-binding portion thereof, that dissociates from human [antigen] with a K_d of $1x10^{-8}$ M or less and a K_{off} rate constant of $1x10^{-3}$ or less, both determined by surface plasmon resonance, and neutralizes human [antigen] cytotoxicity in a standard in vitro L929 assay with an IC_{50} of $1x10^{-7}$ M or less, said antibody comprising a heavy chain variable region comprising a contiguous sequence from CDR1 through CDR3 as represented in SEQ ID NO:14."

In such a claim, the reader would consult the attached patent specification to identify the specific sequence of amino acids that make up the critical portion of the claimed antibody.

[19] An example of a biotechnology claim to a method of treatment could be drafted in the following form:

" A method for inhibiting the growth of human tumor cells that express human [factor] receptors and are mitogenically stimulated by [factor], the method comprising administering an effective amount of an anti-neoplastic agent and an effective amount of a monoclonal antibody to a human cancer patient having said tumor cells; (i) wherein said antibody binds to the extra-cellular domain of the human [factor] receptor of said tumor cell; (ii) wherein the antibody is not conjugated to the anti-neoplastic agent; and (iii) wherein the antibody inhibits the binding of [factor] to the [factor] receptor."

[20] An example of a biological composition claim could be as follows:

" A pharmaceutical composition for parenteral administration to a human patient comprising human [enzyme] with catalytic activity and in a therapeutically effective dosage to treat a patient suffering from [syndrome]; and a pharmaceutical carrier, the composition being free of other human proteins present in its natural environment."

[21] An example of a biological product-by-process claim could be:

"A bacterin-toxoid vaccine against [bacterial strain] infection produced by culturing [bacterial strain] for a time sufficient for said culture to reach the late-logarithmic phase of growth; harvesting culture supernatant therefrom comprising leukotoxin, capsular antigen, soluble antigens, and [bacterial] cells at a density ranging from about 10^3 to about 10^8 cells per ml; and adding an inactivating agent."

[22] An example of a biotechnological process claim could be drafted as follows:

processes by which biologics are made are highly specific, complex, and determine many of the biologic's functional and structural characteristics, such as the way the protein is folded; the presence and position of sugar or fatty acid side chains; the way proteins aggregate; the way both ends of the protein's amino acid chain are truncated or extended; the presence of protein isoforms in the final preparation, or its impurity profile, and the like. Such product characteristics can often be expected to affect the product's safety, purity, and efficacy profile, and thus are integral to the approval of the product itself. Thus, many important inventions are made as biologics manufacturers work out optimal processes to reliably and reproducibly make, purify, and process a biologic molecule. In contrast to the Hatch-Waxman Act, which does not permit listing of process patents and excludes them from the Act's patent resolution procedures, FOBs legislation should contain adequate provisions to account for the importance of process patents in the biologics space, and allow for the pre-marketing resolution of disputes over such patents.

(f) Claims that protect manufacturing technology: Non-process claims. The high importance of process technology is also illustrated by the existence of patents on inventions that must be practiced as part of the technology platform necessary to make and use the biologic, such as claims to the isolated and purified DNA or RNA polynucleotide that encodes the recombinant protein, to the vector used to insert it into host cells, to the host cell that secretes it, to the promoter that drives its expression, and the like. The existence and importance of such claims relate to the way biotechnology inventions are made as the technology progresses through clinical and process development to market approval. The discovery of a new receptor on certain cancer cells, for example, may lead to the isolation and purification of the receptor protein and the sequencing of its amino acid sequence and of the gene that encodes it. To transform such basic discoveries into real-world therapeutic products, biologics manufacturers must develop a technology platform that can involve a number of independently patentable inventions, such as hybridoma cells that secrete antibodies to the drug target, the construction of vectors useful to transfer it to cultured cells, techniques to regulate its expression, and the like. This way, developing, making and using a biotechnology product can involve multiple patentable inventions that all must be practiced together. Patents on such inventions play a more prominent role in the portfolios that protect biologic drugs compared to the small molecule sector.[23] Despite

---

"A process of making a conjugate that comprises a [protein] glycoprotein having an N-terminal alpha-amino group and one poly(ethylene glycol); said process comprising: a) expressing and fermenting a recombinant [protein] that has an N-terminal peptidic extension that includes a proteolytic cleavage sequence, b) protecting the .epsilon.-amino groups, c) proteolytically cleaving the N-terminal peptidic extension, d) pegylating the N-terminal .alpha.-amino group, and e) deprotecting the .epsilon.-amino groups of the [protein] glycoprotein; wherein the recombinant [protein] comprises a sequence selected from the group consisting of the amino acid sequences SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO 4: and SEQ ID NO: 5."

[23] Examples of DNA or host cell claims that are part of the technology platform for manufacturing a therapeutic protein could be drafted as follows:

"An isolated DNA molecule encoding a protein comprising a sequence of amino acids selected from the group consisting of amino acids 1-142 of SEQ ID NO:1 and amino acids 1-226 of SEQ ID NO:3, wherein said protein is capable of binding [receptor]."

"A eukaryotic host cell containing DNA encoding an antibody molecule, said antibody being capable of being expressed in said eukaryotic host by said DNA, wherein said antibody has specificity for the antigen bound by the

their importance to the protection of biologics process technology today, it is possible that the relevance of such patents would be diminished under a FOBs regime where many FOB products would be produced overseas, as more fully explained in BIO's answer to Question #3 in the patent section, below.

Deposits of biological material are another aspect without correlate in the small molecule space. Every patent must contain a technical disclosure sufficient to enable other skilled persons to make and use the invention without undue experimentation. In biotechnology, however, inventions may not always be easily reproducible. For example, during a transfection experiment (a form of experimental gene transfer) it is not possible to predict exactly where, and how, a piece of foreign DNA will be integrated into the chromosomes of the host cell. Each successfully transfected cell will be unique in its own way, and may be near impossible to exactly reproduce by repeating the experiment. Other biotechnology inventions involve complex biological materials that cannot sufficiently be described by words alone. In such situations, the patent law requirement that a patent "enable" other skilled persons to make and use the invention can be satisfied by providing a sample of the biological material to a depository that is approved by the World Intellectual Property Organization, such as, for example, the American Type Culture Collection, where it can be accessed and studied by others. Some biologic drug claims that reference deposited biologic materials are narrowly limited in their scope to only what was deposited.[24]

Other aspects of patent law, too, impact the way biologic drugs are claimed and the amount of experimental work that must be done to obtain comprehensive patent protection. Patent applicants who seek broader biotechnology claims must often conduct more experiments, do more work, and provide more in-depth explanation of the underlying biological processes and structure-function relationships than their colleagues in the small molecule field. This work must be done to satisfy the so-called "written description" and "enablement" requirements – a task that can be particularly difficult in biotechnology, where the unpredictability of biological processes may not allow other scientists to extrapolate from just a few described examples to the full scope of a broadly-claimed invention, and to practice it across its full scope without undue experimentation. Many biotechnology patent practitioners feel that the "written description" and "enablement" requirements operate to limit the breadth of claims available to patent applicants.[25] Stringent application of these requirements by patent examiners may also force patent applicants to retreat from an initially broader claim scope to a much narrower claim scope during the course of patent examination. Because such surrendered claim scope can be difficult or impossible to

---

antibody produced by hybridoma [###] as deposited with the ATCC, and wherein said antibody has cytolytic activity."

[24] An example of a biotechnology claim that includes a limitation to a specific deposit could be drafted as follows:

"A method for treatment of [specific cancer] comprising the step of administering a therapeutically effective amount of immunologically active anti-[antigen] antibody to a patient in need thereof, said antibody being derived from a hybridoma as deposited with the ATCC, deposit number [###]."

[25] For a recent interpretation of the so-called "written description" requirement, see *Carnegie Mellon University et al. v. Hoffmann-La Roche Inc. et al.*, Slip op. (Fed Cir. Sept. 8, 2008); available at: http://www.cafc.uscourts.gov/opinions/07-1266.pdf.

regain during enforcement in later litigation, patentees may find themselves confined to the literal limits of their issued claims, and unable to assert that even a close equivalent of their own, patented product infringes the patent.[26]

In summary, while sharing some common features with small molecule patents, biologics patents more commonly include functional claim limitations, may be limited in scope to specific deposited biological materials or specific recited sequences, and often face unique challenges in meeting the written description and enablement requirements. When viewed as a whole, the patent portfolios that protect biologic drugs today are often more complex than those found in the small molecule space. These differences cannot be disregarded when crafting any follow-on biologics approval pathway. However, for the reasons set forth in BIO's answer to Question #3 in the patent section, below, it does not follow that higher complexity in the innovators' patent estates would always translate into more complex patent litigation. Instead, differences in the way patent disputes would be resolved would predominantly be grounded not in portfolio complexity, but in the way these portfolios operate under different approval standards for generic drugs and FOBs. In the small molecule space, a patent that claims an innovator's new molecular entity almost certainly also covers the generic drug applicant's molecule, because both must, by law, be "the same." Under a follow-on biologics regime, FOB products would likely be approvable under a less stringent standard that may provide FOB applicants with significantly wider latitude to design around innovator patents, and to manufacture FOB products that are different enough to avoid patent infringement, yet similar enough to benefit from the reference product's safety and efficacy record and obtain abbreviated approval. Thus, the differences between patent portfolios that claim small molecule drugs and biologics must always be examined in the regulatory context in which these portfolios will be brought to bear. This context must be taken into account when designing patent resolution procedures in any FOBs regime.

A7. Are the regulatory exclusivities currently provided to pharmaceutical drug products in the FDCA appropriate for new biologic drugs and/or significant improvements to existing biologic products? Are they appropriate for specific types of biologics? Why or why not?

BIO believes that the balance between innovation and generic competition struck by the Hatch-Waxman Act can provide valuable insights for the development of a follow-on biologics approval pathway. The Hatch-Waxman Act provides innovators and generic competitors a range of statutory, patent, and litigation-based incentives that, as described in response to a previous question, operate to create de facto protection against generic competition for, on average, 13.5 years. However, to achieve that same balance in the follow-on biologics context, the law must reflect the differences between small molecule drugs and biologics and differences between generic drugs and follow-on biologics. Under the 1984 Hatch-Waxman Act, a generic version of a small molecule drug may be approved for marketing only if its active ingredient is the "same" as in the innovator product. Thus, the patents that cover the innovator's active ingredient generally will apply to the generic version. Accordingly, the generic drug manufacturer cannot

[26] For a recent discussion of developments in the patent law doctrines relating to prosecution history estoppel and equivalence, see, e.g., John R. Allison and Mark A. Lemley, The (Unnoticed) Demise of the Doctrine of Equivalents, 59 Stan. L. Rev. 955 (2007).

gain FDA approval of its product by demonstrating that the active ingredient is the same as the innovator product and then claim in the patent context that it is different from the innovator's drug. In addition, the Hatch-Waxman Act contains provisions that can extend the term of an innovator patent to cover a period of 14 years following approval of an innovative drug. As noted above, new molecular entities today do not face generic market competition until 13.5 years post-FDA approval on average, evidencing that the mix of policy tools employed by the Hatch-Waxman Act has come remarkably close to achieving the 14-year mark deemed appropriate under the Act for innovators to recoup their substantial investments prior to generic entry.

In contrast, under the various statutory frameworks being considered for follow-on biologics, a follow-on will not be required to be the "same" as the innovator product due to the high degree of complexity of biologics. Instead, the follow-on product will only have to be similar or highly similar to the innovator product. This similarity standard for follow-on biologics creates a significant risk that a follow-on competitor will circumvent or "design around" the innovator's biotech patents – meaning that the follow-on may be outside of the scope of the innovator's patent claim. As a result, a follow-on biologic may be sufficiently similar to the innovator biologic to rely to some degree on the safety and effectiveness of the innovator product and thus receive abbreviated regulatory approval. Yet, it may still be different enough from the innovator product to avoid a patent infringement claim and, thus, reach the market well in advance of innovator patent expiration. For these reasons, patents may provide less comprehensive protection for innovative biologics under a follow-on biologics regime than they do for small molecules in the generic drug context.

Accordingly, if data exclusivity in a follow-on biologics regime were limited to the 5 years under the Hatch-Waxman Act, it would severely undermine incentives to invest in biotech innovation. Instead, BIO believes that a 14-year period of data exclusivity should be granted for biologics in any follow-on biologics regime. Such an approach would ensure that biologics receive the same degree of effective market protection from follow-on competition that small molecules receive today from generics, as described above. For more detailed information, please see BIO's response to Questions #4 above and #8 below, as well as our white paper on exclusivity and patent protection in a follow-on biologics regime, found at the following URL:

- http://bio.org/healthcare/followonbkg/FOBSMarket_exclusivity_20070926.pdf

A8. What are the appropriate factors to consider when determining the optimal length of regulatory exclusivity periods for biologic drug products? Do these factors change based on the type of referenced product involved, the extent of competition facing the referenced product, or patent portfolios claiming the referenced product, and if so, how?

The biotechnology industry in the U.S. is still relatively nascent and largely unprofitable: the companies that comprise it are primarily small, private start-ups heavily reliant on venture capital and years away from product commercialization. It is these small companies – many of which will never see a product come to market or turn a profit – that are undertaking the bulk of early development gambles, challenging the boundaries of current medical knowledge toward new and exciting mechanisms of disease treatment amid overwhelming odds. *In fact, small biotechnology*

companies (all biotechnology companies but the top ten) account for two-thirds of the industry's future clinical pipeline.[27]

This enormous reservoir of biotech innovation is critically important to the future of healthcare, the U.S. economy, the biotechnology industry, and, of course, patients. Thus, in crafting a follow-on biologics approval pathway, it is important to err on the side of incentivizing innovation, particularly in light of the unique elements of the biotechnology industry. These companies already bear enormous costs and a very high degree of uncertainty, not only in product development and manufacturing, but also in raising the necessary capital to fund innovative research. Thus, as compared to the broader pharmaceutical industry, biotechnology companies are more vulnerable to the type of changes in investment incentives that could result from a poorly-crafted follow-on biologics regime.

The industry's heavy reliance on private equity also is notable. In 2005, there were 1,415 biotechnology companies in the U.S., but only 329 were publicly traded. In aggregate, even the publicly traded companies have not yet turned a profit:[28,29]

Year	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Net Loss ($B)	3.6	4.1	4.6	4.5	4.1	4.4	5.6	4.6	9.4	5.4	6.8	1.4	3.5

Given these unique challenges, patent protection (including patent term restoration under current law) is not sufficient to ensure adequate incentives for biotech innovation under a follow-on biologics regime. Rather, any statutory pathway for follow-on biologics must establish a substantial period of data exclusivity to preserve incentives for research, development, manufacture, and approval of new biologic therapies. As discussed in response to Questions #4, 6 and 7, this is necessary because, under a statutory framework allowing for follow-on biologics, there is a very real risk that the manufacturer of a follow-on product may be able to secure abbreviated regulatory approval based at least in part on the innovator's prior approval, and, at the same time, avoid infringing the patents that protect the innovator's product. That likelihood exists because of the confluence of critical factors not present in the Hatch-Waxman Act construct for generic small molecule drugs. Unlike a generic drug which must be the same as an innovator product, a follow-on biologic will only be required to be "comparable," "similar' or "highly similar" to the corresponding innovator product. Compared to generic drugs, the emerging follow-on biologics framework thus provides applicants with significantly more leeway to design around the patents that claim the reference product and make products that are

[27] The Boston Consulting Group: Rising to the Productivity Challenge, July 2004.

[28] Ernst and Young LLP, Annual biotechnology industry reports, 1995 – 2006. Financial data based primarily on fiscal-year financial statements of publicly-traded companies.

[29] Only about 20 biotech companies are currently profitable: Parexel's Bio/Pharmaceutical Statistical Sourcebook 2006/2007, pg. 39.

sufficiently different to avoid patent infringement, but sufficiently similar to get abbreviated regulatory approval.

In light of this potential gap in patent protection for biologics under a follow-on biologics regime, data exclusivity must be substantially longer than the five years currently afforded to small molecule drugs under the Hatch-Waxman Act. Failure to provide substantial data exclusivity would fundamentally alter the ability of biotechnology companies to continue to innovate because these companies, in order to secure the necessary resources from venture capital firms and other funding sources, must have some certainty that they can prevent free-riding on their investment in the development of new breakthrough therapies for a substantial period of time. Without sufficient data protection, companies and investors will have a great deal of uncertainty as to whether they will be able to recoup the – on average – $1.2 billion in research and development costs that are necessary to bring a biologic to market.[30] This large amount of uncertainty will cause companies and investors to direct their investments to other areas where there is a higher degree of certainty that they will obtain a fair return on their investment. If this occurs, society as a whole will suffer, as fewer cures and therapies for cancer, Alzheimer's, Parkinson's, AIDS and many rare or unmet medical conditions will be developed.

As stated above, BIO believes that the best data available support a 14-year period of data exclusivity – not an "exclusive marketing" period – for biologics under a follow-on biologics regime. Several independent factors support this position. First, we know that the breakeven point for return on investment in a biologic occurs after it has been on the market between 12.9 and 16.2 years,[31] and thus competition from follow-on biologics prior to that time period would clearly undermine incentives for such investment in the first place. Second, in 1984, Congress enacted patent term restoration provisions to provide pharmaceuticals with up to 14 years of patent protection following marketing approval. This time period was selected so that "research intensive companies will have the necessary incentive to increase their research and development activities."[32] As a result, the average period of time for marketing a drug product with patent protection now is 11.5 years,[33] and new molecular entities are, on average, marketed in the U.S. for 13.5 years before the entry of generic competition.[34]

---

[30] DiMasi, Joseph and Henry Grabowski. "The cost of biopharmaceutical R&D: is biotech different?" Managerial and Decision Economics 28(4-5), pages: 469-479 (2007).

[31] Grabowski, Henry. "Data Exclusivity for New Biological Entities," Duke University Department of Economics Working Paper. June 2007.

[32] H.R. Rep. No. 98-857, at 41 (1984).

[33] Congressional Budget Office. A CBO Study: How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry. July 1998. Chapter Four, "The Effects of the Hatch-Waxman Act on the Returns from Innovation."

[34] Grabowski, Henry and Margaret Kyle. "Generic Competition and Market Exclusivity Periods in Pharmaceuticals," Managerial and Decision Economics 28(4-5), pages: 491-502 (2007).

Thus, any statutory formula that allows for follow-on biologics should at least guarantee the same degree of effective market protection that Congress found necessary to maintain incentives for innovation in small molecule drugs – and, for the reasons discussed above, that protection can be accomplished most predictably through data exclusivity. Indeed, if the data exclusivity period for biologics is less than the number of years available to drugs under patent term restoration (that is, 14 years), then, because of the potential patent protection gap and the higher risks of biologics development, it will skew investment away from biotech innovation. Because data exclusivity would run concurrently with the patent term for the product, it therefore would create actual protection only in those instances where the follow-on manufacturer would be able to work around the patents held by the innovator but still gain abbreviated approval of its product.

For a fuller discussion of these data and the justification for 14 years of data exclusivity, please visit the following URL:

- http://bio.org/healthcare/followonbkg/FOBSMarket_exclusivity_20070926.pdf

A9. How does the European Medicines Agency's approach to regulatory exclusivities in its abbreviated regulatory approval pathway for follow-on biologics inform the U.S. approach?

As we state in our answers above, we believe that a 14-year base period of data exclusivity is necessary to avoid undermining incentives for the development of innovative biologics. And for the reasons explained more fully below, anything less would jeopardize the U.S.'s leadership role in producing innovative biotechnology medicines for the patients who need them.

The European Union provides eight years following innovator approval during which a generic or biosimilar application cannot be submitted, two further years (i.e., 10 years total) during which a generic or biosimilar cannot be marketed, and one further year if, during the first eight years of data exclusivity, the holder of the reference product obtains an authorization for new therapeutic indication(s) which bring(s) significant clinical benefit in comparison with existing therapies. While we believe that the length of data exclusivity provided in the European Union would be inadequate in the U.S. context, we strongly agree with the provision of a further exclusivity period for new indications, and we also note that the European Union provides 10 (or 11 if appropriate) years of data exclusivity to next- or second-generation products. (See BIO's Response to Question #4 above). We also strongly support the protection against the filing of biosimilar applications too soon after innovator approval, for the reasons described more fully in response to Question #1 below in the patent section).

We believe that if the U.S. adopts incentives for innovation in biologics that are substantially less than those afforded in Europe, the result will be substantially less investment in biotech innovation. Because the U.S. leads the world in this area, the economic impact of reduced investment will be particularly acute here in the U.S. The latest data from Burrill & Company show that the U.S. continues to dominate the biopharmaceutical market, whether the measure is sales, R&D, employees or public companies:

US, European, Canadian, Japanese, Canadian, and Australian Biotech: Global Activity Measures (2005, U.S. dollars)

	U.S.	Europe	Japan*	Canada	Australia
Sales/Revenue	$71.5 B	$7.5 B	$0.82 B	$1.7 B	$1.0 B
Annual R&D	$18.5 B	$4.2 B	-	$0.6 B	$0.1 B
# of Companies	1,473	1,878	464	470	226
# of public companies	363	96	22	81	58
# of employees	146,100	32,470	4,171	7,440	6,393

*Japan – public companies only

The U.S.'s per capita biotech R&D expenditures are 574% higher than the European Union's (EU's) per capita biotech R&D expenditures.[35] It also should be noted that:[36]

- The biotechnology industry's U.S. trade surplus grew from $593 million in 2000 to $1.8 billion in 2004 – an increase of almost 200%. Over the same period of time, overall U.S. trade in advanced-technology products decreased by more than 200% -- going from a net surplus to a net deficit.
- The biotechnology industry's U.S. exports grew from $1.7 billion in 2000 to $3.7 billion in 2004 – an increase of more than 100%.
- Between 2000 and 2004, U.S. jobs in the biopharmaceutical industry rose by 8.3%.
- The biopharmaceutical industry expands U.S. gross domestic product by at least $27 billion annually, on a permanent basis, for every one-time R&D investment of $15 billion. In 2005 alone, the U.S. biotechnology industry invested nearly $20 billion in R&D.

Thus, a follow-on biologics pathway that does not preserve the necessary incentives for innovation (that is, 14 years of data exclusivity) would disproportionately and negatively affect the U.S., the world leader in biotechnology innovation, and would drive investment towards less risky ventures, including those outside of the U.S.

B. Patent Dispute Resolution Issues

B1. Would it be important to have the litigation of any patent disputes proceed concurrently with the abbreviated FDA approval process for follow-on biologics? Why or why not? What has been learned from the experience under Hatch-Waxman about the incentives necessary to encourage early resolution of patent issues?

It would be important to resolve patent disputes concurrently with the approval process, and prior to launch of, a follow-on biologic, because premature launches of such products carry numerous risks that significantly impact the public as well as the private interests of the parties.

[35] R&D figures are from Parexel's Bio/Pharmaceutical R&D Statistical Sourcebook 2006/2007. Population figures estimated as of July 2006.

[36] See URL: http://www.nsf.gov/statistics/seind06/c6/t06-03.htm -- last accessed on February 1, 2008.

A judicial determination of patent infringement for a prematurely-launched FOB product would raise significant concerns about therapeutic disruption for patients. In fact, consistency of product availability is of great importance to patient health and physician prescribing practices and such consistency would be jeopardized by a premature launch without patent resolution.

Premature marketing would not only create unnecessary confusion among physicians, patients, payers and other market participants – it would also lead to great business uncertainty for both parties. From the reference product sponsor's perspective, a premature follow-on biologic launch may lead to a loss of market share and price erosion that cannot be reversed even if a court subsequently were to find the asserted patents valid and infringed. From the follow-on applicant's perspective, a judicial determination of patent infringement could lead to very significant damages awards which may or may not exceed the applicant's financial capacities.

Seen this way, launches of follow-on biologics prior to patent resolution entail huge business risk not only for the innovator, but also for the follow-on applicant – a risk that is exacerbated by the considerable financial investment in FOB development (much larger than the investment required for a generic drug submission) that would already have been made at that point. It stands to reason that only the biggest, financially strongest FOB applicants would tolerate the risk of losing their investment or facing large infringement damages awards. Thus, a FOB framework that routinely envisions patent resolution after FOB market entry would selectively disadvantage smaller, financially weaker FOB applicants and operate to create FOB markets that are dominated by only a few, financially strong players and FOB products.

Sufficient time for resolution of patent disputes prior to follow-on biologic approval must therefore be provided. Ideally, patent disputes would be resolved by the time the innovator statutory exclusivity period expires. This way, the patent resolution could take place without the need for special stays pending litigation during a time when the FOB product could otherwise be launched. Such timing of patent resolution would provide business certainty that a risk-free FOB launch could occur at a fixed point in time. Timing of patent resolution prior to the expiration of the innovator's statutory exclusivity period would also encourage full resolution of patent validity questions on the merits, rather than through settlement, thus providing more patent certainty for subsequent FOB applicants.

However, while patent resolution should be timed so as to be concluded within the innovator's statutory exclusivity period, it should not be timed so as to begin too early. The FOB applicant must be far enough down the road of developing its comprehensive data package, as well as its detailed manufacturing processes, needed for the FOB regulatory submission and for a full exploration of relevant patent-related issues. Further, in order to properly evaluate a FOB application and the heightened concerns regarding immunogenicity in the biologics arena, the FDA will need sufficient experience with the reference product in the marketplace.

It also must be kept in mind that the earliest date on which a FOB application can be submitted during an innovator's data exclusivity period should not be set so early that its final approval, upon expiration of the innovator's exclusivity, is so remote in time that the data on which it relies have become inapposite to the final FOB product due to, for example, subsequent changes to the FOB process technology used in commercial manufacturing. Finally, the likelihood that any

given FOB application would be approvable will be lower than it is today for generic drug applications, and the possibility that the Secretary may require additional clinical studies is greater. Thus, patent litigation would be premature if it were allowed to commence before a determination that the FOB application in question is complete and in condition for review without additional clinical studies.

A focus on triggering "patent challenges" at the earliest possible opportunity, possibly complemented by valuable regulatory exclusivity incentives for doing so, could thus lead to premature litigation as well as premature submission of FOB applications. The focus should be on incentivizing the timely submission of complete, high-quality, approvable FOB applications, not to reward the first "patent challenge." Experience under the Hatch Waxman Act confirms that incentives for early resolution of patent disputes must be crafted carefully to avoid unintended consequences. Premature litigation, both with respect to timing and with respect to the merits, is commonplace today in the small molecule space. For example, a survey of active NDAs for New Molecular Entities (NMEs) approved after March 2000 for which a paragraph IV certification could have been submitted after March 2004[37] shows that about 42% of all NMEs in this sample faced a paragraph IV challenge between the fourth and the seventh year following NDA approval (average 4.6 years). This, it is submitted, is an extraordinarily high litigation burden on both innovators and generic drug applicants that should not occur within just a few years after NME launch, and need not occur at all under a FOBs regime. A rational FOB framework would instead create incentives for timely patent dispute resolution within the innovator's statutory exclusivity period, to proceed in parallel with the FOB approval process, and would account for judicial determinations of patent validity and infringement by making the approval of the FOB application effective on the date of patent expiration or expiration of the innovator's statutory exclusivity period, whichever occurs later.

B2. How long might the approval process for a follow-on biologic application take? What factors might influence this timing?

It has been estimated that the time required for follow-on biologic manufacturers to obtain regulatory approval likely will be three to five years for pre-clinical and clinical testing, and one-and-a-half to two years for FDA review and approval.[38] Note that it also takes four to six years to bring manufacturing capacity on-line (likely developed concurrently with product development schedule).

Following passage of any legislation, FDA will need to create a regulatory scheme, testing requirements, and product-class guidelines. However, we note that, in most cases, the European Union has completed product-group-specific guidance in 12-18 months. While FDA must conduct its own guidance development process, it will have the benefit of what has been and can be learned from the European Union and, in some cases, this may allow FDA to complete guidance in a shorter time. Furthermore, there are administrative processes FDA will have to put

[37] The time for which Paragraph IV certification dates are available from the FDA at http://www.fda.gov/cder/ogd/ppiv.htm

[38] Grabowski, Henry, *et al.* "The Effect on Federal Spending of Legislation Creating a Regulatory Framework for Follow-on Biologics: Key Issues and Assumptions," White Paper, August 2007. See URL: http://bio.org/healthcare/followonbkg/Federal_Spending_of_followonbkg200709.pdf

in place prior to approval of follow-on biologics; these will be separate from any guidance requirement. A guidance requirement would run concurrently with the establishment of these processes and thus would not create any additional delay.

B3. How might differences between patent portfolios for small molecule drugs and biologics affect patent litigation involving follow-on biologics? How long might patent litigation involving a follow-on biologic product take?

Compared to patent litigation under the Hatch-Waxman Act, biologics process patents would be expected to play a more prominent role in conjunction with other patents in the portfolio that protect the reference product. The main differences in the way in which patents would be litigated would, however, not be grounded in portfolio complexity, but in the way small molecule and biologics patent portfolios operate under different approval standards for generic drugs and FOBs. For example, because the reference product and the follow-on product would likely not need to be identical, there would be more frequent litigation of questions of noninfringement, doctrine of equivalents, and prosecution history estoppel. Claim construction would therefore be an even more important aspect of follow-on biologics patent litigation. In addition, it can be expected that the affirmative defenses of patent invalidity and unenforceability would be asserted at the same frequency at which they today occur during Hatch-Waxman litigation.

In another distinction from Hatch-Waxman litigation, biologics patent portfolios do not lend themselves to an Orange Book listing process of the kind relied on as the starting point for generic drug litigation today. Because a FOB product would likely not need to be the same as the reference biologic, and would invariably be made by a different manufacturing process, the innovator should not be forced to "guess" which of its product or process patents would probably cover a future FOB product and which ones might not, with potentially dire consequences for having guessed wrong. Instead, a mechanism that provides confidential access to follow-on product and process data for the sole purpose of identifying relevant patents would seem to be a more rational and practical approach.

Additional questions arise with respect to third parties who are likely to get involved in FOB patent litigation. Patent owners (such as university licensors) who have licensed relevant patents to the reference product sponsor, but who have reserved their patent enforcement rights, may need to be included in the patent resolution process. Early inclusion of such third party plaintiffs would seem to be necessary for a patent resolution process that provides legal certainty for innovators, patent holders, FOB applicants, and market participants prior to marketing of a FOB product.

It is not clear, however, that a relatively high degree of complexity of biologics patent portfolios, or the inclusion of third party patentees, would necessarily translate into a higher rate of litigation, or length of litigation, in the FOBs context. Industry experience over more than two decades of biotechnology patent litigation has shown that, while litigation involving biologic products can indeed be complex, such litigation has not been vastly more complicated than other high-stakes commercial litigation over other valuable products. Biotechnology patent disputes today can be adjudicated within a relatively stable doctrinal framework that is expected to

solidify further as biotechnology matures both as a science and as an industry. Further, some of the aspects that add complexity to biologics patent estates would not necessarily all come to bear in FOBs patent litigation. For example, composition-of-matter patents claiming the DNA that encodes the biologic protein, the host cell used for making it, or the promoter sequence used to drive its expression, etc., may not be relevant in U.S. patent litigation if the follow-on product is imported from India, China, or Europe. Third, the sheer rate of litigation per reference product is likely to be lower for biologics than it is for small molecule drugs. In the Hatch-Waxman context, a single reference product can get involved in multiple patent infringement suits against eight or more generic drug applicants.[39] Due to the complexities and cost inherent in developing biologic products, including FOBs, the number of potential FOB competitors – and the amount of litigation over multiple follow-on applications all referencing the same innovator product – will likely be smaller overall for at least a number of years. Finally, the length of reference product data exclusivity will be an important determinant of the numbers of "relevant" patents, because only patents that have a term longer than the reference product data protection would need to be adjudicated. It stands to reason that substantial periods of reference product data exclusivity would have the beneficial, if incidental, effect of simplifying litigation by taking those patents that expire during the innovator's data exclusivity period "off the table."

No good predictions can be made with respect to length of litigation. Patent litigation length depends on many factors that are highly specific to the parties, the legal issues in the case, the caseload of the court where the action was brought, the way the case is managed by the court, the individual judge to whom the case was assigned, and the like. To be sure, patent litigation generally does consume a lot of time. Experience from the small molecule sector, for example, suggests that the 30-month period envisioned by the Hatch-Waxman Act is not always sufficient to fully litigate a patent case on the merits. In any event, substantial reference product data exclusivity periods would likely be helpful in providing a litigation timeframe in which all key patent disputes could play out prior to FOB approval.

B4. When is it in the interest of a referenced biologic drug manufacturer to resolve patent issues prior to marketing by a follow-on applicant? When is it in the interest of a follow-on biologic applicant to resolve patent issues prior to marketing its follow-on biologic? When is it in the interest of either party to resolve patent issues following commercial marketing of the follow-on product?

For the reasons stated in BIO's answer to Question #1 in the patent section above, both innovators and follow-on applicants would normally be expected to want to resolve patent disputes prior to launch of the FOB. For a more complete discussion of the disadvantages of a process that routinely envisions patent resolution after FOB launch, see BIO's answer to Question #1 in the patent section as well.

---

[39] See, e.g., multiple infringement actions filed on August 12, 2008 by Hoffmann-La Roche, Inc. against Cobalt Pharmaceuticals Inc., 2:08-cv-04054; Gate Pharmaceuticals, 2:08-cv-04058; Mutual Pharmaceutical Company, Inc. 2:08-cv-04060; Genpharm Inc. 2:08-cv-04052; Teva Pharmaceuticals USA, Inc. 2:08-cv-04059; Orchid Chemicals & Pharmaceuticals Ltd. 2:08-cv-04051; Apotex Inc. 2:08-cv-04053; Dr. Reddy's Laboratories, Ltd. 2:08-cv-04055; in the U.S. District Court for the District of New Jersey relating to defendants' Paragraph IV certifications as part of ANDAs to manufacture generic versions of Roche's Boniva® (ibandronate sodium) once-monthly tablets.

B5. What are the legal impediments facing a follow-on biologic applicant that has not been sued for infringement to obtaining a declaratory judgment on patent infringement or invalidity issues prior to commercial marketing of its follow-on product?

Appropriate follow-on biologics legislation would provide opportunities for innovators to protect their intellectual property rights – and for both parties to resolve disputes over them – before the FDA allows a follow-on product on the market. By making the filing of a FOB application an act of infringement, innovators and patentees would have a cause of action for infringement. Likewise, FOB applicants who have a justiciable case or controversy could seek legal and business certainty under the available Article III jurisdiction, as interpreted by the Supreme Court and the U.S. Court of Appeals for the Federal Circuit. By ensuring that these two complementary mechanisms would operate during the innovator's statutory exclusivity period, patents that claim the FOB product could be tested in litigation, thus ensuring patent and business certainty for the FOB applicant and innovator, and market certainty for patients, providers, and payers.

B6. Are regulatory exclusivities needed to encourage follow-on biologic applicants to challenge patents? Why or why not?

The emphasis should not and need not be on "challenging patents." The 180-day exclusivity under the Hatch-Waxman Act was designed to incentivize generic drug applicants to take on the cost of patent litigation because of free-rider concerns over other generic drug applicants that would benefit from this litigation investment. While it can fairly be asked whether the benefit of being able to exclusively market a first generic drug without significant price erosion for six months is commensurate with the cost of patent litigation,[40] many believe that the 180-day exclusivity has created an unnecessarily litigious environment by placing a high premium on bringing the earliest possible patent challenge, often by multiple filers who cannot afford to cede valuable generic exclusivity for a profitable drug to their generic competitors. 180-day exclusivity rewards the earliest possible challenge, not the one with the highest merits. In BIO's view, the award of regulatory exclusivity or similarly powerful incentives merely for "challenging patents" carries a significant risk of operating in multiple unintended ways that, in the Hatch-Waxman context, have already led to significant litigation, regulatory scrutiny, and legislative intervention.

BIO cautions against the creation of such misguided and unwise patent litigation incentives. FOB legislation should encourage and facilitate investment in bringing FOB products to market rather than "challenging patents." The logic for creating special patent challenge incentives under the Hatch-Waxman Act does not apply to FOBs because no two biologic drugs made by different manufacturers using different processes will be identical. Therefore, patent litigation over one FOB product will not necessarily apply to another FOB product, and the risk of

[40] This question can even more squarely be posed in light of the MMA Amendments of 2003, which confer 180-day exclusivity for the mere first filing of a paragraph IV certification, regardless of whether litigation ensues.

litigation free-riders faced in the generic context will be much diminished under a FOB framework.

Further, compared to a generic drug submission, the data package that will need to be assembled for a follow-on biologic application will be much more comprehensive and expensive. Also, regulatory approval of a follow-on biologic application will likely be less certain than it is for an average generic drug application, and further investment may be necessary to conduct any additional studies the Secretary may require, whether pre- or post-approval. In short, having made a very significant investment in its follow-on biologic technology, a follow-on applicant will be sufficiently motivated to challenge any patent barriers to entry even in the absence of artificial "patent challenge" incentives.

While it is thus unlikely that FOB applicants need special incentives to challenge patents, if Congress were to decide that a special regulatory exclusivity incentive is appropriate, the conditions under which such exclusivity would be triggered or forfeited would need to be carefully defined. In any case, such incentives should be designed to stimulate investment in FOB development and the submission of quality, approvable FOB applications, not the submission of naked patent challenges at the earliest possible opportunity.

Conclusion:

BIO appreciates this opportunity to respond to FTC's questions regarding competition provided by developing a regulatory approval pathway for follow-on biologic drugs. We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/s/

John M. Taylor, III
Executive Vice President, Health
Biotechnology Industry Organization

ATTACHMENT B

A FOLLOW-ON BIOLOGICS REGIME WITHOUT STRONG DATA EXCLUSIVITY[1] WILL STIFLE THE DEVELOPMENT OF NEW MEDICINES

BIO recognizes the importance of providing the fruits of science and innovation in healthcare for the benefit of all American citizens. BIO represents both small and large biotechnology companies: some with products already on the market and most with their lead products still at the development stage with many years ahead of them before they can expect marketing approval. BIO's goals are to ensure that those companies with approved products are able to receive an appropriate return on their investment, and that the development stage companies can continue to finance their operations through accessing the venture and equity markets with the opportunity for an appropriate return in the future. This enormous reservoir of innovation is critically important to the future of healthcare, the U.S. economy, the biotechnology industry, and, of course, patients.

Central to achieving these goals, any statutory pathway for follow-on biologic products ("FOBs") must establish a substantial period of data exclusivity to preserve incentives for research, development, manufacture, and approval of new biologic therapies. This is necessary because, under a statutory framework allowing for FOBs, there is a very real potential that the manufacturer of a FOB may be able to secure abbreviated regulatory approval based at least in part on the innovator's prior approval, and, at the same time, avoid infringing patents that protect the innovator's biotech product. That likelihood exists because of the confluence of two critical factors not present in the Hatch-Waxman construct for generic small molecule drugs. First, unlike a generic drug which must be the same as an innovator product, a FOB will only be required to be "similar" or "highly similar" to the corresponding innovator product. Second, because of the nature of biologic products – large molecules produced by living cells and organisms – patent protection is often narrower and easier to "design around" than that afforded to small molecule drugs.

In light of this potential gap in patent protection for biologics, data exclusivity in a FOB regime must be substantially longer than the five years currently afforded to drugs under the Hatch-Waxman Act. Biotechnology companies must have some certainty that they can protect their investment in the development of new breakthrough therapies for a substantial period of time in order to secure the necessary resources from venture capital firms and other funding sources. As described below, that period should be no less than 14 years if biologics are to receive the same length of effective market protection as drugs, and thus avoid skewing investment away from higher risk biologics research and development. Indeed, in striking the appropriate balance, Congress should err on the side

[1] Definition of data exclusivity: the time period after approval of the innovator's product during which the FDA may not approve a follow-on biologic product relying to any degree on the safety and effectiveness of the innovator product.

of protecting incentives for biomedical innovation because, as compared to the broader pharmaceutical industry, the biotechnology industry is largely comprised of small companies that are, for many reasons discussed herein, more vulnerable to changes in investment incentives.

The Need for Substantial Data Exclusivity for Innovator Biologics in any FOB Statutory Scheme

The Problem: The Similarity Standard for FOBs Creates a Gap that May Allow for Regulatory Approval without Adequate Patent Protection

Under the 1984 Hatch-Waxman Amendments to the Federal Food, Drug and Cosmetic Act, a generic version of a small molecule drug may be approved for marketing only if its active ingredient is the "same" as in the innovator product. Thus, the patents that cover the innovator's drug molecule necessarily apply to the duplicate, generic version, and a generic may not enter the market until the innovator's patent expires. Indeed, the manufacturer of a generic drug may not have it both ways – it cannot gain FDA approval of its product by demonstrating that the active ingredient is the same as the innovator product and then turn around and claim in the patent context that its product is different from the innovator's drug. In this respect, the Hatch-Waxman exclusivity provisions work in concert with the patent system to provide market protection to innovator drugs.

In contrast, under the statutory framework being considered for FOBs, the same level of protection will not be available to innovator biological products. Unlike a small molecule generic drug, a FOB will not be required to be the "same" as the innovator product. Instead, it will only have to be "highly similar" to the innovator product. While the meaning of "highly similar" may vary between legislative proposals, there is no question that it falls short of the degree of sameness required of generic drugs. In fact, under one current legislative proposal, "highly similar" is defined in a manner that would allow for approval of FOBs with potentially significant differences from the innovator product. As a result, a FOB may be sufficiently similar to the innovator biologic to rely to some degree on the safety and effectiveness of the innovator product and thus receive abbreviated regulatory approval. Yet, it may still be different enough from the innovator product to avoid a patent infringement claim and, thus, get on the market well in advance of innovator patent expiration – undermining incentives to invest in innovation. The pace of medical advancement and the patients who stand to benefit from it would likewise suffer.

The Gap in Protection for Innovator Biologics Will Widen as Patent Law Yields Increasingly Narrow Patent Claims

Because of the nature of biologic products – produced by living cells and organisms – patent protection is different from and may be weaker than that afforded to small medicinal molecules.[2] First, because of current limitations of patentability of naturally

[2] This is so because the so-called "utility," "written description," and "enablement" requirements of the Patent Act are interpreted more stringently for biotechnology inventions than for most other technologies.

occurring substances, many biologics are protected only by process patents that may be easier to "design around." Moreover, under rules of patentability specific to biotechnology inventions, patent claims on biologics must often be narrowly drawn to the specific innovative aspect (e.g., a specific protein or nucleotide sequence) to be allowable. By contrast, patents on small medicinal molecules can often claim a whole class (a so-called genus) of related molecular structures and thereby provide a "penumbra" of patent protection covering the innovator small molecule.

These distinctions in patent protection for biologics are especially significant because, through a series of court decisions, the patent law is leading inexorably to narrower allowable claims. While this trend impacts all products, it is especially relevant to questions surrounding protection of innovator biologics in a FOB regime. That is because narrower patent claims for such products will result in a wider gap through which a FOB may be able to receive regulatory approval while still eluding an innovator's patents.[3] Furthermore, the sheer size of biologic products – often several hundred- or thousand-fold larger than small molecule drugs – increases the number of possible ways of altering the product such that it would be similar enough to the original product to qualify as a FOB but different enough to be outside the scope of the patents on the original product. Disputes over patent claim coverage that are likely to arise from this situation would lead to an increase in litigation expenses and add to the uncertainty that biotechnology companies could protect their investment.

Strong Data Exclusivity Will Preserve the Balance that Congress Found Necessary to Stimulate Innovation in the Pharmaceutical Industry

With passage of the Hatch-Waxman Amendments in 1984, Congress recognized that normal patent protection alone is insufficient to provide small molecule pharmaceutical innovators with sufficient market exclusivity to allow them to recoup clinical research and development costs. To address this problem, Congress established a period of data exclusivity for drugs, and it created a mechanism allowing for the extension of patents on innovator drugs and biologics for up to 14 years following approval of the product.[4] In providing for patent extensions of up to 14 years, Congress acknowledged that – unlike most other industries – the pharmaceutical industry rarely benefited from the full length of normal patent protection (then 17 years) due to the long development and regulatory approval process for drugs. Given that Congress has previously concluded that 14 years of patent protection is appropriate for drugs and biological products, any statutory

---

Moreover, patents cannot claim something that occurs naturally. Therefore, because many biotech products are "artificial" (recombinant) versions of naturally occurring proteins, the patent claims must be narrowly crafted (i.e., limited to specific isolated and purified DNA sequences, proteins, or clonal cell lines) in order to avoid encompassing naturally produced molecules. In contrast, most of the small medicinal molecules are synthetic. It is in part because they never existed before in nature that the claims to such synthetic small molecules may be drafted more broadly than claims to biotechnology products.

[3] Manheim, Granahan, and Dow. "'Follow-On Biologics': Ensuring Continued Innovation in the Biotechnology Industry," Health Affairs, March/April 2006.

[4] Extension is calculated by taking: ½ of the time spent diligently from IND effective date to NDA submission; and the full NDA review period; patents cannot be extended by more than 5 years. The patent extension also cannot result in a patent that has a term of more than 14 years post-NDA approval.

formula that allows for FOBs should at least guarantee that same degree of effective market protection – and, for the reasons discussed above, that protection can be accomplished most predictably through data exclusivity.

The presence of substantial data exclusivity also would serve as an additional incentive to research and prove the safety and effectiveness of new indications for existing biologics. Data exclusivity for new indications is critical in areas such as cancer research, where initial marketing approval generally focuses on late-stage disease, and research and development activities for early-stage or adjuvant therapies most often occur much later in time. It is important to provide substantial exclusivity for the original treatment in order to support the expensive further development for these later indications, as well as an additional period of exclusivity – no less than two years beyond the standard 14 year period – to provide the proper incentives to research and bring to market the vibrant pipeline of treatments that can allow cancer patients to live longer and healthier lives.

It also is important to note that this length of data exclusivity for innovators in any FOBs regime would not operate as an extension of exclusivity. Rather, the period of data exclusivity would run concurrently with the patent term for the product, which itself may run at least 14 years. Data exclusivity would create actual market protection for the innovator product only in those instances where the follow-on manufacturer is able to work around the patents held by the innovator but still gain approval of its product as a follow-on. In this respect, a 14-year period of data exclusivity serves essentially as an insurance policy that provides the innovator with some certainty of protection, given that a FOB can be approved on the basis of a less stringent standard of similarity. Thus, 14 years of data exclusivity is an essential component of a balanced statutory pathway for FOBs, making possible their introduction and use in the market while appropriately safeguarding incentives for biotechnology innovation.

Empirical Data Support a 14-Year Period of Data Exclusivity for Biologics

In 1998, the Congressional Budget Office found that the average period of time for marketing of a drug product with patent protection is 11½ years[5], and new molecular entities, on average, are marketed in the U.S. for 13.5 years before the entry of generic competition.[6] Further, the breakeven point for a biologic occurs after it has been on the market between 12.9 and 16.2 years.[7] As described below in more detail, biotechnology companies bear enormous costs and risk to develop life saving products. As a result, it is essential that the period of effective market protection for drugs – 14 years – be extended to biologics. Indeed, if the data exclusivity period for biologics is less than that, then, because of the higher risks of biologics development, it will skew investment options away from biotechnology.

---

[5] Congressional Budget Office, A CBO Study: How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry, July 1998, Chapter Four, "The Effects of the Hatch-Waxman Act on the Returns from Innovation."

[6] Grabowski, Henry and Margaret Kyle. "Generic Competition and Market Exclusivity Periods in Pharmaceuticals," Managerial and Decision Economics (*forthcoming*).

[7] Grabowski, Henry. "Data Exclusivity for New Biological Entities," Duke University Department of Economics Working Paper. June 2007.

Strong Protection for Innovative Biologic Products Is an Essential Incentive for Investment in Biomedical Innovation

In crafting a FOBs regime, it is important to err on the side of incentivizing innovation due to the unique elements of the biotechnology industry, which is largely comprised of small, privately-funded start-up companies without reliable revenue streams. These companies already bear enormous costs and a very high degree of uncertainty, not only in product development and manufacturing, but also in raising the necessary capital to fund innovative research. Thus, as compared to the broader pharmaceutical industry, biotechnology companies are more vulnerable to the type of changes in investment incentives that could result from a poorly-crafted FOBs regime.

Biotechnology Companies Bear Enormous Costs and High Uncertainty

- Cost of Capital: The cost of capital for small biotechnology companies is much higher than the cost of capital for large pharmaceutical firms. While large pharmaceutical companies have product revenue streams that they reinvest in the research and development of new pharmaceuticals, the vast majority of biotechnology companies, as shown below, do not have any marketed products and have very limited revenues.

  The lack of a product revenue stream coupled with risk of early product development drives up biotechnology companies' cost of capital:

  - Whereas the cost of capital for a large pharmaceutical company averages 15.7%, biotechnology companies with at least one drug approved have an average cost of capital of 18.7%
  - Biotechnology companies with only a drug candidate in clinical phase II or III trials have a cost of capital averaging 27.4%.[8]

  The higher cost of capital coupled with failure to give an adequate data exclusivity period to biotech products could result in shifting investment away from small, innovative biotechnology companies.

- Production Costs: Biologics, as opposed to pharmaceuticals, are produced using biologic processes such as cell cultures or fermentation and are then purified. Indeed, cell culture facilities:

  - Take on average three to five years to construct
  - Cost between $250 million and $450 million
  - Must often be constructed before drugs enter clinical testing[9]

[8] Grossmann, Martin. Entrepreneurship in Biotechnology, Physica-Verlag NewYork, 2003.
[9] Grabowski, Henry, Iain Cockburn and Genia Long. "The Market for Follow-On Biologics: How Will It Evolve?" Health Affairs, 25(5).

Further, the cost of materials to produce a biologic is 20 to 100 times more than the materials used to produce a small molecule pharmaceutical.[10]

- Manufacturing Uncertainties: Biologics manufacturing necessitates far more planning, investment and skilled personnel and, thus, can be much riskier than small-molecule manufacturing.[11] "A typical manufacturing process for a chemical drug might contain 40-50 critical tests. The typical process for a biologic, however, might contain 250 or more critical tests…Consequently, construction and validation of new facilities is disproportionately expensive and time-consuming."[12]

- Late-Stage Failures: The success rate for late-stage biotechnology products is lower than for pharmaceuticals. From 2001 – 2005, the success rate of a Phase III trial for the average pharmaceutical was 65% to 75%; whereas, the success rate of a Phase III trial for biotechnology produces was 54% to 58%.[13] These failures occur at the last stage of product development – after years of research and hundreds of millions of dollars have been spent.

The Biotechnology Industry is Comprised Mostly of Small, Start-ups

The biotechnology industry in the U.S. is still relatively nascent: the companies that comprise it are primarily small, private start-ups heavily reliant on venture capital and years away from product commercialization. It is these small companies—many of which will never see a product come to market or turn a profit—that are undertaking the bulk of early development gambles, challenging the boundaries of current medical knowledge toward new and exciting mechanisms of disease treatment amid overwhelming odds. *In fact, small biotechnology companies (all biotechnology companies but the top ten) account for two-thirds of the industry's clinical pipeline.*[14]

The statistics speak to the challenges this emerging industry faces: in 2005, there were 1,415 biotechnology companies in the U.S., but only 329 were publicly traded. In aggregate, even the publicly traded companies have not yet turned a profit:[15,16]

Year	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
$B Net Loss	3.6	4.1	4.6	4.5	4.1	4.4	5.6	4.6	9.4	5.4	6.8	4.1

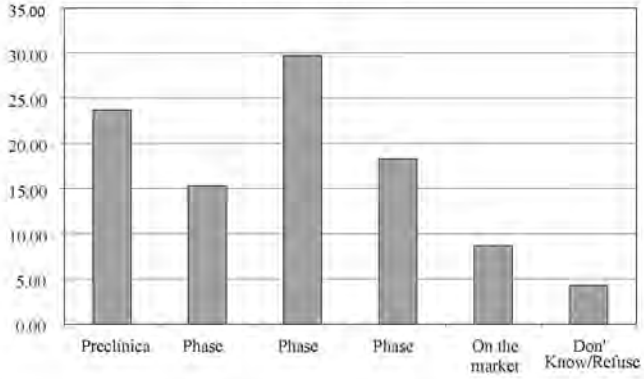
[10] U.S. Bancorp Piper Jaffrey. "The Road Ahead for Biologics Manufacturing," January 1, 2002.
[11] Lakshmikanthan, Jayant. "Outsourcing: Biologics Manufacturing: The CMO Advantage," International BioPharm, Feb. 1, 2007.
[12] Webster, Christopher, et al. "Can There Be an Abbreviated Applications, Generics or Follow-On Products?" BioPharm International, July 2003.
[13] Parexel's Bio/Pharmaceutical R&D Statistical Sourcebook 2006/2007.
[14] The Boston Consulting Group: Rising to the Productivity Challenge, July 2004.
[15] Ernst and Young LLP, Annual biotechnology industry reports, 1995 – 2006. Financial data based primarily on fiscal-year financial statements of publicly traded companies.
[16] Only about 20 biotech companies are currently profitable: Parexel's Bio/Pharmaceutical Statistical Sourcebook 2006/2007, pg. 39.

A 2006 Biotechnology Industry Organization (BIO) representative survey of 300 small biotech companies showed:

- **Company Size:** 65% of the companies surveyed have fewer than 50 employees. 40% of the respondents reported that their company's revenue from all sources was less than $150,000 in the previous year, and 66% had revenues under $1 million annually. Additionally, of those companies that do have revenue, the only revenue streams for the vast majority of the companies were milestone and royalty payments.

- **Product Development:** Of the companies surveyed, less than 10% have a product on the market. The chart below shows the distribution of latest phase of lead product development, which represents each individual company's most fully developed product:

Latest Phase of Lead Product



Thus, while the biotechnology industry continues to grow and expand, the vast majority are emerging enterprises, relying on the investment community and the talents of their dedicated employees to bring much-needed treatments to fruition. Failure to provide substantial data exclusivity could fundamentally alter the ability of these small companies to continue to innovate.

U.S. Public Policy Should Encourage a Growing Biotechnology Industry

The U.S. leads the world in biotechnology innovation:

	U.S.	Europe	Canada	Australia

Annual R&D	$18.5 B	$4.2B	$1.7 B	$1.0 B
No. of Companies	1,473	1,878	470	226
No. of Public Companies	363	96	81	58
No. of Employees	146,100	32,470	7,440	6,393

Source: Burrill & Company, Ernst & Young

Indeed, the per capita biotechnology R&D is 574% higher in the U.S. than in the European Union.[17] U.S. public policy thus should support this important U.S. industry and employer and encourage its growth through effective market protection from unfair and premature competition by generic companies. Only in this way will the U.S. continue to lead the world in biotechnology innovation.

Conclusion

Continued U.S. leadership in biotechnology innovation, made possible through sound public policy as outlined here, will enable further progress in the research and discovery of breakthrough therapies to improve the health and lives of patients across the globe. Today, as the legislative framework for follow-on biologics comes into view, it is critical that data exclusivity of no less than 14-years be included as a central component of that framework, given the uncertainties of effective patent-based protection and the higher risks associated with investment in biotechnology.

[17] Based on EU's population of approximately 457 million people and the U.S. population of 298 million people – both figures estimated in July 2006.

ATTACHMENT C

Data Exclusivity Periods for Biologics:

Updating Prior Analyses and Responding to Critiques

Duke University Department of Economics Working Paper, No. 2008-10

December 22, 2008

Authors:

Henry Grabowski
Professor of Economics and Director of the Program in Pharmaceuticals and Health Economics
Duke University
grabow@econ.duke.edu
Corresponding Author

Genia Long
Managing Principal
Analysis Group, Inc.
glong@analysisgroup.com

Richard Mortimer
Vice President
Analysis Group, Inc.

Acknowledgments

This research was supported in part by the Pharmaceutical Research and Manufacturers of America (PhRMA). The design, analysis, and composition of the analyses and manuscript were conducted independently and entirely by the authors, and we are solely responsible for any errors.

The authors thank Alex Brill for sharing his data.

I. SUMMARY

Recent discussion, including at the November 21, 2008 Federal Trade Commission Roundtable on Follow-on Biologic Drugs, has addressed the question of the appropriate duration of data exclusivity (also called data protection) for innovative biologics. This paper proposes that the breakeven financial analysis outlined in an earlier paper is an appropriate framework for the assessment of different data exclusivity periods being proposed in the context of an abbreviated regulatory approval pathway for biosimilars.[1] Among the key parameters in this model are: the cost of capital;[2] expected margins produced by marketed biotech products (contribution margin);[3] and other financial parameters such as required pre-marketing and post-marketing R&D investments. Applying this model led to the conclusion that a representative portfolio of biologics would "break even" or just cover its costs of development, manufacturing and sales, together with the industry's cost of capital, in 12.9 to 16.2 years, thereby providing support for a substantial data exclusivity period.

A recent critique, which adopts the same model and framework for its assessment of the appropriate duration of data exclusivity periods, suggests that alternative values for the cost of capital and contribution margin parameters are more appropriate and that, applying them

---

[1] Grabowski, H., "Follow-on Biologics: Data Exclusivity and the Balance between Innovation and Competition," *Nature Reviews Drug Discovery*, 7, 479 – 488 (2008).
[2] The cost of capital is the annual rate of return that an investor would require on average in order to make a given investment. In the case of biologics, this accounts for the risks associated with potential failure to develop or market the biologic candidate product successfully.
[3] The contribution margin is a measure of how much a company earns in sales, after subtracting costs for labor and materials (cost of goods sold), and selling, general and administrative expenses. Contribution margin is not equivalent to profit margin, which also subtracts the costs of R&D, and interest, taxes and all other expense items.

supports a lower breakeven period, and therefore, a lower data exclusivity period.[4] It also considers the effects on breakeven periods of different assumptions for innovator product share and price impacts resulting from biosimilar entry. This paper corrects computational problems and inconsistencies in Brill's critique of the breakeven period. Furthermore, it disputes his claim that a 10% cost of capital and an average 60% contribution margin assumption are reasonable and appropriate baseline valves, and performs a number of sensitivity analyses using a range of input values. Together, these analyses suggest that limiting the data exclusivity period to less than 12 to 16 years results in failure of the representative portfolio of biologics to break even within an extended period, under reasonable assumptions.

The remainder of this paper is organized as follows:

- **Section II** discusses the importance of data exclusivity to biologics, including why patents alone may be insufficient to provide protection for biologics;
- **Section III** summarizes why the portfolio cash flow approach adopted in this paper is an appropriate framework for analysis of the impact of data exclusivity limits on investment and competition in the biotech industry;
- **Section IV** summarizes the key points in a recent critique of the previous "breakeven" analysis published in *Nature Reviews Drug Discovery* (hereafter referred to as the *Nature* model) and identifies four problems and implausible assumptions in this critique;
- **Sections V and VI** refute key assumptions from this critique, including the a cost of capital that is too low (Section V) and contribution margins that are too high (Section VI);
- **Section VII** notes that the critique fails to take into account other countervailing assumptions in the prior *Nature* analysis that tend to understate expected breakeven periods;
- **Section VIII** extends the previous *Nature* analysis to incorporate other impacts associated with biosimilar entry, and summarizes the results of sensitivity analyses on the extended model;
- **Section IX** summarizes the overall results of the additional analysis in this paper; and
- A brief **Appendix** addresses the critique's computational inconsistencies

---

[4] Brill, A., "Proper Duration of Data Exclusivity for Generic Biologics: A Critique," unpublished manuscript, November 2008.

II. THE IMPORTANCE OF DATA EXCLUSIVITY TO BIOLOGICS

Data exclusivity is the period of time between FDA approval and the point at which an abbreviated filing for a biosimilar relying in whole or in part on the innovator's data on safety and efficacy can receive final approval. Data exclusivity is designed to preserve innovation incentives, and recognize the long, costly, and risky process necessary for the innovator to gain FDA approval. Data exclusivity is a critical issue for the future of biologics, with different provisions for data exclusivity in recent legislative proposals ranging from zero to 14 years. All bills other than H.R. 1038, sponsored by Representative Henry Waxman of California, proposed combined periods of at least 12 years.[5, 6]

Data exclusivity periods are essential to compensate for some important shortcomings in patent protection for biologics. Data exclusivity extends from the date of product approval, and this protection period runs concurrently with any remaining patent term protection for the biologic. That is to say, data exclusivity provides additional protection to the innovator when the remaining patent length is shorter than the data exclusivity period at the time of approval (which can occur due to lengthy preclinical and clinical research required to obtain FDA approval), or to

---

[5] Although H.R. 1038 contains no data exclusivity period at all, its absence did not necessarily indicate opposition to a provision, according to coverage at the time, but rather a desire to hold off on backing a specific figure until more was learned about what an appropriate period should be. See summary in *Inside Health Policy,* "Boston University Study Criticizes Exclusivity Measures in Biogenerics Bills," September 30, 2008. Access October 29, 2008 at www.insidehealthpolicy.com/secure/health_docnum.asp?f=health_2001.ask&docnum=9302008_boston&DOCID=9302008_boston.

[6] Recent legislative proposals for establishing an abbreviated pathway for biosimilar entry consider both permissible filing dates and overall market protection periods. For example, the bill S.1695, sponsored by Senator Kennedy, allows for four years before an abbreviated filing can occur, during which the FDA cannot rely on innovator's data on safety and efficacy to review an abbreviated biosimilar application, followed by an additional eight years during which FDA review of the application can take place but the application cannot be approved, for a total of 12 years of data exclusivity.

the extent that the patent is circumvented by a biosimilar prior to its expiry. Patent protection alone may be insufficient for biologics in the context of biosimilars for two primary reasons:

(1) The standard for FDA approval of biosimilars is likely to be based on *similarity* rather than *sameness*, allowing for greater differences between the biosimilar and the reference product than are allowed between an AB-rated generic small-molecule drug and its reference product. As a result, development of a biosimilar may allow for greater deviations from the reference product and greater opportunity to deviate slightly from the patented technology, thereby sidestepping patent infringement while still benefiting from an abbreviated FDA application process. In 2007 remarks before the Committee on Oversight and Government Reform, Dr. Janet Woodcock of FDA noted, "Because of the variability and complexity of protein molecules, current limitations of analytical methods, and the difficulties in manufacturing a consistent product, it is unlikely that, for most proteins, a manufacturer of a follow-on protein product could demonstrate that its product is identical to an already approved product."[7]

(2) Patents for biologics, unlike for small-molecule drugs, do not typically protect the entire molecule or class of related molecular structures. Biologics are much more complex than small-molecule drugs, and the patents protecting biologics tend to focus on certain aspects of the protein or ways of producing the protein rather than on protecting the entire molecule.[8]

Data exclusivity provides investors with an "insurance policy" against the potential failings of patent protection for biologics. Recent evidence suggests that the effective marketing

---

[7] Woodcock, J. "Follow-on Protein Products" Statement before the Committee on Oversight and Government Reform, U.S. House of Representatives, 26 March 2007, FDA web site (online), http://www.fda.gov/ols/2007/rotein32607.html, (2007).
[8] Manheim, H., Granaham, P., and Dow, K., "Follow-on Biologics: Ensuring Continued Innovation in the Biotechnology Indnstry," Health Affairs, 25:394-404 (2006).

exclusivity period for small-molecule drugs (the time between launch and first generic entry) is approximately 12 years on average.[9] Data exclusivity for small-molecule drugs is generally not the constraint on generic entry (although in recent years, it has become increasingly important for small molecules due to the rise of Paragraph IV challenges under the Hatch-Waxman Act), whereas it is expected to be more determinative for biologics due to the nature of their patent protection.[10]

III. A PORTFOLIO DISCOUNTED CASH FLOW APPROACH IS AN APPROPRIATE FRAMEWORK FOR ANALYSIS OF THE IMPACT OF DATA EXCLUSIVITY LIMITS ON INVESTMENT AND COMPETITION IN THE BIOTECH INDUSTRY

In evaluating the impact of data exclusivity periods of different durations on the incentives for innovation, an appropriate perspective to adopt is that of a potential investor who weighs alternative investments, together with their expected risks, costs and returns. Venture capital and private equity are the primary sources of early stage investment in biotech start-ups, which account for many new pipeline biologics. Venture capital-backed firms constitute 40 percent of employment in biotechnology.[11] Such investors account for the low probabilities of success of any individual opportunity by investing in a long-term portfolio of opportunities, most of which ultimately will not succeed, but one or two of which may earn significant returns years later. Larger established firms, as well as venture investors, need to take a portfolio approach,

---

[9] Grabowski, H. and Kyle, M., "Generic Competition and Market Exclusivity Periods in Pharmaceuticals," *Managerial and Decision Economics*, 28: 491-502 (2007). For drugs with first-generic entry in 2005, the average market exclusivity period (MEP; the time between product launch and first-generic entry) was 11.5 years (drugs with sales greater than $100 million) to 13.0 years (all drugs).
[10] Grabowski, H. "Are the Economics of Pharmaceutical R&D Changing? Productivity, Patents, and Political Pressures, *PharmacoEconomics*, Vol. 22, Suppl. 2, 2004, pp. 15-24.
[11] Lawton R. Burns, Michael G. Housman, and Charles A. Robinson, "Market Entry and Exit by Biotech and Device Companies Funded by Venture Capital," *Health Affairs* 28, no. 1 (2009): w76-w86.

given the low probability of success for new biological candidates, and the skewed distribution of sales revenues for approved marketed candidates. Venture capital firms use discount rates that vary by stage of investment, and account for a decreasing level of risk as products approach launch and commercialization. An empirical analysis of this issue found that discount rates vary from 70% down to 25%, depending on stage of finance (start-ups to IPOs).[12] Similarly, established biotech or pharmaceutical firms apply a portfolio approach to their selection of which candidate molecules to advance in development and to the valuation of licensing and acquisition opportunities, using a risk-adjusted cost of capital, as discussed below.

This approach was outlined in an article recently published in *Nature Reviews Drug Discovery* (Grabowski, 2008; henceforth referred to as the *Nature* article). In a recent unpublished white paper, Alex Brill utilizes the same framework to comment on the optimal data exclusivity period. Brill accepts the basic premise of the *Nature* article, namely that data exclusivity times should be guided by the time necessary for a representative new biological entity to just cover its expected R&D, sales and marketing investments, together with the industry-wide cost of capital. This is defined as the "breakeven lifetime" in the parlance of economics and financial studies.

Brill also accepts the appropriateness of a portfolio approach to evaluating R&D investment decisions, like the one performed in the analysis in the *Nature* article. Accordingly,

---

[12] Sahlman,W.A., "The Structure and Governance of Venture-Capital Organizations," *Journal of Financial Economics*, 27(1990) pp. 473-521, Table 6 at p. 511.

he also focuses on the returns for a representative biological product from a portfolio based on the historical distribution of R&D costs and revenues.[13]

IV. BRILL'S ANALYSIS

As discussed, the analysis presented in the 2008 *Nature* article results in breakeven returns for the representative biologic between 12.9 years and 16.2 years. This is depicted in Exhibit 1, which is Figure 7 from the *Nature* article. This diagram shows the cumulative net present values over a 30-year period from the beginning of the R&D investment period through market launch and over the product life cycle. As shown in this diagram, it takes 12.9 years after launch, at a discount value of 11.5%, for the cumulative net present value (NPV) to become positive in terms of value from cash flow, and 16.2 years for breakeven at a discount value of 12.5%. Alternatively stated, it takes 12.9 to 16.2 years for the firm to earn a rate of return which is just equal to its risk-based cost of capital.

A. DESCRIPTION OF BRILL'S ANALYSIS

In his white paper, Brill makes three changes from the analysis presented in the *Nature* article that affect the breakeven point calculation:

---

[13] In particular, his basic inputs include average R&D investment from DiMasi and Grabowski, 2007 (DiMasi, J., and Grabowski, H., "The Cost of Biopharmaceutical R&D: Is Biotech Different?" *Managerial and Decision Economics*, Vol. 28, Issue 4-5, pp. 469-479), sales revenue distribution for biologics based on Grabowski, 2003 (Patents and New Product Development in the Pharmaceuticals and Biotechnology Industries," *Science and Cents*, edited by John Duca, Federal Reserve Bank of Dallas, 2003, pp. 87-104), and post approval R&D costs and product launch expenditures based on Grabowski, Vernon and DiMasi, 2002 (Grabowski, H., Vernon, J., DiMasi, J., "Returns on Research and Development for 1990s new Drug Introductions," *Pharmacoeconomics*, Vol. 20, Supplement 3, 2002, pp. 11-29).

(1) First, he assumes that the innovator's product will retain a significant share of its pre-entry sales after the market entry of biosimilars, and bases his estimates in this regard on recent assumptions from the Congressional Budget Office (CBO).[14]

(2) Second, he utilizes a 10% baseline real cost of capital for the representative biotechnology firm, compared to the 11.5% to 12.5% range utilized in the *Nature* article.

(3) Third, he utilizes a 60% contribution margin for the representative biologic product, compared to a 50% baseline value in the *Nature* article.

The *Nature* article estimates a breakeven lifetime of between 12.9 and 16.2 years for the representative biological product. With the above changes in assumptions, Brill claims that relatively short exclusivity periods would still be compatible with significant innovation incentives. In particular, he claims that a seven-year data exclusivity period with subsequent biosimilar entry would still allow firms to break even in just over ten years.

However, Brill's analysis is subject to computational problems and inconsistencies, as well as implausible assumptions. When these are corrected and accounted for, his implication that short data exclusivity periods, coupled with rapid biosimilar entry, still provide strong innovation incentives is not valid. In this paper, we perform alternative sensitivity analyses on particular inputs and assumptions, and confirm the importance of a substantial data exclusivity period for biologics.

---

[14] Congressional Budget Office, Cost Estimate: S.1695 Biologics Price Competition and Innovation Act of 2007, June 25, 2008.

B. CRITIQUE OF BRILL'S ANALYSIS

Exhibit 2 is taken from Brill's white paper (it is Figure 3 in his paper and appears with results uncorrected). This exhibit uses the same framework as Exhibit 1, but reflects the changes Brill implemented to incorporate biosimilar entry (including his calculation errors and implausible assumptions). In particular, for the specific case presented in this exhibit, there is a hypothesized data exclusivity period of seven years, after which biosimilars are assumed to enter. Brill relies on a discussion of shares and prices from the CBO bill-scoring document to make assumptions on innovator share and price erosion following biosimilar entry. Brill assumes that, on average, biosimilars will capture a 10% share of the market in the first year of entry, growing to a steady state of 35% within 4 years. He further assumes that price (sales-weighted) would decline by 20% in the first year, and reach a steady state of a 40% price discount by the fourth year. The analysis is also performed under Brill's assumption of a 10% cost of capital and a 60% contribution margin. As shown by the dotted line in this diagram, Brill finds the firm can still break even in year 10, and earn increasingly positive cash flow values after that point.

The four problems and implausible assumptions in Brill's analysis are:

(1) ***Brill's calculations include a significant computational problem and inconsistency in incorporating assumptions made by the CBO in its scoring of follow-on biologics bill S. 1695 into the Nature model; correcting these problems does not yield his results as reported and does not support a seven year data exclusivity period.*** Since the publication of the *Nature* article, the CBO has published a bill-scoring estimate that includes some discussion of potential market shares and price discounts with biosimilar entry. Brill references the CBO discussion in his assumptions of biosimilar shares and price discounts, which

are used to evaluate whether particular data exclusivity periods are compatible with eventual breakeven returns. In doing so, however, the treatment of price discounts and margin changes in Brill's analysis are inconsistently incorporated into the investment returns model in the *Nature* article. This in turn results in a significant underestimation of breakeven times.

(2) ***Brill's assumption on the cost of capital is not reasonable and is at odds with most current best thinking on the subject and with other commonly used industry metrics***. Indeed, the most sophisticated analysis in the current literature, together with accepted published industry metrics, suggests real costs of capital for biotech firms are well above the 11.5% to 12.5% assumed in the *Nature* article. (Golec and Vernon, 2007; Ibbotston Annual Cost of Capital Yearbook, 2008)[15] Brill also fails to acknowledge the large subsample of private and public biotech firms without marketed products that need to rely on venture funding and financial instruments at very high costs of capital.

(3) ***Brill's assumption for the average contribution margin relies on results from six of the most profitable biotech firms, and fails to consider the high degree of variability in profits even among this small, upwardly biased sample. His approach also puts inordinate weights on two of the most successful biotech firms***[16]. As a result of these sample selection issues, his 60% margin can be viewed as being an extreme value, or upper bound, rather than being a plausible baseline value.

---

[15] Golec, J., and Vernon, J., "Financial Risk in the Biotechnology Industry," *Journal of Applied Economics and Health Policy*, forthcoming; also NBER Working Paper # 13604, November 2007. Ibbotson, *Cost of Capital Yearbook*, Morningstar, 2008.

[16] Together, Amgen and Genentech alone receive 67 percent of the overall weights in Brill's calculation of the average.

(4) ***Brill ignores countervailing assumptions already reflected in the Nature article breakeven analysis, which have the effect of producing estimated breakeven periods that are shorter than likely actual breakeven periods***. For example, the representative portfolio modeled reflects the mean values observed for only the top four ranked quintiles of the sales distribution of established biotechnology drugs, with the bottom quintile excluded. Excluding all biologics in the lowest tail of the distribution biases breakeven periods downward. In addition, the *Nature* model assumes that firms can use existing plant assets to produce the biologics in the modeled portfolio at commercial scale and that capital costs are captured fully by depreciation charges subsumed in the contribution margin. This approach also biases breakeven periods downward, as some new plant construction or retrofitting would be required. The cost of a new multi-product manufacturing plant for large-scale commercial production is substantial. It has been estimated elsewhere that a new manufacturing plant can take three to five years to construction and can cost $250 million or more.[17] Even retrofitting existing plant assets can cost between $50 and $100 million. Finally, the *Nature* model assumes a 3.5% reduction in branded biologic share each year, beginning in the 10th year to account for therapy obsolescence. Vigorous dynamic competition in the therapeutic areas with high unmet need (such as rheumatoid arthritis, oncology and other areas) typically served by biologics, and the high numbers of pipeline products in these areas suggest actual rates of share attrition may be higher in the coming years.

---

[17] Molowa, D.T. The State of Biologics Manufacturing. J.P. Morgan Securities, Equity Research Healthcare Note. 16 February 2001.

C. CORRECTING LOGICAL INCONSISTENCIES IN BRILL'S ANALYSIS

Brill's first point concerning innovator sales after biosimilar entry can be viewed as a logical extension or sensitivity analysis to the breakeven analysis. In the *Nature* article, various qualifying points that had countervailing effects on the breakeven lifetime were presented.[18] One such qualifying point was that, for the foreseeable future, innovative firms may retain significant shares of the market after the entry of biosimilars. This is in contrast to the current experiences of small-molecule drugs, where as behavior under Hatch-Waxman has evolved over the years, high sales products now often lose 90 percent of the market to generics within just a few months (Grabowski, 2004; Silver, 2008).[19] Over time, the markets for biosimilars may evolve to more closely resemble the now intensely competitive ones for generic chemical entities (Grabowski, Cockburn and Long, 2006).[20] In the meantime, however, current biologics may be able to earn potentially significant revenues after biosimilar entry, prolonging the innovative product's life beyond the expiration of data exclusivity periods. Therefore the impact of innovator sales and price erosion on the breakeven calculation needs to be further investigated.

Brill's analysis of these issues, however, has inconsistently implemented how the price erosion assumption will affect the model results presented in the *Nature* article. In calculating changes in contribution margins, Brill assumes that the innovator will discount the price of the brand biologic in response to biosimilar entry, by the same amount as the sales weighted price of

---

[18] Most of the other qualifying points in Grabowski (2008) operate in an opposing manner as discussed below, and these points were ignored by Brill.

[19] Grabowski, H., "Are the Economics of Pharmaceutical R&D Changing? Productivity, Patents and Political Pressures," *Pharmcoeconomics*, Vol. 22, Suppl. 2, 2004, pp. 15-24. Silver, R., "A Wall Street Perspective on Generics," 2007 GPhA Annual Meeting, March 1-3, 2007, available at http://www.gphaonline.org/AM/CM/ContentDisplay.cfm?ContentFileID=593.

[20] Grabowski, H., Cockburn, I., Long, G., "The Market for Follow-On Biologics: How Will it Evolve?," *Health Affairs*, 25, no. 5 (2006), pp. 1291-1301.

the biosimilar entrants. However, he fails to correspondingly reduce the level of assumed brand biologic sales in his modification to the model by the same price discount. This inconsistent computational approach means that he multiplies margins that take the price erosion assumptions into account by revenues that do not.[21]

As discussed in the sensitivity analysis later in this paper, Brill's interpretation of the CBO assumptions on the brand's price response is open to question. The CBO report states that biosimilar entry will constrain innovator prices, but does not specify by how much it will do so.[22] Hence, this is a subject for further sensitivity analysis that we undertake in Section VIII. In this section, however, we examine the effects of the logical inconsistency in Brill's analysis, given his interpretation that the innovator price will be the same as the sales weighted average of the biosimilars. Further details and an illustrative example of this computational problem are presented in the Appendix.

Correcting Brill's computational problems and inconsistencies has a substantial impact on his findings. Applying his overstated baseline profit margin assumption of 60% and understated baseline cost of capital assumption of 10% to the corrected model, and maintaining his assumption of a seven-year exclusivity period results in a breakeven period of over 13 years, not the just over 10 years that he reports. Furthermore, he erroneously states that even with a cost of capital of 11.5% and a seven-year exclusivity period (and his other assumptions

---

[21] These issues are discussed more specifically in the Appendix to this paper. In the updated *Nature* model calculations presented in this paper, we assume that costs are reduced proportionately with reductions in output.

[22] In a telephone conversation on December 22nd, CBO confirmed that the appropriate interpretation of the assumption in their report that the availability of biosimilars will constrain brand-name prices is that brand-name prices will be lower than they would otherwise be without any biosimilar entry. However, the CBO has not released any quantitative assumptions in this regard and are still analyzing the issue in light of new information.

unchanged), a breakeven period (of unspecified magnitude) results. In fact, when his calculation error is corrected, there is no breakeven period in the first 50 years when applying an 11.5% cost of capital assumption and a seven-year breakeven period.[23]

D. SENSITIVITY OF BRILL'S RESULTS

After correcting for calculation problems and inconsistencies, Brill's findings are extremely sensitive to small changes in his assumptions. Exhibit 3 uses the same framework as Exhibit 2, but corrects for Brill's calculation error. Using reasonable assumptions, a seven-year exclusivity period is insufficient:

- Keeping all of his assumptions unchanged but reducing the margin assumption from 60% to 55% results in ***no breakeven period within the first 50 years***.
- Similarly, increasing just his cost of capital assumption from 10% to 11.5% (and keeping his margin assumption at 60%), again results in ***no breakeven period within the first 50 years***.

Even if Brill's margin and cost of capital assumptions were reasonable, which they are not, such high sensitivity in findings to small changes in those assumptions would be of significant concern.

It is also important to keep in mind that while biosimilar penetration rates and/or brand price discounts may be modest in the near term (as reflected in estimates for existing products by

[23] Whether or not a breakeven period exists beyond 50 years following launch of the brand was not investigated, as it is unlikely that investors will consider projects with such a lengthy term to break even regardless of the discount rate.

the CBO or others), they could very well exceed those assumed by Brill in the longer run.[24] Data exclusivity provisions are focused on innovation incentives for the long-term. Many of these molecules will not reach the market for a decade or more, and biosimilar entry will be even further removed in time from market launch. Over time, attrition rates may increase for biologics as the FDA develops a larger experience base, and private and public reimbursement systems evolve for biosimilars.

Even if one accepts Brill's cost of capital and contribution margin assumptions, increasingly aggressive biosimilar entry following the expiration of data exclusivity periods would result in longer breakeven periods over time or no breakeven period at all over a reasonable timeframe.

V. 10 PERCENT COST OF CAPITAL IS NOT CREDIBLE FOR BIOTECH FIRMS

The *Nature* article's estimates of the real cost of capital, 11.5% and 12.5%, are substantially below reliable broad industry estimates of the cost of capital for biotech R&D investments. These original estimates were based on a small group of biotech firms that had multiple FDA-approved biologics and a history of positive operating profits over the past decade, and understate cost of capital for the industry more broadly, which includes smaller biotech firms with few or no biologics on the market. As noted in the *Nature* article, for these reasons, the values used for the real cost of capital are conservative, meaning they are below those faced by most firms. In addition, recent best academic literature estimates the real cost of capital for

[24] The CBO's estimate focuses on a 10-year timeframe beginning with the present when the initial implementation of a regulatory pathway for biosimilars would be developed and implemented and the first biosimilars would enter the market.

biotechnology firms to be no lower than 13.25%, and in some cases much higher when the focus is small to mid-size biotechnology firms:

- Golec and Vernon (2007) estimate costs of capital for the biotechnology industry generally, relying on a three-factor Fama French model (as opposed to a CAPM model), which is the generally accepted, appropriate methodology for estimating cost of capital.[25] Golec and Vernon (2007) estimate a nominal cost of capital of 16.75% for biotech R&D investment, and Vernon recently noted that this corresponds to a real cost of capital of 13.25%, significantly higher than the 11.5% and 12.5% figures used in the *Nature* models.[26]
- Ibbotson's Cost of Capital 2008 Yearbook, a widely accepted general industry source for cost of capital estimates, reports a similar nominal three-factor Fama-French estimate of 17.49% for the median publicly-traded company within the biotechnology SIC code (2836). Assuming a 3% annual inflation rate, this figure would correspond to a 14.07% real cost of capital.

---

[25] Fama-French three factor return models are considered to be far superior for estimating cost of capital in industries such as biotechnology. As noted in Golec and Vernon (2007), the finance literature has established that "[s]ingle factor models such as the Capital Asset Pricing Model (CAPM) do not capture all of the types of systematic risk that influence firm cost of capital. In particular, the CAPM does not reflect the empirical evidence that supports both a size-related and a book-to-market related systematic risk factor."

[26] As estimated by Vernon in comments filed with the FTC during its comment period. This is consistent with Myers and Shyum-Sunder, 1996 (Myers, S., and Shyum-Sunder, L., "Measuring Pharmaceutical industry risk and the cost-of-capital," In: RB Helms, editor, *Competitive Strategies in the Pharmaceutical Industry*, Washington, DC, AEI Press (1996), pp. 208-237), who estimate a 14% real cost of capital for seven medium-sized publicly traded biotech and pharmaceutical firms for 1989. Brill cites this paper, but neglects to mention the 14% estimate in the paper or their corresponding analysis of "small" firms (including Biogen, Cetus and Genentech, along with other firms like Scherer and Mylan, with lower average betas than the true biotechs); the small firm sample had real equity costs of capital of 16.1% (p. 228), and higher if one just used biotech firms.

- Grossman (2003) estimates the cost of capital for smaller biotechnology firms and finds that biotechnology firms without a marketed product but with one or more biologic candidates in Phase II or III trials have an average nominal cost of capital of 27.4%.[27] He also estimates a nominal cost of capital for biotechnology firms with at least one biologic approved of 18.17%.[28] Again assuming a 3% annual inflation rate, these figures would correspond to real costs of capital of 23.69% and 15.24%, respectively.

Consistent with these findings, many small biotechnology firms rely heavily on venture capital for financing, which typically implies very high cost of capital requirements, and biotechnology firms are facing increasing difficulties obtaining this financing in the face of the current credit crunch.[29] Table 1 summarizes biotechnology industry cost of capital figures from a wide range of sources.

Brill relies on a real cost of capital of 10%, which is far lower than estimates typically reported in the academic or trade literature for the biotechnology industry. His results are also highly sensitive to increases in this estimate.[30] Brill claims to substantiate his 10% cost of

---

[27] Grossmann, M., *Entrepreneurship in Biotechnology*, Physica-Verlag New York, 2003.

[28] Myers and Howe (1997) similarly find that smaller biotech firms had much higher betas (measures of risk) than larger biotech companies, which would result in substantially higher cost of capital for smaller firms. They estimate an average beta in 1992 of 1.38 for "mature" biotech firms, 2.38 for biotech firms with drug candidates in advanced stages of clinical testing, and 2.17 for biotech firms without drug candidates in advanced stages of clinical testing.

[29] See for example, Boyle, C., "Credit Crunch Threatens Investment in Medicines," TimesOnline, October 27, 2008.

[30] Brill's claim in footnote 9 of his paper that breakeven still occurs with a cost of capital of 11.5% and a 7 year data exclusivity period is not accurate (even if one relies on his assumed 60% profit margin). Prior to correcting for errors in Brill's calculations, his model yields a 17 year breakeven period with a cost of capital of 11.5% rather than 10%; after correcting the calculations in his model but keeping all inputs other than cost of capital unchanged there is no breakeven in the first 50 years.

capital assumptions by citing the paper, DiMasi and Grabowski (2007), along with Myers and Shyam-Sunder (1995), and by citing a website maintained by Damodaran:

- Brill's interpretation of DiMasi and Grabowski,(2007) as being consistent with a 10% cost of capital is not correct. The 10% estimate is the lowest of several estimates found (other estimates included 12 and 12.5%) and reflects a period of low risk-free rates and risk premiums. Investors will consider *long-term* investment conditions, however, and the lower observed short-term period of risk-free rates and risk premiums are unlikely to be a reliable guide as to long-term future rates and premiums. Furthermore, the estimate is based on relatively large, publicly traded biotech and pharmaceutical companies and does not reflect the cost of capital of small or mid-sized biotechs.
- In discussing DiMasi and Grabowski (2007), Brill also cites Myers and Shyam-Sunder (1995), but ignores their 1989 analysis of "small" firms that finds a real equity cost of capital of 16.1%, or even higher if one examines just biotech firms. Their "small" firm sample actually includes several well-established companies that are now leaders in the biotech field.[31]
- Using data on a website maintained by Damodaran, Kotlikoff (2008) finds the real cost of capital as of January 2008 to be 12.7% for biologic firms. To calculate this cost of capital he uses a risk-free rate based on U.S. Treasury inflation protected securities ("TIPS") of 2%. Brill relies on the same data but estimates a real cost of capital of 10.25%, apparently suggesting that Kotlikoff's estimates are overstated. To arrive at a lower cost of capital than Kotlikoff, it is likely the case that Brill is assuming a lower

[31] Such as Biogen and Genentech, along with other firms like Scherer and Mylan with lower average betas than the true biotechnology firms.

risk-free rate and a lower equity premium. In fact, Brill's risk-free rate would need to approach zero to account for the difference between his and Kotlikoff's cost of capital estimates, as the other input data currently available from Damodaran's website appear to be unchanged from those relied on by Kotlikoff.[32] Biotech firms and early stage investors cannot and do not change their R&D investment decisions based on monthly changes in U.S. Treasury rates, however, as would be suggested by Brill's analysis of the Damodaran data. In comparison, the 13.25% real cost of capital estimate found by Golec and Vernon (2007) reflects a superior approach that is longer-term in focus and less susceptible to such volatility.

Relying on cost of capital inputs that do not accurately reflect the actual biotech industry cost of capital to determine an exclusivity period risks adverse effects on financing. This would severely restrict investment in the development of new therapies and have a potentially strong negative effect on competition. As discussed earlier, the costs of capital for firms without marketed products exceed the industry average substantially and would be particularly adversely affected.

---

[32] The sample of companies that Damodaran relies on for the biotechnology industry includes a number of firms that are not true biotechs for the purposes of this paper, including: Luminex, a bioassay testing firm; Martex Biosciences, which markets supplements; Ista, primarily focused on small molecule opthamalic products; and Mamatech, which develops breast tumor detection products.

VI. CONTRIBUTION MARGINS OF 60 PERCENT ARE TOO HIGH AND REFLECT THE EXPERIENCE OF ONLY A FEW OF THE LARGEST AND MOST SUCCESSFUL FIRMS

The *Nature* article simulations rely on a 50% contribution margin,[33] which is based on the contribution margins realized by the eight largest biotech firms with multiple products on the market. However, few biotech companies are actually profitable, and the universe of biotech firms is populated with development-stage companies whose principal assets are their human capital and intellectual property. These companies would be expected to experience lower contribution margins than a firm with an established line of approved products as represented by the sample that reflects even a 50% margin.

Brill argues for a much higher contribution margin of 60%, which is not reflective of the expected profit potential for most biotechnology products. He bases this estimate on a market-capitalization-weighted average of large and very successful companies, which has the effect of biasing his figure upward and is not representative of the sector.

Brill's use of market-capitalization weighting means that his average margin primarily reflects just two biotech firms with large market capitalizations relative to the other firms in his sample. Even among Brill's six highly successful companies, many of them earn margins well below his 60% average, and there is considerable variation in margins from 43.4% to 63.7%.

---

[33] As noted earlier, the contribution margin is a measure of how much a company earns in sales, after subtracting costs for labor and materials (cost of goods sold), and selling, general and administrative (SG&A) expenses. It is expressed as a ratio of sales, less cost of goods sold and less SG&A, to sales. Contribution margin is not equivalent to profit margin, which also subtracts the costs of R&D, and interest, taxes and all other expense items. All calculations of the contribution margin in this paper were based on publicly available sources.

Furthermore, three of the six firms identified by Brill earn margins of 50% or less over the 2001 to 2007 time period that he examines.

Two of the largest biotechnology not identified in Brill's sample that qualify for inclusion and were independent firms during the time period examined earned average margins of 36% and 35%, respectively, during the 2001 to 2007 period, substantially lower than Brill's 60% margin assumption.[34] Including these two additional firms, the range in margins over the time period would be 33.6% to 63.7% with five of the eight biotechnology firms reviewed earning margins of 50% or less.

Not only do a number of highly successful biotech companies fail to earn contributions margins consistent with his 60% assumption, but contribution margins for medium and smaller biotechnology companies would also be far lower than 60%.

Relying on Brill's overly optimistic contribution margin assumption to determine appropriate exclusivity periods for biologics would result in estimated breakeven periods that are too low. If these figures are used to determine data exclusivity period limits, it would have the effect of making investment in some potentially important innovative biotech products too unattractive to warrant the cost and risk of investment..

VII. BRILL HAS IGNORED OTHER COUNTERVAILING ASSUMPTIONS IN THE PRIOR *NATURE* ANALYSIS

The *Nature* analysis imposes a number of countervailing assumptions that are likely to overstate expected revenues and understate expected costs, resulting in breakeven periods that err on the side of being shorter than what would actually be experienced in the biotechnology

[34] These firms are MedImmune and Chiron.

industry. Brill fails to note any of these countervailing assumptions in his critique, or the fact that reasonable alternative assumptions result in longer breakeven periods, and potentially no breakeven point using his cost of capital, contribution margin, and seven-year data exclusivity assumptions. These countervailing assumptions include:

(1) ***The lowest quintile of sales is excluded when estimating the expected average revenue stream.*** Excluding the lowest quintile results in estimates that potentially overstate expected revenues, and understate expected breakeven periods.

(2) ***A very low rate of product obsolescence from new biologics is assumed.*** Specifically, the *Nature* model assumes no product obsolescence in the first 10 years following release, and only a 3.5% annual reduction in sales after 10 years. The recent surge in the biologic product pipeline and R&D growth for biologics suggests that a faster rate of new product introduction, and therefore a higher rate of obsolescence (shorter product life cycles) may apply than that assumed in the *Nature* model. Currently, over 600 biologics are in development.[35] This low rate of product obsolescence further serves to potentially overstate the expected revenue stream from successful biologics. Including the effect of more robust brand-to-brand competition would produce longer required breakeven periods.

(3) ***Finally, the Nature model assumes that firms are able to utilize existing plants with no retrofitting costs.*** The *Nature* model assumes that product validation costs are the only costs required to produce successful biologic products. In actuality, many firms may face

---

[35] The Pharmaceutical research and Manufacturers of America (PhRMA). Medicines in Development – Biotechnology 2008. PhRMA web site (online), http://www.phrma.org/images/110308%20biotech%202008.pdf (2008).

substantial upfront capital investment costs. The model may therefore understate expected costs of bringing a biologic product to market and, thus, understate expected breakeven periods.[36]

VIII. SOME FURTHER EXTENSIONS AND SENSITIVITY ANALYSIS OF THE *NATURE* MODEL

Data exclusivity periods should be established that are robust to alternative reasonable assumptions for contribution margin, cost of capital, biosimilar share, and brand price discounts in response to biosimilar entry. Brill relies on the following assumptions:

- Contribution margin of 60%
- Biotech cost of capital of 10%
- Biosimilar shares increasing from 10% in the first year to 35% by the fourth year of biosimilar entry
- Brand price discounts increasing from 20% in the first year to 40% by the fourth year of biosimilar entry.

This section presents the results of sensitivity analyses on a range of potential values for each of these key assumptions.

A. SENSITIVITY ANALYSES ON COST OF CAPITAL AND MARGIN ASSUMPTIONS

Table 2 presents the results of sensitivity analyses on breakeven period findings for different cost of capital and contribution margins, and also includes Brill's cost of capital and

[36] Alternatively, this approach is akin to assuming production is outsourced with a contract manufacturing charge equal to book depreciation charges. This also would be a conservative assumption since contractors would have to obtain a margin above depreciation costs to be a viable business.

data exclusivity assumption for comparison. The breakeven periods are reported for data exclusivity periods of 7 years, 10 years, 12 years, 14 years, and 16 years. The results reflect the same biosimilar share and brand price erosion assumptions that Brill uses (i.e., a biosimilar share of 10% in the first year of biosimilar entry, increasing to 35% by year 4, and a 20% brand price discount in the first year of biosimilar entry increasing to 40% by year 4, reflecting a branded competition model). Results indicate that a data exclusivity period of 12 to 16 years is required for breakeven periods of less than 50 years, under reasonable assumptions.

The cost of capital and margin assumptions applied in the sensitivity analyses include:

- The best current estimate now available of the cost of capital for the biotechnology industry is 13.25%, as supported by Golec and Vernon (2007). Breakeven periods are estimated under cost of capital assumptions including the 11.5% and 12.5% assumptions from the *Nature* article, Golec and Vernon's finding of 13.25%, and a real cost of capital estimate of 14.1% based on Ibbotson's median three-factor Fama-French measure. As stated, the 11.5% and 12.5% assumptions are lower than the best current estimates for cost of capital in the biotechnology industry, and therefore would have the effect of understating breakeven periods.
- A contribution margin of 50% is reasonable based on large successful biotechnology companies. Half of the companies in the sample of very successful biotechnology companies used by Brill earn contribution margins of 50% or less. Furthermore, small biotechnology companies typically have margins that are substantially lower. As a result, 50% likely overstates the margin that would be earned by an average biotechnology company. The sensitivity of findings is tested by applying average contribution margins of 60%, 55%, 50%, 45%, and 40%.

The cost of capital and contribution margin sensitivities are reported relying on the same biosimilar share and brand price erosion assumptions that Brill implements (his interpretation of the CBO's assumptions in its cost estimate of S. 1695). In addition, sensitivities with respect to alternative biosimilar share and brand price discount assumptions are also calculated in the next section.

In general, results confirm the importance of a substantial data exclusivity period to R&D returns. Notably, with an exclusivity period of 7 years, the *only* combination of assumptions that yields a breakeven point of less than 50 years is the one used by Brill (i.e., a cost of capital of 10% and a contribution margin of 50% or lower). Even with a 12-year exclusivity period, reasonable breakeven periods are possible only under the more extreme assumptions (e.g., if the best current estimate of the cost of capital of 13.25% is assumed, breakeven is achieved only when the contribution margin assumption is 60%, and breakeven is achieved at 17 years).

Exhibits 4(a), 4(b) and 4(c) present the results for cumulative net present value over time for selected data exclusivity periods, assuming costs of capital of 11.5%, 12.5% and 13.25%, respectively, and a 50% average contribution margin. Exhibit 4(a) shows that the cumulative net present value of returns to the innovator approaches a value just above zero when a cost of capital of 11.5% is assumed and a 12-year exclusivity period is applied. The innovator fails to break even if a cost of capital of 12.5% is assumed under either a 12-or 14-year data exclusivity period (Exhibit 4(b)), and if a 13.25% cost of capital is assumed, the innovator does not break even with a 12-, 14-or even a 16-year data exclusivity period (Exhibit 4(c)).

Exhibits 5(a), 5(b) and 5(c) present the same sensitivities as in Exhibit 4 but assume a 55% average contribution margin. With the higher assumed contribution margin, the innovator would be able to break even with a 12 year data exclusivity period but only if the cost of capital

is 11.5% or 12.5% (Exhibits 5(a) and (b)). In this regard, breakeven is achieved for the combination of a 12.5% cost of capital and 12 year data exclusivity period in approximately 17 years (Exhibit 5(b)). Assuming instead the preferred Golec Vernon-derived 13.25% cost of capital, the innovator breaks even only with a 16-year data exclusivity period, but fails to do so with shorter exclusivity periods of 12 and 14 years (Exhibit 5(c)).

B. SENSITIVITY ANALYSES TO ALTERNATIVE BIOSIMILAR SHARE AND BRAND PRICE EROSION ASSUMPTIONS

1. Biosimilar Share and Brand Price Erosion Assumptions

In this section, we report alternative assumptions on biosimilar share and brand price erosion reported in the literature. We calculate the impact of some alternative assumptions on breakeven results in a series of sensitivity analyses.[37] Before presenting these calculations, as background, it is useful to review the CBO report assumptions, together with other studies that have considered the competitive effects of biosimilar entry.

Table 3 shows the peak market penetration and biosimilar price discount estimates from four recent studies. Each of these studies is focused on established biologic products that could experience biosimilar competition over the next several years. Most studies generally acknowledge that biosimilar penetration rates are expected to increase as markets evolve from a regulatory, scientific, and reimbursement perspective. Hence, these estimates tend to underestimate penetration rates for the products which are now in discovery and development. Peak biosimilar penetration rates reflected in various recent studies range from 35 to 60%, with

[37] All of the assumptions in the sensitivity analyses are guided by the existing literature, economic theory, and the judgements of the authors.

the CBO estimate being the most moderate. Some of these figures reflect biosimilar penetration rates only among the largest selling products, however, while the CBO estimate is described as a sales-weighted average. All of the studies are based on comparators that may be imperfect predictors of the future biosimilar market.

Table 3 also displays the corresponding assumptions on biosimilar price discounts relative to the pre-biosimilar entry price of branded products. In this case, the CBO estimate is generally consistent with other sources at least in terms of initial year price discounts. All of the studies shown expect discount rates to reach at least 25 percent over time, especially for larger-selling products where more entrants are expected.

In terms of the branded products' competitive response to biosimilar entry, only one of the sources in Table 3, Avalere, provides an initial estimate of expected branded product's price impacts. [38] In general the Avalere study predicts that the reference brand will decrease prices in response to biosimilar entry.[39] Economic theory suggests that a competitive price response on the part of the innovator is expected, where there is a small number of entrants in these markets.[40]

Given these considerations and possibilities, further sensitivity analyses appear warranted on biosimilar share and the brand's price response.

---

[38] Ahlstrom, A., et al., "Modeling Federal Cost Savings from Follow-On Biologics, White Paper, Avalere Health, April, 2007 < http://www.avalerehealth.net/research/docs/Modeling_Budgetary_Impact_of_FOBs.pdf >, accessed December 20, 2008.
[39] Avalere has indicated they are refining their estimates on branded share and price impacts as new information becomes available.
[40] Grabowski, H., Ridley, D., and Schulman, K., "Entry and Competition in Generic Biologics," *Managerial and Decision Economics*, 2007, 28(4-5), pp. 439-451.

2. Results of Sensitivity Analyses

Table 4 presents the breakeven period findings for alternative assumptions on biosimilar share and brand price erosion. Specifically, we test the following brand share and price erosion assumptions:

- ***Biosimilar share*** is assumed to be 10% in the first year of entry regardless of scenario, but we test alternative steady-state biosimilar shares in year 4 of 25%, 35%, 45%, and 55%. The 35% assumption is consistent with Brill's assumptions; other values are associated with other recent estimates shown in Table 3.
- ***Brand price erosion*** is assumed under three scenarios: to be 0% in all years (i.e., no increase or decrease in real brand prices from the point of biosimilar entry); to be a 10% brand price decrease in year 1, increasing to a steady-state decrease of 25% by year 4; or to be a 20% decrease in year 1, increasing to a steady-state decrease of 40% in year 4, relative to real prices at the point of biosimilar entry.[41] The scenario that assumes brand price erosion increasing from 20% to 40% in the first four years is consistent with Brill's assumptions.

As shown in Table 4, a 10 year data exclusivity period is consistent with breakeven only in the extreme case where both the cost of capital and margin assumptions fall beyond the best baseline estimates.

All of the above described sensitivity analyses reflect a cost of capital of 13.25% and a contribution margin of 50%. The breakeven periods are reported for data exclusivity periods of

---

[41] Since over time nominal prices for biologics are expected to be adjusted for inflation and other factors, reductions have been reflected on a real, or inflation-adjusted, basis in the *Nature* model. Assuming no real price changes implies nominal price will increase only with inflation.

7 years, 10 years, 12 years, 14 years, and 16 years. As in the earlier sensitivity analyses, the results for these brand share and price erosion sensitivity analyses suggest that limiting the data exclusivity period to less than 12 to 16 years results in failure of the representative portfolio of biologics to break even within an extended period of time, under reasonable assumptions.

As a further sensitivity analysis, Table 5 presents results for similar calculations as those presented in Table 4, but assuming a lower cost of capital of 12.5% and a higher contribution margin of 55%. The results in Table 5 are likely to understate breakeven periods as the cost of capital is lower than the best estimate for biotechnology investments and the contribution margin is higher than for many biotechnology companies. Nevertheless, data exclusivity periods of less than 12 to 16 years are still associated with long, or no, breakeven period. For data exclusivity periods of 7 years, breakeven periods of less than 50 years only occur with no brand price discounts and limited biosimilar shares. For data exclusivity periods of 10 years, breakeven periods of less than 20 years only occur with no brand price discounts; and breakeven periods of less than 50 years occur with moderate brand price discounts (10% to 25%) and limited biosimilar shares.

The analysis presented by Brill and the sensitivity analyses that are presented in this paper are based on worldwide revenues, and it should be noted that these worldwide revenues will be affected by variation in data or market exclusivity periods worldwide. In a review of top selling biologic drugs, the U.S. market is by far the most significant, varying substantially depending on where the drug is in its life cycle.[42] As a result, because volume is a key driver,

---

[42] According to a December 12, 2008 telephone call with a Sanford C. Bernstein & Co. analyst, in 2008, U.S. sales as a percentage of world-wide sales for all tracked biologic products are expected to average

U.S. data exclusivity periods are likely to have the most significant impact on biologic revenues and investor decisions.

IX. SUMMARY AND CONCLUSIONS

Identifying an appropriate data exclusivity period for biologics is an important component of any bill meant to establish an abbreviated regulatory pathway for biosimilar entry. The data exclusivity period is an essential component in allowing investors to earn a market return on biotechnology investments. As a result, continued investment in biotechnology research, and the valuable new products that such investment will produce, is dependent upon the establishment of an appropriate data exclusivity period in conjunction with any legislation establishing an abbreviated biosimilar regulatory approval pathway.

Appropriately modifying the Nature article breakeven model to consider the effects of biosimilar entry on market shares and prices indicates that limiting the data exclusivity period to less than 12 to 16 years results in failure of the representative portfolio of biologics to break even within an extended period, under reasonable assumptions. An adequate exclusivity period is necessary to maintain incentives to invest in the development of innovative new biologic products.

This finding is in stark contrast to the seven-year data exclusivity period suggested by Brill and others, and reflects the correction of errors in Brill's application of the model and the sensitivity of Brill's results to small changes in the key assumptions.

66%. Danzon and Furukawa (2006) previously report that U.S. biologics spending represented 63% of the ten countries examined in 2005.

As discussed in the earlier *Nature* article, analyses of breakeven lifetimes, based on historical cost and revenue data, are only one guidepost for selecting appropriate data exclusivity periods. The future environment for biologic innovation may differ from the past in many important ways – including the cost of development, prices and sales revenue, and the intensity of competition from branded therapeutic alternatives and from biosimilars. Nevertheless, a substantial data exclusivity period also appears to be consistent with a few core principles and facts that were outlined in that article and the introduction to this paper:

- Biologic introductions have been among the most novel therapies directed at life threatening and disabling diseases and offer hope for many important unmet medical needs for thousands of patients.
- There is currently a rich pipeline of product candidates in discovery and development from a spectrum of small start-up firms to larger established entities. Most of this pipeline emanates from firms without marketed products whose investors are very sensitive to expected future returns and risks, as many product candidates never make it to market, and there is no guarantee that those that do will be successful. Even for larger firms, the risk and investment associated with biologics research and development is large.
- The nature of patent protection for biologic products necessitates a strong complementary data exclusivity form of protection.

Given the tremendous potential benefits to patient from new biologics, setting a sufficient data exclusivity period to maintain investment incentives under a range of reasonable assumptions about expected returns should be an important consideration.

Appendix – A Note on Brill's Computational Inconsistencies

The sales and price erosion assumptions that Brill relies upon require three modifications to the model presented in the *Nature* article based on the time of biosimilar entry:

(1) Brand biologic revenues must be reduced based on the assumed brand price discount in response to biosimilar entry, and according to the time path of assumed price discounting. This adjustment reflects the fact that even if the same number of units of the brand product are sold, those sales generate less revenue due to the price discount.

(2) The assumed profit margin earned by the brand biologic must be adjusted to reflect the fact that brand price discount results in a smaller margin. Moreover, in computing margins one also expects costs to decline given changes in output and sales. It is reasonable to assume that production and other costs will decline in proportion to output reductions.

(3) Brand biologic revenues must be reduced by the assumed share of sales that the biosimilar is assumed to capture, and according to the time path of assumed biosimilar penetration. This adjustment reflects the fact that fewer units of the brand may be sold following biosimilar entry. Similarly, non-R&D production costs must be adjusted proportionately.

Brill makes the second and third of these modifications, but fails to implement the first. As a result, he overstates the level of brand biologic revenues following biosimilar entry that would be implied by his assumptions.

As an example for purposes of illustration, assume the following set of facts, and perform the associated calculations:

- Assume brand revenues in absence of biosimilar entry are $1,000.
- Further assume that with biosimilar entry, the biosimilar captures 35% of unit sales and the brand reduces its price by 40%.
- Brand revenues for determining cash flow in the presence of biosimilar entry are then $390, calculated as: $1,000 x (1 – 35%) x (1 – 40%) = $390, to which one would then apply the appropriate profit margin. Assuming that after taking account of the price changes, the appropriate margin in this illustrative example of 50% , the total margin contribution would be $195.

Brill's calculation error would instead yield the incorrect figure of $650 in brand revenues, calculated as $1,000 x (1 – 35%), and $325 in total margin contribution, again assuming a 50% margin.[43]

[43] The margin is assumed to not be affected by the share penetration of the biosimilar; that is, the share of unit sales captured by the biosimilar is assumed to reduce costs and revenues proportionally. Conversely, the brand price decline is assumed to reduce revenues but not costs, resulting in a lower margin.

Table 1

Cost of Capital Estimates for the Biotechnology Industry

Source	Sector/Group	Model	Cost of Capital Nominal	Cost of Capital Real
Golec & Vernon (2007)	Biotech industry-wide	Fama-French	16.75%	13.25%
Ibbotson [1]	Median	Fama-French	17.49%	14.07%
Grossman (2003) [2]	Large drug companies	CAPM	15.70%	12.33%
	Biotech with ≥1 drug approved	CAPM	18.70%	15.24%
	Biotech drugs in phase II or III trials	CAPM	27.40%	23.69%
	Medium-sized publicly traded	CAPM	19%	14%
Myers and Shyam-Sunder (1995)	Small firms	CAPM		16%
Grabowski (2008) [3]	Biotech industry-wide	CAPM		11.5%-12.5%

Notes:

Highlighted cells indicate calculated estimates of real cost of capital based on reported nominal values and assuming a 3% annual inflation rate.

[1] The reported number is for the WACC; Ibbotson includes 73 firms in SIC 2836.

[2] Grossman (2003) relies on a nominal risk free rate of 6.8% and a risk premium of 8.6%.

[3] Grabowski (2008) estimates are based on DiMasi and Grabowski (2007).

Table 2
Breakeven Periods in Years

Alternative Cost of Capital and Contributions Margin Assumptions
Seven-and Ten-Year Data Exclusivity Periods

7-Year Data Exclusivity Period:

Cost of Capital	Contribution Margin 60%	55%	50%	45%	40%
10%	13.5	>50	>50	>50	>50
11.5%	>50	>50	>50	>50	>50
12.5%	>50	>50	>50	>50	>50
13.25%	>50	>50	>50	>50	>50
14.1%	>50	>50	>50	>50	>50

10-Year Data Exclusivity Period:

Cost of Capital	Contribution Margin 60%	55%	50%	45%	40%
11.5%	10.6	14.5	>50	>50	>50
12.5%	17.4	>50	>50	>50	>50
13.25%	>50	>50	>50	>50	>50
14.1%	>50	>50	>50	>50	>50

Sources:
[1] Calculations based on the *Nature* model and Brill's interpretation of CBO assumptions for market share and price decline.
[2] Real costs of capital:
11.5% and 12.5% - Grabowski (2008)
13.25% - Golec and Vernon (2007) and Vernon (2008)
14.1% - Ibbotson median Fama-French WACC for SIC 2836, assuming 3% inflation.

Notes:
[1] Cells highlighted in yellow reflect a breakeven period of under 50 years.
[2] Cells highlighted in pink reflect no breakeven within a 50 year period.

Table 2 (Continued)
Breakeven Periods in Years

Alternative Cost of Capital and Contributions Margin Assumptions
Twelve-, Fourteen-, and Sixteen-Year Data Exclusivity Periods

12-Year Data Exclusivity Period:

Cost of Capital	Contribution Margin 60%	55%	50%	45%	40%
11.5%	10.4	11.4	14.2	>50	>50
12.5%	11.9	17.3	>50	>50	>50
13.25%	17.1	>50	>50	>50	>50
14.1%	>50	>50	>50	>50	>50

14-Year Data Exclusivity Period:

Cost of Capital	Contribution Margin 60%	55%	50%	45%	40%
11.5%	10.4	11.4	12.9	>50	>50
12.5%	11.9	13.5	>50	>50	>50
13.25%	13.6	>50	>50	>50	>50
14.1%	>50	>50	>50	>50	>50

16-Year Data Exclusivity Period:

Cost of Capital	Contribution Margin 60%	55%	50%	45%	40%
11.5%	10.4	11.4	12.9	15.4	>50
12.5%	11.9	13.5	16.3	>50	>50
13.25%	13.6	16.4	>50	>50	>50
14.1%	18.9	>50	>50	>50	>50

Sources:
[1] Calculations based on the *Nature* model and Brill's interpretation of CBO assumptions for market share and price decline.
[2] Real costs of capital:
11.5% and 12.5% - Grabowski (2008)
13.25% - Golec and Vernon (2007) and Vernon (2008)
14.1% - Ibbotson median Fama-French WACC for SIC 2836, assuming 3% inflation.

Notes:
[1] Cells highlighted in yellow reflect a breakeven period of under 50 years.
[2] Cells highlighted in pink reflect no breakeven within a 50 year period.

Table 3

Biosimilar Assumptions
In Several Recent Studies

Source [1]	Peak Biosimilar Penetration Rate	Basis	Biosimilar Price Discount (Relative to Pre-Entry Brand Price)
CBO (2008)	10% (year 1) to 35% (year 4)	Similar market situations	20% (year 1) to 40% (year 4)
Grabowski, et. al. (2007)	10 - 45%	Higher estimates correspond to complex small molecules	10% - 30% (year 1)
Express Scripts (2007)	49%	Therapeutic alternatives	25% (year 1)
Avalere Health (2007) [2]	60%[2]	Average small molecule generic drug penetration rates	20% (year 1) to 51% (year 3)

Notes:

1. Congressional Budget Office, Cost Estimate: S.1695 Biologics Price Competition and Innovation Act of 2007, June 25, 2008.
   Grabowski, H.,Cockburn, I., Long, G. and Mortimer, R. "The Effect on Federal Spending of Legislation Creating a Regulatory Framework for Follow-on Biologics: Key Issues and Assumptions," Duke University, Department of Economics Working Paper, August, 2007.
   Miller, S., and Houts, J., "Potential Savings of Biogenerics in the United States," whitepaper, Express Scripts, February 2007.
   Ahlstrom, A., et al., "Modeling Federal Cost Savings from Follow-On Biologics," whitepaper, Avalere Health, April, 2007.
2. This estimate is for largest selling products. Avalere Health is conducting further analysis.

Table 4
Breakeven Periods in Years

Sensitivity of Findings to Price and Share Assumptions
13.25% Cost of Capital and 50% Contribution Margin

Biosimilar Share (year 4 and beyond)	Brand Price Discount (Year 1 to Year 4 and beyond): No Price Decline	10% year 1 to 25% year 4+	20% year 1 to 40% year 4+
7-Year Data Exclusivity Period:			
25%	>50	>50	>50
35%	>50	>50	>50
45%	>50	>50	>50
55%	>50	>50	>50
10-Year Data Exclusivity Period:			
25%	>50	>50	>50
35%	>50	>50	>50
45%	>50	>50	>50
55%	>50	>50	>50
12-Year Data Exclusivity Period:			
25%	>50	>50	>50
35%	>50	>50	>50
45%	>50	>50	>50
55%	>50	>50	>50
14-Year Data Exclusivity Period:			
25%	30.3	>50	>50
35%	>50	>50	>50
45%	>50	>50	>50
55%	>50	>50	>50
16-Year Data Exclusivity Period:			
25%	25.9	>50	>50
35%	28.7	>50	>50
45%	37.7	>50	>50
55%	>50	>50	>50

Sources:
[1] Calculations based on the *Nature* model
[2] Real costs of capital 13.25% - Golec and Vernon (2007) and Vernon (2008)

Notes:
[1] Cells highlighted in yellow reflect a breakeven period of under 50 years
[2] Cells highlighted in pink reflect no breakeven within a 50 year period
[3] Biosimilar share is assumed to be 10% in year 1 for all scenarios.

Table 5
Breakeven Periods in Years

Sensitivity of Findings to Price and Share Assumptions
12.5% Cost of Capital and 55% Contribution Margin

Biosimilar Share (year 4 and beyond)	Brand Price Discount (Year 1 to Year 4 and beyond): No Price Decline	10% year 1 to 25% year 4+	20% year 1 to 40% year 4+
7-Year Data Exclusivity Period:			
25%	16.9	>50	>50
35%	19.6	>50	>50
45%	27.2	>50	>50
55%	>50	>50	>50
10-Year Data Exclusivity Period:			
25%	14.5	20.7	>50
35%	14.9	24.2	>50
45%	15.5	42.7	>50
55%	16.4	>50	>50
12-Year Data Exclusivity Period:			
25%	13.7	14.4	16.7
35%	13.7	14.5	17.3
45%	13.7	14.5	18.1
55%	13.8	14.6	19.4
14-Year Data Exclusivity Period:			
25%	13.5	13.5	13.5
35%	13.5	13.5	13.5
45%	13.5	13.5	13.5
55%	13.5	13.5	13.5
16-Year Data Exclusivity Period:			
25%	13.5	13.5	13.5
35%	13.5	13.5	13.5
45%	13.5	13.5	13.5
55%	13.5	13.5	13.5

Sources:
[1] Calculations based on the *Nabury* model
[2] Real costs of capital 12.3% - Grabowski (2008)

Notes:
[1] Cells highlighted in yellow reflect a breakeven period of under 50 years
[2] Cells highlighted in pink reflect no breakeven within a 50 year period.
[3] Biosimilar share is assumed to be 10% in year 1 for all scenarios.

Exhibit 1

Cumulative Net Present Value of Cash Flows for Representative Biotech Drug

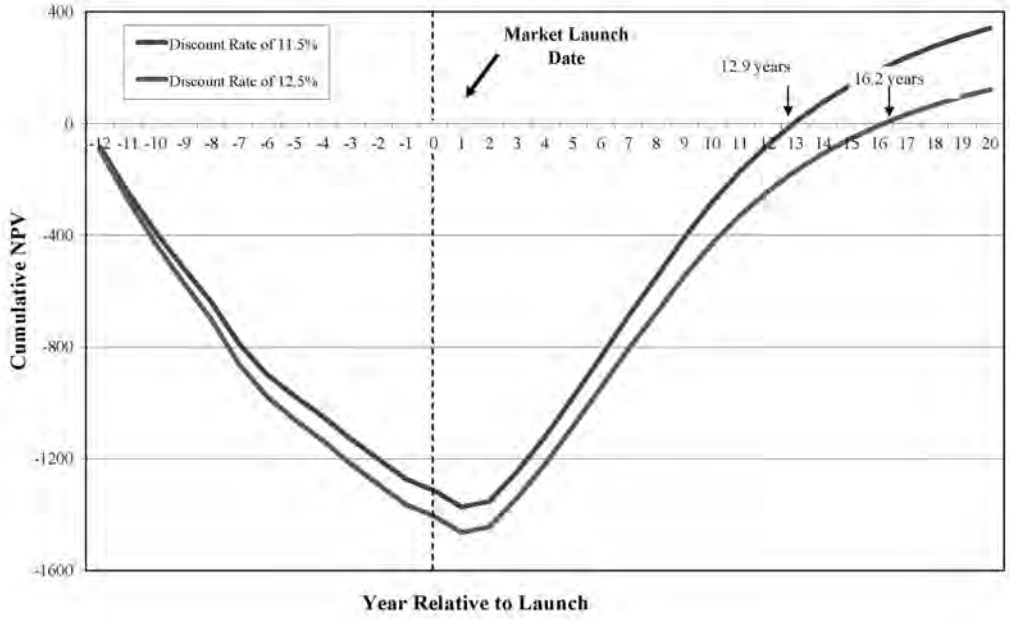
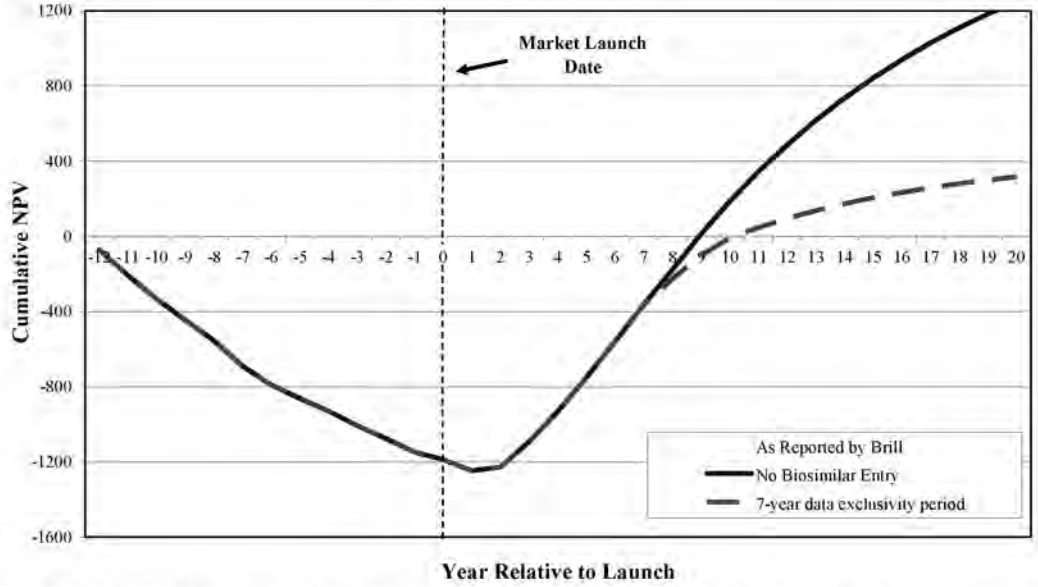


Exhibit 2

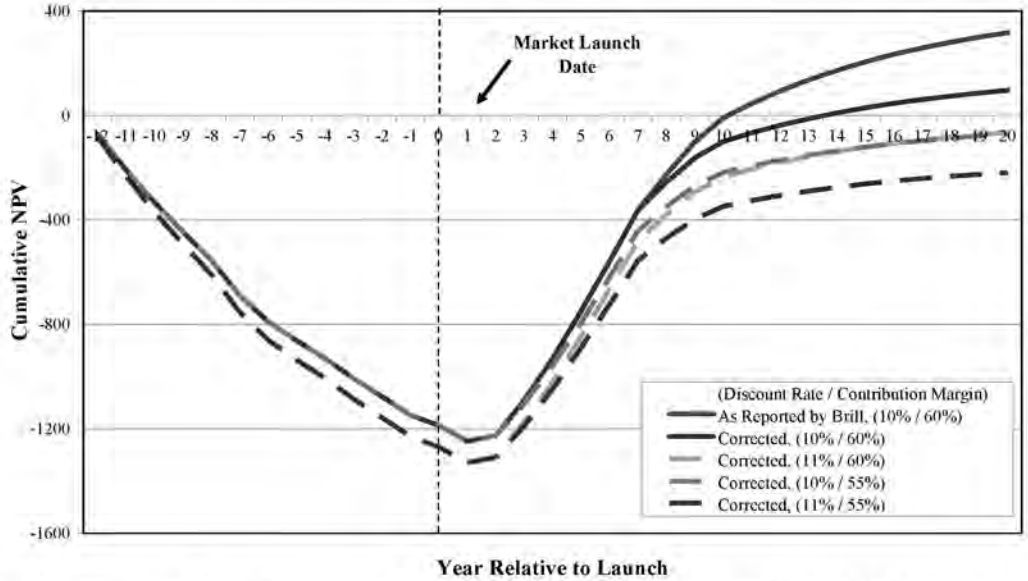
Cumulative Net Present Value of Cash Flows for Representative Biotech Drug
Brill Representation



Note: All scenarios maintain Brill's assumption of a 7-year data exclusivity period and biosimilar share and innovator price discounts, based on his interpretation of CBO share and price assumptions.

Exhibit 3

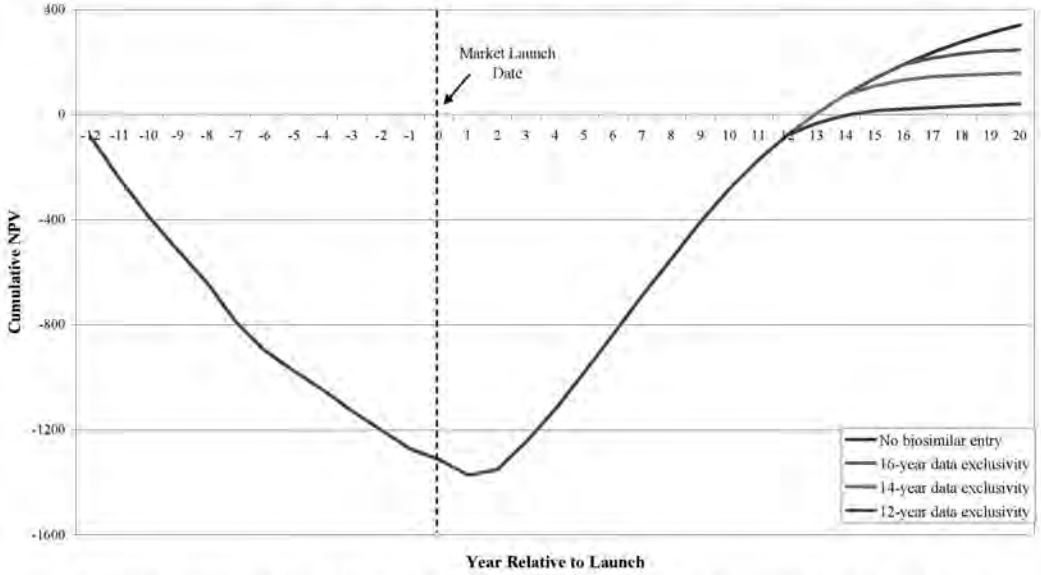
Cumulative Net Present Value of Cash Flows for Representative Biotech Drug
Brill Representation



Note: All scenarios maintain Brill's assumption of a 7-year data exclusivity period and biosimilar share and innovator price discounts, based on his interpretation of CBO share and price assumptions. The innovator does not breakeven within 50 years with either an 11% discount rate, a 55% long-run contribution margin, or both.

Exhibit 4(a)

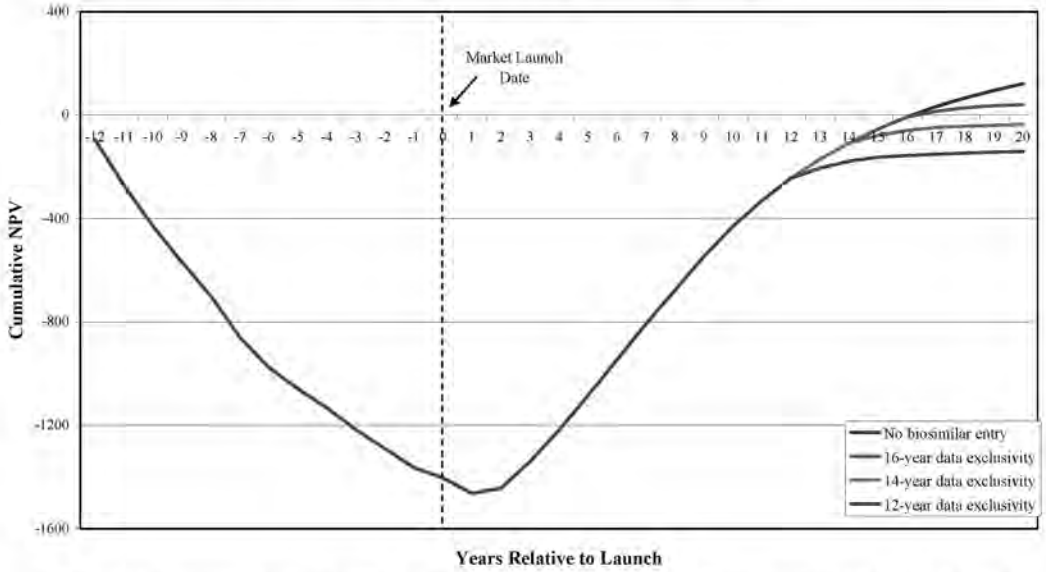
Sensitivity Analysis of Cumulative NPV of Cash Flows for Representative Biotech Drug
(50% Average Contribution Margin, 11.5% Cost of Capital)



Note: Biosimilar is assumed to capture 10% share in first year, increasing to 35% by year 4. Innovator price is assumed to decline 20% in first year of biosimilar entry, and 40% by year 4. Assumptions reflect Brill's interpretation of CBO assumptions.

Exhibit 4(b)

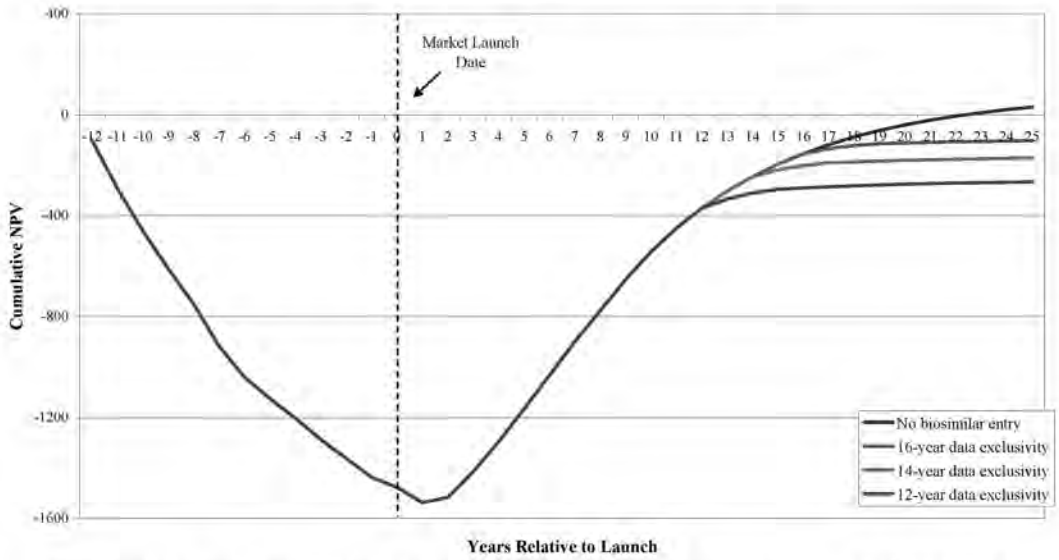
Sensitivity Analysis of Cumulative NPV of Cash Flows for Representative Biotech Drug
(50% Average Contribution Margin, 12.5% Cost of Capital)



Note: Biosimilar is assumed to capture 10% share in first year, increasing to 35% by year 4. Innovator price is assumed to decline 20% in first year of biosimilar entry, and 40% by year 4. Assumptions reflect Brill's interpretation of CBO assumptions.

Exhibit 4(c)

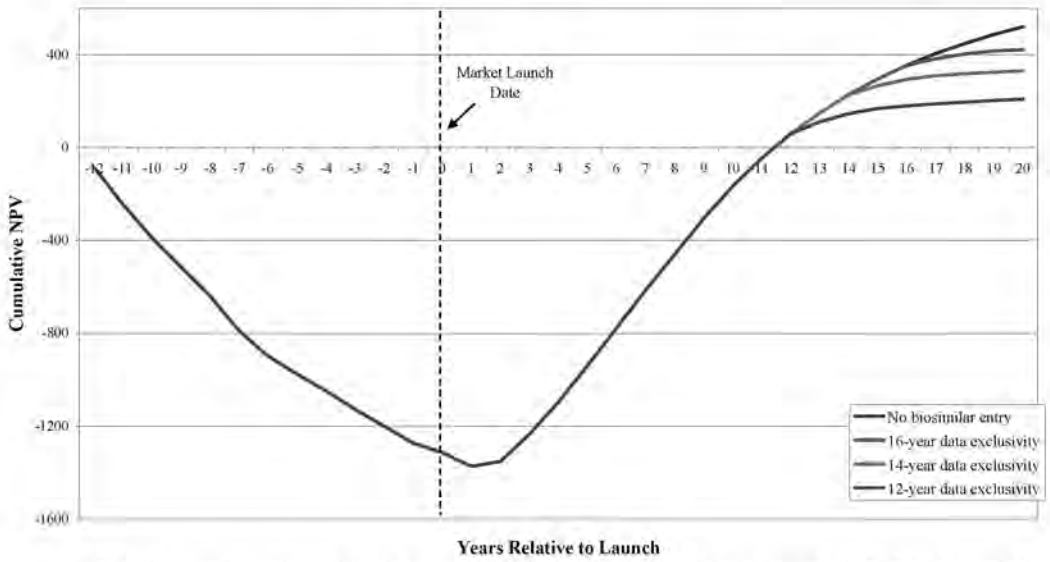
Sensitivity Analysis of Cumulative NPV of Cash Flows for Representative Biotech Drug
(50% Average Contribution Margin, 13.25% Cost of Capital)



Note: Biosimilar is assumed to capture 10% share in first year, increasing to 35% by year 4. Innovator price is assumed to decline 20% in first year of biosimilar entry, and 40% by year 4. Assumptions reflect Brill's interpretation of CBO assumptions.

Exhibit 5(a)

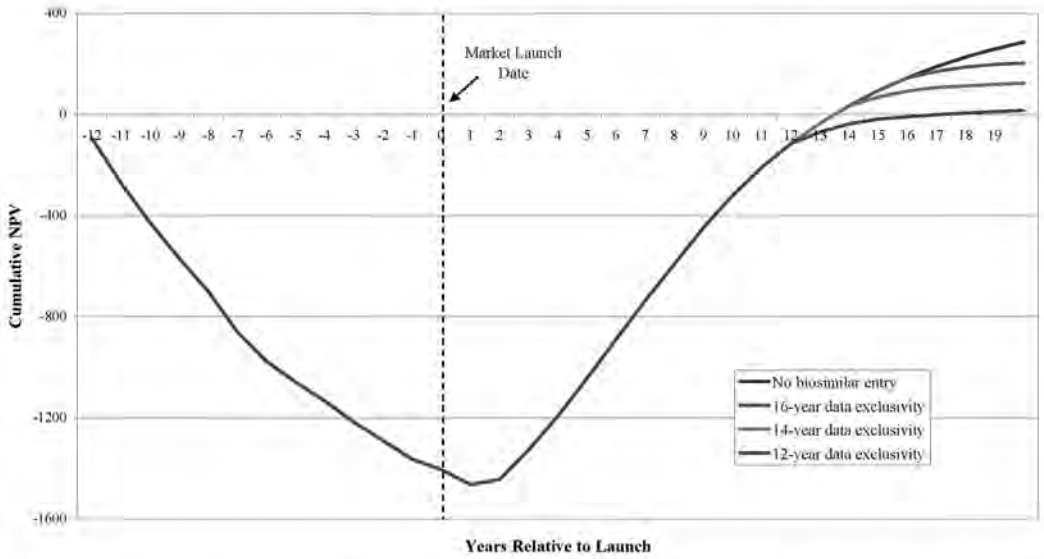
Sensitivity Analysis of Cumulative NPV of Cash Flows for Representative Biotech Drug
(55% Average Contribution Margin, 11.5% Cost of Capital)



Note: Biosimilar is assumed to capture 10% share in first year, increasing to 35% by year 4. Innovator price is assumed to decline 20% in first year of biosimilar entry, and 40% by year 4. Assumptions reflect Brill's interpretation of CBO assumptions.

Exhibit 5(b)

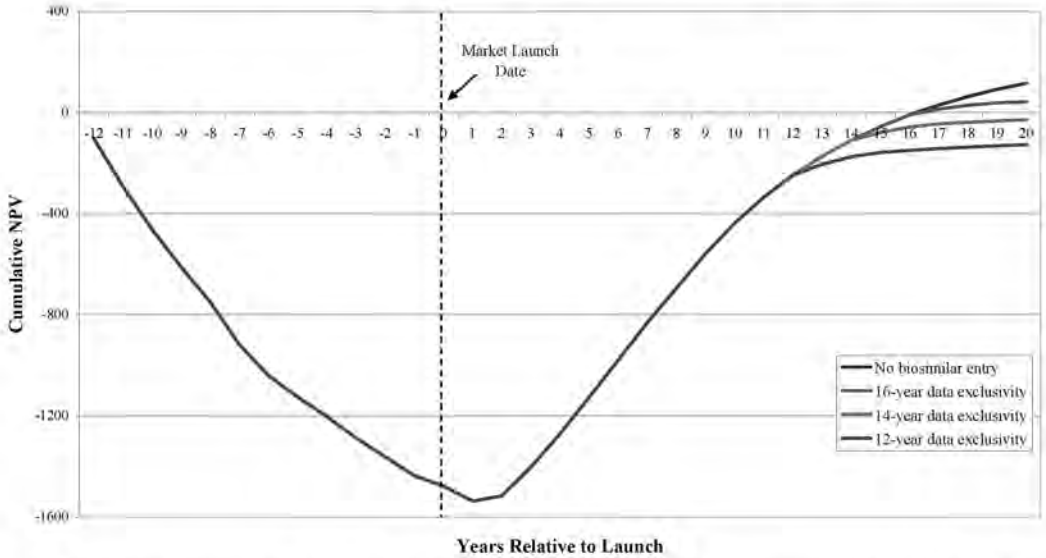
Sensitivity Analysis of Cumulative NPV of Cash Flows for Representative Biotech Drug
(55% Average Contribution Margin, 12.5% Cost of Capital)



Note: Biosimilar is assumed to capture 10% share in first year, increasing to 35% by year 4. Innovator price is assumed to decline 20% in first year of biosimilar entry, and 40% by year 4. Assumptions reflect Brill's interpretation of CBO assumptions.

Exhibit 5(c)

Sensitivity Analysis of Cumulative NPV of Cash Flows for Representative Biotech Drug
(55% Average Contribution Margin, 13.25% Cost of Capital)



Note: Biosimilar is assumed to capture 10% share in first year, increasing to 35% by year 4. Innovator price is assumed to decline 20% in first year of biosimilar entry, and 40% by year 4. Assumptions reflect Brill's interpretation of CBO assumptions.

ATTACHMENT D

FTC BIOSIMILARS REPORT REBUTTAL

FTC: Given that biosimilar competition with a pioneer biologic drug is likely to resemble brand-to-brand competition among biologics, the question arises whether provisions that "delay" biosimilar entry and "restrict competition" are necessary to benefit consumers. No economic arguments suggest that such provisions are necessary to foster pioneer drug innovation.

FACT: We agree with the FTC that the market dynamics of biosimilars are more akin to brand-to-brand competition in terms of likely number of entrants, price competition, and market share erosion, at least for the short-term. But this is NOT brand-to-brand competition in one critical respect that the FTC report 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, will be given a scientific and regulatory short-cut that, while still more demanding than small molecule generic drug entry, will be 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 do we 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 also phrases its question in a way that is destined to lead to the wrong answer. It is not whether the Congress should enact provisions that delay entry and restrict competition – of course, Congress shouldn't. The proper question is at what point Congress should, when enacting a new pathway designed to facilitate additional competition from biosimilars, allow follow-on manufactures to "free ride" off the work of pioneer companies.

FTC: Nothing about the introduction of biosimilar drug products changes the relationship of pioneer biologic drug products to the patents protecting them. As a result, patent protection should continue to incentivize biotechnology innovation, even after enactment of an approval process for biosimilar drugs.

FACT: In the small molecule, generic drug context, patents do provide the incentives for continued innovation and the period of data exclusivity is less important, because the regulatory approval standard for generics ("sameness") and the patent system (with appropriate term extensions permitted under Hatch-Waxman) work in concert to provide protection against premature generic competition – on average for 12-14 years, as the FTC notes. However, the regulatory approval standard for biosimilars creates a "patent protection gap" that may allow for abbreviated regulatory approval of a biosimilar which does not infringe an innovator's patents. That likelihood exists because of the confluence of two critical factors not present in the Hatch-Waxman construct. First, unlike a generic drug which must be the same as an innovator product, a biosimilar will need only be "similar' to the corresponding innovator product. Indeed, some of the proposed legislation would permit the approval of products that are not very similar to the innovator biologic at all. For example, H.R. 1427, introduced by Energy & Commerce Committee Chairman

Henry Waxman, has a very broad and undefined view of similarity. While the Waxman bill provides for approval of a biosimilar that is highly similar structurally and has the same mechanism of action, dosage form, and strength, it also expressly allows for any or all of these requirements to be waived. Accordingly, the biosimilar product could be quite dissimilar from the innovator's product in structure, in route of administration, mechanism of action, dosage form or strength – or in all of these characteristics – yet still theoretically gain abbreviated approval. This uncertainty will raise substantial questions about the effectiveness of innovator patent protection – a fact that is completely ignored by the FTC report. Second, because of the nature of biologic products – large molecules produced by living cells and organisms through highly specific processes – patent protection is often narrower and easier to "design around" than that of small molecule drugs, and the trend is towards increasingly narrow biotech patents.

FTC: There is little empirical evidence that patent design-arounds have occurred in biologics to any greater degree than with respect to small molecule drugs.

FACT: There is currently no abbreviated biologics approval pathway, and hence much less financial motivation to develop competing "me too" products specifically designed to exploit gaps in the innovator's patent protection. The cost and risk of such an approach in today's market is high, and thus it is unsurprising that there are not many existing cases of biotech patent work-arounds. Yet even without the major incentives of an abbreviated approval pathway, successful biotech design-arounds have occurred (see Hormone Res. Found. v. Genentech, 904 F.2d 1558; Novo Nordisk v. Genentech 77 F.3d 1364; Geneutech, Inc. v. Wellcome Foundation Ltd., 29 F.3d 1555; Amgen v. Hoechst Marion Roussel, 314 F.3d 1313; Biogen v. Berlex, 318 F.3d 1132; Genzyme v. TKT, 346 F.3d 1094). These cases illustrate that courts have indeed sometimes taken a very a narrow view of biotechnology patent claims, under which even very 'close' products were determined not to infringe a valid patent. The FTC report focuses on what has happened to date, while ignoring the fundamentally changed incentives once a biosimilar pathway is created.

FTC: Even if the biosimilar manufacturer were to design around the patents claiming a pioneer biologic drug product and enter prior to patent expiration, the pioneer manufacturer will continue to earn significant revenues after biosimilar entry; thus, the effect on the pioneer manufacturer caused by biosimilar entry is not nearly as great as it is with small-molecule generic drug entry and there is no need for data exclusivity to prevent the earlier competitive entry.

FACT: A peer reviewed, published study by Duke University Professor Henry Grabowski looked at this precise question, and found that, even with expected smaller market erosion based on Congressional Budget Office estimates, innovators will not be able to recoup their investment in a reasonable period of time without 12 – 14 years of data exclusivity. While the FTC report offers a critique of this study on other grounds, it never offers any economic data or support for its conclusion that, simply because innovators will still receive substantial revenues after biosimilar entry, there is no need for data exclusivity protections. The FTC report never addresses the fundamental questions raised about the impact of premature biosimilar entry on investment incentives.

FTC: 12-14 years of data exclusivity is too long to promote innovation.

FACT: In fact, the exact opposite is true – 12-14 years of data exclusivity is necessary to continue to foster long-term innovation. The FTC contends that a long period of data exclusivity will hurt innovation. However, currently – with no pathway – there are an unlimited number of years of data exclusivity. Under the current regime, there has been tremendous innovation with the developments of treatments for many diseases such as cancer, rheumatoid arthritis, Crohn's disease to name but a few. The danger of setting the number of years too low is stifling medical advancement and innovation. There is absolutely no evidence that adequate data exclusivity of 12 – 14 years will hamper innovation. In the small molecule world, innovators do not face generic competition for an average of 12-14 years. A similar data exclusivity period for biologics is needed to mitigate against the increased risk created by the similarity standard and patent work-arounds, and achieve parity between small molecule and biotech therapies. Without such parity, there is a real risk that investment incentives will be skewed away from biotechnology – an industry that is largely made up of small companies without profits that are heavily reliant on private investment to fund the R&D process and therefore are particularly susceptible to negative changes in investment incentives.

FTC: Special procedures to resolve patent issues between pioneer and follow-on manufacturers prior to FDA approval are unnecessary and could undermine patent incentives and harm consumers.

FACT: Again, the opposite is true. The early resolution of patent disputes benefits patients, physicians, insurers, follow-on manufacturers and innovators alike. Without a mechanism to resolve patent disputes early – before FDA approval of follow-on products – follow-on products would systematically have to enter the market under a cloud of patent uncertainty. Once on the market, patent disputes over such products would have to play out in high-stakes litigation, causing confusion for patients, physicians, and insurers about the long-term availability of certain products. Congress has recognized that patent disputes over medicines must be resolved as early as possible, and in 1984 created a specific mechanism to litigate patents before generic small molecule drugs are released to the public. The same should be true for biosimilars, so that patients can have the assurance that such products, once released, are there to stay.

Mr. JOHNSON. Thank you.
Mr. Brill, please proceed with your testimony, sir.

TESTIMONY OF ALEX M. BRILL, RESEARCH FELLOW, AMERICAN ENTERPRISE INSTITUTE (AEI), WASHINGTON, DC

Mr. BRILL. Thank you.

Thank you, Chairman Johnson, Ranking Member Coble, and other Members of the Committee for the opportunity to appear before the Committee today to testify on an important matter currently before Congress, creating a pathway to allow for more competition within the biologic drug sector.

My name is Alex Brill, and I am a research fellow at the American Enterprise Institute.

Biologic drugs offer great promise for improving outcomes in health care. While it is costly and risky to produce products for development, they offer some of the best hopes for treating some of the Nation's most deadly and debilitating diseases.

As you noted in your opening statement, Mr. Chairman, currently there is no expedited process by which a biogeneric product could enter the U.S. market. While many experts who discuss the expected market dynamic for biogeneric competition make reference to small-molecule drugs and generic small-molecules that emerged after enactment of Hatch-Waxman legislation, it is important to understand the critical differences between traditional pharmaceutical and biologics drug markets.

Not only are there scientific differences between these drugs, as Congresswoman Eshoo described in her testimony, but because of the cost, uncertainty and complexity in biologic drug development, a competitive biologic drug market will be very different than the market for small-molecule generics.

As described in the recently released FTC report on this issue, "Competition from follow-on biologic drug entry is likely to resemble brand-to-brand competition rather than generic drug competition. Branded manufacturers are likely to continue to reap profits after follow-on biologic entry."

As the FTC reports, high barriers to entry will limit the number of generic competitors to only a few. The result, according to FTC, will be price declines for biogenerics of 10 to 30 percent. However, in small-molecule drugs, generic prices typically decline up to 80 percent. These more modest price effects on a percent basis relative to small-molecule drugs means that the need for additional market protection for biologic drugs facing competition is weaker as innovator drug companies will continue to be able to profit from their innovations after a follow-on competitor has entered the market.

The additional protections granted by the Hatch-Waxman legislation for small-molecule drugs gives innovators greater confidence that they would have sufficient time to generate the necessary rents to recoup their R&D costs. This additional protection was deemed necessary due to the particular dynamics of that industry.

However, the FTC argues that biologic drug patents are collectively stronger than small-molecule drug patents, making the need for additional protections unnecessary. In the eyes of the FTC, none of the problems inherent to small-molecule drug patents apply to biologic drugs, and they advocate no additional protection beyond that given by the patent system.

I do not take as strong a stand against an exclusivity period as does the Federal Trade Commission. The cost of providing modest

additional intellectual property rights to drug originators will likely outweigh the potential costs.

Research I conducted demonstrates that an exclusivity period of 7 years is sufficient to ensure that innovator drug companies continue to earn the necessary economic rents. Modeling included in the recent FTC report further extends that model and finds support for the view that 7 years of market exclusivity will be sufficient. Proposals that establish a long period of market protection will lead to unreasonably large rent for originator drug companies and provide no additional benefit to consumers.

Ultimately, it is a balancing act, promoting innovation by shielding the company from market competitors, and promoting innovation and price competition by allowing market entrance.

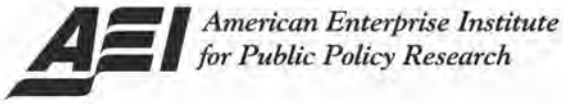
Yet as these proposals have become more complex, another important issue has come to the fore, that of tiered exclusivity. Post-launch R&D involves costs, albeit less than the original development costs, and should be encouraged, since it only stands to reason that a drug's original developer has the best knowledge of their own invention.

However, when thinking about the optimal amount of protection to give an improvement to an existing drug, we must once again return to the basic question of the particular market dynamic. An improvement that enlarges market share would increase profits further, thereby mitigating the amount of needed exclusivity. Furthermore, the more exclusivity that is expected to be attached to a drug for its improvements, the shorter the period that needs to be given to a newly approved drug initially. In my view, the total exclusivity period, including extensions, should be close to 7 years.

Thank you. That concludes my statement. I look forward to your questions.

[The prepared statement of Mr. Brill follows:]

PREPARED STATEMENT OF ALEX M. BRILL



Statement before the Judiciary Committee

Subcommittee on Courts and Competition

On Biologics and Biosimilars: Balancing Incentives for Innovation

Alex Brill

Research Fellow

American Enterprise Institute

July 14, 2009

U.S. House of Representatives

House Judiciary Subcommittee on Courts and Competition Policy

2141 Rayburn House Office Building

Washington, DC

The views expressed in this testimony are those of the author alone and do not necessarily represent those of the American Enterprise Institute.

Chairman Johnson, Ranking Member Coble and other Members of the Committee:

Thank you for the opportunity to appear before the Committee today to testify on an important matter currently before Congress, creating a pathway to allow for more competition within the biologic drug sector. My name is Alex Brill and I am a research fellow at the American Enterprise Institute (AEI).[1] My testimony will address 4 topics:

1. The size, scope and importance of the biologic drug industry;
2. A framework for understanding the likely market dynamics for biogeneric competition;
3. An economic model for understanding the appropriate amount of exclusivity to provide innovator biologic drugs;
4. Views on proper data exclusivity, tiered exclusivity schemes and the negative consequences from granting "too much" exclusivity

To avoid the building of any undue suspense, I will begin with my conclusion. Biologic drugs offer great promise for improving outcomes in healthcare. While they are costly, time consuming and risky products to develop, they offer some of the best hopes for treating some of the nation's most deadly and debilitating diseases.

A properly designed pathway for biogeneric entry will, over time, lead to additional market entrants, lower prices, increased access to drugs and a few billion dollars a year in reduced spending. The largest single purchaser of biologic drugs is the federal government and a large share of total savings will be taxpayer dollars.

It is important to ensure adequate incentives for innovative drug companies to undertake the risk and expense of developing new drugs and a market exclusivity period can be a well

[1] The opinions expressed in this testimony are solely mine and do not necessarily represent AEI, or any other individuals or organizations.

designed tool for that purpose. Excessive exclusivity that needlessly blocks competition is a government built monopoly that unduly interferes in the marketplace.

The Market for Biologic Drugs

Biologic drugs are large, complex molecules derived from living organisms.[2] Recently, U.S. sales of biologic drugs exceed $40 billion annually[3] and global sales were over $112 billion[4]. Sales are concentrated among a few blockbuster products as just 27 biologic products represent approximately 87 percent of total biologic drug sales.[5] While a biologic drug may compete with other brand biologic products, there is currently no expedited process by which a biogeneric product could enter the U.S. market.[6]

Biologic drugs contains the promise to fight some of our most dangerous diseases, including anemia, hemophilia, cancer, diabetes, HIV, rheumatoid arthritis and thrombosis. Top selling biologics include Avastin and Herceptin (cancer); Enbrel, Remicade, and Humira (arthritis); and Epogen and Procit (anemia). However, biologic drug development is a costly process, with an expected development expense of about $1.2 billion for an approved product[7]. Similarly, the cost of purchasing a biologic drug is also often very expensive and annual treatment costs frequently are tens of thousands of dollars.

---

[2] According to Department of Health and Human Services, a biologic drug is defined as follows: "A biological product subject to licensure under the Public Health Service Act is any virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, applicable to the prevention, treatment or cure of diseases or injuries to humans. Biological products include, but are not limited to, bacterial and viral vaccines, human blood and plasma and their derivatives, and certain products produced by biotechnology, such as interferons and erythropoietins." See: "What is a Biologic?" at http://www.hhs.gov/faq/drug/drugs/414.html (accessed July 12, 2009).

[3] Federal Trade Commission, "Emerging Health Care Issues: follow-on biologic drug competition," FTC Report, June 2009, p. 3.

[4] FTC 2009, p. 4.

[5] Ibid.

[6] A pathway for biosimilars does exist in other markets including the EU.

[7] "Average Cost to Develop a New Biotechnology Product is $1.2 billion." Tufts Center for the Study of Drug Development, Recent News, November 9, 2006. [http://csdd.tufts.edu/NewsEvents/NewsArticle.asp?newsid=69]

The Market Dynamic for Competition in Biologics

As noted above, an approved biologic drug in the U.S. market currently faces no direct competition. But, brand biologic drugs may compete with other brand drug products or other treatment modalities. In general, however, brand biologic drugs enjoy strong monopoly pricing power.

While many experts who have discussed the expected market dynamic for biogeneric competition make reference to the market development in small-molecule drugs that emerged after enactment of Hatch-Waxman legislation, it is important to understand critical differences between traditional pharmaceutical and biologic drug markets. Because of the cost, uncertainty and complexity in biologic drugs (both for discovery and manufacturing), a competitive biologic drug market will be very different than a competitive small-molecule market.

While competition results in price declines of up to 80 percent[8] and over 10 new entrants[9] for a popular small molecule drug, biologic drug competition can be expected to be quite different.

As described in the recently released FTC report, *Emerging Health Issues: Follow-on Biologic Drug Competition*, "Competition from FOB drug entry is likely to resemble brand-to-brand competition rather than generic drug competition…Branded manufacturers are likely to continue to reap profits after FOB entry."[10]

As the FTC reports, high barriers to entry, will limit the number of generic competitors to only a few and only among relatively large markets. The result, FTC estimates, will be price

---

[8] Federal Trade Commission, "Prepared Statement," United States Senate, Committee on the Judiciary, Hearing on: Anticompetitive Patent Settlements in the Pharmaceutical Industry: the benefits of a legislative solution, January 17, 2007, p. 8. [http://www.ftc.gov/speeches/leibowitz/070117anticompetitivepatentsettlements_senate.pdf]

[9] David Reiffen and Michael R. Ward, "Generic Drug Industry Dynamics," Review of Economics and Statistics 87 (1), 37-49.

[10] FTC 2009, pp. 13-14.

declines of 10 to 30 percent. The Congressional Budget Office estimates that follow-on prices will decline as much as 40 percent compared with branded prices.[11] These more modest price effects (on a percent basis) relative to small molecule drugs means that the need for additional market protection for biologic drugs facing competition is weaker, as innovator drug companies will continue to be able to profit from their innovations after a follow-on competitor has entered the market.

Protecting Innovators from Competition

Determining the optimal length of market protection is a crucially important regulatory problem. Too little market protection has the potential to make drug companies unwilling to take costly risks to develop life-saving drugs, while too much allows branded drugs the opportunity to obtain excessive monopoly rents, driving up prices for patients in need and healthcare costs to the U.S. government.

As University of California, Berkeley economist, Professor Richard Gilbert, and his co-author Alan Weinschel note, "[I]nnovators need to be compensated for their innovative efforts, and this sometimes requires practices that may exclude potential competitors. At the same time, one must be careful not to lean too heavily on practices that focus on rewards to innovation, because these practices incur costs in the short run by limiting the use of innovations and possibly in the long run by raising the costs for future innovators who use protected innovations as inputs into their own innovative efforts."[12]

---

[11] Congressional Budget Office. S. 1695: Biologics Price Competition and Innovation Act of 2007. Congressional Budget Office Cost Estimate. June 25, 2008. [http://www.cbo.gov/ftpdocs/94xx/doc9496/s1695.pdf]

[12] Richard J. Gilbert and Alan J. Weinschel. "Competition Policy for Intellectual Property: balancing competition and reward," University of California at Berkeley Working Paper, September 2007. [http://repositories.cdlib.org/cgi/viewcontent.cgi?article=1078&context=iber/cpc]

Before entering into a specific discussion on the balance of promoting innovation and promoting competition in the biologic drug market, I would like to describe the right way to think about the problem of market protection, more generally. A common refrain in the debate over an exclusivity period is the concern over being able to "free ride" on the innovator's data.

However, I want to stress that free-ridership is certainly not always a problem. A follow-on product -- in any industry -- takes advantage of the research and development of their predecessors, and we don't always identify this "free-riding" as problematic. It is through this process that products are improved upon and refined, in the end making everyone better off. A 2003 report by the Federal Trade Commission notes, titled *To Promote Innovation: The Proper Balance of Competition and Patent Law Policy* notes, "[I]n the real world, innovation is an ongoing process, with one invention frequently providing a building block for the next."[13]

When a person shares a ride home with a neighbor, they are (literally) free riding. The alternative would be that each person drive themselves separately, thereby consuming twice as much gasoline. Free riding is only a problem when, due to the potential lessened profits of the originator product caused by expected competition from a follow-on product, the originator product itself is expected to be unprofitable. We typically combat this problem through the patent system, which is intended itself to create the incentives to innovate by granting exclusive rights for a limited time.

Pharmaceutical R&D and Market Dynamics

The Hatch-Waxman legislation grants innovator, small molecule drugs an exclusivity period beyond the protection granted by the patent system to give innovators greater confidence

---

[13] Federal Trade Commission, "To Promote Innovation: the proper balance of competition and patent law and policy," FTC Report, October 2003, p. 32. [http://www.ftc.gov/os/2003/10/innovationrpt.pdf]

that they would have sufficient time to generate the necessary rents to recoup the cost of R&D. This additional protection was deemed necessary due to the particular dynamics of the small molecule drug industry. First, once generic competitors enter the market, the price of the originator drops so much that profit, measured as the price of the drug less the combined costs of all inputs, including the opportunity cost of money, drops to near zero. Second, the strength of the patent protection may be insufficient. Therefore, without adequate market protection allowing originator drugs to recoup their R&D costs before competition enters the market, drug companies would refuse to undertake the costly R&D required to develop these innovative drugs.

The FTC argues that biologic drug patents are, collectively, stronger than small molecule drug patents, making the need for additional protection unnecessary. Therefore, in the eyes of the FTC report, neither of the problems inherent to small molecule drug patents apply to biologic drugs, and they advocate no additional protection beyond that given by the patent system, i.e., no data exclusivity.

Furthermore, Georgetown Law professor John Thomas' research supports the FTC's conclusions on the strength of biologic drug patents. Based both on historical experience and legal theory, Thomas notes that "marketing exclusivities should be granted only in circumstances where the patent system, under its own terms, cannot protect activities that promote public health," and concludes: "The proposition that patent protection is inferior with respect to biologics has not been demonstrated."[14]

Economic model for estimating exclusivity

I do not take as strong a stand against an exclusivity period as the FTC. There is an immense importance to sufficiently encouraging healthcare innovation and the costs of

[14] John R. Thomas, "Toward a Theory of Marketing Exclusivities," mimeo, pp. 31-33.

Mr. JOHNSON. Thank you, Mr. Brill.
Next, Mr. Lasersohn, please proceed.

TESTIMONY OF JACK W. LASERSOHN, GENERAL PARTNER, VERTICLE GROUP, ON BEHALF OF NATIONAL VENTURE CAPITAL ASSOCIATION (NVCA), ARLINGTON, VA

Mr. LASERSOHN. Mr. Chairman, thank you for inviting me to testify today on behalf of the National Venture Capital Association,

which represents nearly 500 venture capital firms who in turn invest more than 90 percent of all venture capital in the United States.

Last year, we invested over $3 billion in over 100 new biotechnology companies and currently manage over 1,000 biotechnology companies in our portfolios.

It is probably not well-known that the venture community is the primary founder and funder of biotechnology in the United States. Indeed, it is not an exaggeration to say that venture capitalists founded the biotechnology industry in the 1970's and 1980's. For example, both Amgen and Genentech were founded by venture capital firms, and even today supply nearly all of the capital for early-stage biotechnology companies.

In turn, our entrepreneurial biotechnology companies discover and develop the overwhelming majority of new biological drugs in the world. I cannot emphasize this point enough. The last time we looked at this, these companies were responsible for 80 percent of the new biological drugs in the entire pipeline of biotechnology development.

While we have been actively involved in this behind the scenes, we have in fact not participated in testimony before the Congress before, and we did not have an opportunity to testify to the FTC. If we had, we would have said the following:

We absolutely support a well-designed FOB process that will ultimately lower prices and improve access for biologicals for consumers while preserving investment in discovery and development of revolutionary new biotechnology drugs.

The FOB system endorsed by the FTC will absolutely not accomplish these goals. Instead, it will result in a dramatic reduction in our ability to fund new drug discovery, leading to a Pyrrhic victory in which we have very cheap versions of old biologics and a vast reduction in the pipeline of new drugs which have the potential to revolutionize medicine. Both goals are important.

Now, this may sound like a rehash of arguments against Hatch-Waxman in 1984, but this really is different. First, the current biotechnology industry bears no resemblance to the pharmaceutical industry in 1984. Most small-molecule drugs were discovered by large pharmaceutical companies in those days, and still are today.

As I said, in contrast, virtually all new biological drug development today are discovered by small, private, VC-funded start-ups. This is an absolutely critical difference. These companies have no cash flow and depend entirely upon us for financing. We in turn invest in these incredibly risky, illiquid and very long-term investments, and usually lose money on about 50 percent of them.

To justify this risk and time, we must produce a return that is much higher than you can get from less risky investments and much higher than large biotechnology and pharmaceutical companies need to make. If we don't get those returns, in turn our investors will not give us money to invest in biotechnology, and indeed, that is already beginning to happen.

This return is our cost of capital and is much more than the 10 percent that has been assumed by supporters of other more aggressive FOB systems. In fact, it is over 20 percent, as a new Harvard and Boston University report showed that was just published last

week. All of the published models demonstrate that with a 20 percent cost of capital, or even a blended cost of capital of 10 to 12 to 15 percent, we cannot break even on these enormously risky investments if generic follow-on biologicals competition can enter the market immediately or as little as 7 years after our drugs. If we cannot break even, we cannot invest.

The second difference is how patents work in this system as compared to the generic biological system. The difference is obvious and simple. Under Hatch-Waxman, a simple composition-of-matter patent gives you enormous certainty that you can preclude generic competition during the life of the patent. It gives you a reasonable period to recoup your investment. Under an FOB system, you have no such certainty, because an FOB does not have to be identical with the approved drug. So a composition-of-matter patent, which is the strongest type of patent, may be completely irrelevant and unprotective.

The FTC dismisses this point by arguing that other biological patents may offset this risk. Unfortunately, this is just speculation with which many experts disagree. And what matters to us most is it creates uncertainty, which is what actually affects our investment decisions, venture capital investment decisions. I can tell you, despite the what the FTC argues, that I and other VCs cannot rely on patents alone to continue to make investments in early-stage biotechnology companies.

The data exclusivity period of 12 years that we are requesting is merely insurance against the possibility the FTC and the proponents of more radical FOB systems are wrong in their speculations about how strong patents will be. If they are correct, patents will give us 12 years anyway and the data exclusivity will be completely irrelevant. But if they are wrong, the data exclusivity will simply give us the same period to recoup our investments that the pharmaceutical industry already has under Hatch-Waxman. This seems to us like a prudent compromise to avoid the enormous unintentional—unintended damage to our entire entrepreneurial biotechnology industry.

Thank you for your attention, sir.

[The prepared statement of Mr. Lasersohn follows:]

PREPARED STATEMENT OF JACK W. LASERSOHN

National Venture Capital Association

House Committee on the Judiciary
Subcommittee on the Courts and Competition Policy

Hearing on Biologics and Biosimilars: Balancing Incentives for Innovation
July 14, 2009

Jack Lasersohn, General Partner, Vertical Group
Board Member, National Venture Capital Association

Chairman Johnson, Ranking Member Coble and Members of the Subcommittee, my name is Jack Lasersohn and I am a partner at The Vertical Group, a venture capital firm based in Summit, New Jersey and Palo Alto, California that focuses investment in the life sciences sector. I was originally trained as a physicist and have been an active venture capital investor since 1981. I am also a Board Member of the National Venture Capital Association (NVCA), which represents over 460 venture firms across the country. It is my privilege to be here today and to have the opportunity to share the view of the venture capital community on the crucial role that biosimilars legislation will play in future investment and development of biological products.

As Congress considers the creation of a biosimilars approval pathway at the Food and Drug Administration (FDA), the central question is how to balance the public's interest in lower prices for biological drugs, with continued vigorous investment in the development of new medical treatments and cures for patients suffering from debilitating diseases such as cancer, Parkinson's and multiple sclerosis.

NVCA supports the principle of a biosimilars approval system to reduce excessive costs of biologic drugs, particularly arising from inflated earnings streams extending far beyond the reasonable expectations of market exclusivity. However, in seeking this result, NVCA believes that we must also carefully balance the countervailing need to ensure continued development of and patient access to innovative biologic therapies.

Venture Capital Investing is Critical to Innovation

For the last four decades, the venture capital community has served as a founder and builder of companies, a creator of jobs, and a catalyst for innovation in the United States. This contribution has been achieved through high-risk, long-term investment of considerable time and dollars into small, emerging growth companies across the country and across industry sectors, including information technology, communications, biotechnology, medical technology and more recently the "cleantech" industry. According to the econometrics firm Global Insight 2009 study, venture-backed companies accounted for 12.1 million jobs and $2.9 trillion in revenue in the United States in 2008 representing 11 percent of U.S. private sector

employment. In fact, it was the venture capital industry that created the biotechnology industry including companies like Genentech and Amgen.

In addition to providing early stage funding to young biotech businesses, venture capitalists also take an active role in guiding these companies through their start-up and expansion phases. Accordingly, we have a valuable perspective on the hurdles that these emerging businesses confront and the environments that promote or stifle growth and innovation. Given the role that we play at various points in a biotech company's life cycle, venture capitalists have the opportunity to provide a unique perspective on the importance of providing adequate incentives for innovator products in biosimilars legislation.

My testimony today focuses on the critical role that "data exclusivity" in biosimilars legislation will play in the development of the next generation of innovator biological products. If an adequate period of data exclusivity is not included in the legislation, the "return on capital" (expected return that the provider of capital actually earns on their investment) will be too low to support continued VC investment in the biotech industry. This will stifle, perhaps even cripple, the emerging biotech industry, and delay the development of life-saving therapeutics. This is especially true when one considers that patent protection on biologics is simply too uncertain to sustain, by itself, VC investment in the biotech sector.

The Cost-of Capital for Biotech Drugs Supports a Lengthy Period of Data Exclusivity

The NVCA believes that in determining the appropriate period of data exclusivity, it is critical to understand what factors affect investment in new drug development, including, in particular, the "cost of capital" of the innovation sector of the biotechnology industry. Prior attempts to address this question have failed to recognize two key issues:

First, in contrast to the pharmaceutical sector, the biotechnology industry is overwhelmingly comprised of private, venture capital funded, small, entrepreneurial companies. Thus, conclusions about how a biosimilars system will affect innovation in this sector cannot be drawn directly from experience with Hatch-Waxman in the pharmaceutical sector. In other words, one must carefully examine the unique circumstances involved in biotech investment and innovation when crafting biosimilars legislation.

Second, one of the most important distinctions between the pharmaceutical and biotech sectors is their respective "cost of capital." The cost of capital is the minimum required return that the provider of capital needs to earn on their investment. Because data on actual cost of capital for the small, privately held biotech companies which comprise the majority of the biotech industry is proprietary, current estimates about the cost of capital in the biotech industry are based on publicly traded companies. This substantially understates the cost of capital for the small public and privately held firms because large public companies are intrinsically more mature and less risky than the average private VC funded company, and also because such a sample introduces "survivor bias" by excluding from the data all the private companies who do not survive to become public.

A recent study from professors at Harvard Business School and Boston University School of Management found that the cost of capital of the small private biotech VC funded sector is at least 20% and is likely higher. This is in sharp contrast to the 10% assumed in all prior

analyses. The report also found that 44% of VC investments in biotech result in either partial or total loss of capital. Most disturbing, the report concluded that the VC fundraising rate for all sectors has declined by 50% in 2009, but that the VC biotech investment rate has declined by 75% in 2009.

Since the clear goal of any biosimilars system is to produce lower prices for biologics, it follows that such a system will reduce the flow of earnings from an innovator biologic as compared to what it would be in the absence of a biosimilars system. If the reduction in the expected flow of earnings reduces the value of the earnings stream below the "cost" of inventing the drug, no one will invest to invent the drug in the first place. That is obvious and simple.

If the biosimilars legislation has the intended result of reducing the stream of earnings from a future biological product, the key question is whether the value of that "return" has been reduced below the relevant investor's cost of capital, in this case the biotech segment of the venture capital industry. In its recent report on follow-on biologics drug competition, the Federal Trade Commission never even raised this question, let alone attempted to answer it. However, this question is the central issue in this debate.

The cost and return of capital analysis has been examined in numerous academic studies, including one commissioned by the generic drug industry,[1] a strong supporter of the proposed biosimilars system. That study assumed a biotech cost of capital of 10%, based on publicly traded biotech companies, and determined that on average a "data exclusivity" period of seven-years would permit an investor with a 10% cost of capital to make a positive return on its investment in the development of new biologics. That means that with a seven year data exclusivity period, an investor with a cost of capital of 10% or less would continue to make investments in new drug development. Unfortunately and more importantly, it also means that investors and companies with cost of capital above 10%, including the small, privately owned, VC-backed biotech sector (20% cost of capital), will drastically reduce investments and shift remaining funds to less risky and less innovative opportunities. In other words, VCs will invest in something other than the development of innovative biologics that will be used to treat those with unmet medical needs.

In short, recent studies showing that the cost of capital for the majority of the biotech industry is higher than previously expected indicate that a lengthy period of data exclusivity (at least greater than seven years) is necessary to support continued biotech innovation. For the reasons outlined below, NVCA believes that 12 years of data exclusivity is needed for innovator biologics.

12 Years of Data Exclusivity Protection Is Necessary to Sustain Innovation

NVCA believes that no less than a 12 year data exclusivity period for innovator products is critical to preserving biotech innovation. The recently released Federal Trade Commission (FTC) report entirely dismisses the need for data exclusivity by concluding, in part, that existing patent protection will provide equivalent or even stronger barriers to entry for biological drugs as compared to small molecule pharmaceuticals.[2] However, in the absence of an assured

[1] Brill, Alex M. "Proper Duration of Data Exclusivity for Generic Biologics: A Critique," November 2008.
[2] Federal Trade Commission, Authorized Generics: An Interim Report, June 2009, available at www.ftc.gov/opa/2009/06/generics.shtm.

period of data exclusivity, patent protection is not sufficient to sustain innovation in the biotech sector.

The FTC's conclusion is largely based upon past examples of biologics innovator-on-innovator patent litigation where patents have been successfully asserted. The report acknowledges that there have been examples to the contrary but concludes that, on the whole, substantial data exclusivity is not needed because there is no evidence that past biologics patents have been designed around more frequently than those claiming small molecule drugs. Also, the FTC found no evidence that biologics have suffered from a lack of patentability, or that market forces have been insufficient to incentivize the development of new biologics in the past. The flaws of this logic are obvious: the question is not whether patent protection and market forces have stimulated biotechnology innovation in the past – the question is whether reliance on patents alone continues to be justified even under a new abbreviated biologics approval pathway that completely alters the business incentives for pioneering developers and subsequent competitors alike.

With no abbreviated approval pathway today, biologics developers have little incentive to incur staggering development costs only to create me-too biologics that are marketed as merely "similar" to existing products with no opportunity for product differentiation. The creation of an abbreviated approval pathway would change that – it would create powerful incentives for biologics competitors to identify and exploit gaps in each others' patent portfolios that could be filled with "similar" products, developed at a fraction of today's costs. In other words, "patent pressure" will increase by orders of magnitude – pressure on originators to develop only those biologics that have the best patent protection, and pressure on subsequent competitors to tear down or design around these same patents. Thus, it is by no means assured that a patent system that enables abundant biotechnology innovation today will continue to do so under a biosimilars system that incentivizes biologics competitors to invade rather than avoid each others' patent space, and to develop similar rather than different products. The answer to whether reliance on patents alone is justified under such a new system allows no margin for error.

In concluding that patents alone are sufficient, the FTC glosses over the most relevant point with respect to patent protection for biologics under a biosimilars system. Unlike under Hatch-Waxman, biological biosimilars will *not* need to be identical to the pioneer drug. As a result, composition of matter patents are less likely to protect against biosimilars competition as they do in the case of Hatch-Waxman. In the small molecule drug space, composition of matter patents are usually extremely strong and easy to enforce because proof of infringement is rarely an issue. This most potent patent protection is much more easily avoided in the biosimilars context because the biosimilar developer has more design alternatives, i.e. greater opportunities to modify the innovator's molecule in ways that avoid the patent but are still similar enough for abbreviated approval. Regardless of how one weighs all the other intangible patent questions, it is clear that this factor alone will make the patent rights of pioneer developers much less certain compared to their rights under Hatch-Waxman.

Even if one could conclude that the increased uncertainty of patent rights is somehow offset by the greater diversity of typical biotechnology patent portfolios, as the FTC seems to do, the FTC conclusion that this eliminates the need for data exclusivity completely ignores the fact that the proposed exclusivity is not additive to patent protection, it is merely a parallel right. The patent

rights and data exclusivity terms would run concurrently. In other words, if patents are strong and cannot be designed around, data exclusivity would not matter. Long experience under Hatch-Waxman has already demonstrated that existing patent barriers for small molecule drugs delay generic entry for 12 years. If the FTC is correct that patent rights for biologics will be at least as strong as those of small molecule drugs facing generic challenge, the data exclusivity will be irrelevant because it will provide no exclusivity beyond that provided by patent rights. But if the FTC is wrong and, as most experts expect, the patent rights are less certain, then a 12 year period of data exclusivity will merely protect biologics pioneers for the same 12 years that small molecule drug makers achieve under Hatch-Waxman. For this reason, NVCA strongly supports no less than 12 years of data exclusivity for innovator biologic products.

Moreover, in its discussion of innovator exclusivity, the FTC overlooks the difference between market exclusivity and data exclusivity. Market exclusivity bans all competitor products from being marketed in the U.S., and thus provides the innovator with a virtual monopoly for a period time. In contrast, data exclusivity, which is the concept considered by the pending legislative proposals, delays approval of a biosimilar only if it relies on the innovator's safety and efficacy data rather than on new safety and efficacy data generated by the secondary applicant at its own expense. A data exclusivity period protects the innovator, for a limited period, from the free rider effect of allowing the biosimilar applicant to exploit the innovator's $1 billion investment in developing a pioneering biologic; it is not unrestricted immunity from competition. There is, therefore, a valid public policy served by data exclusivity which cannot be achieved through patent protection alone.

Considering the financial vulnerability of the biotech industry, the difficulty of predicting exactly how the balancing of patent rights will evolve, and the separate rationale for data exclusivity in addition to patent protection, data exclusivity is a prudent effort to insure against undermining this nation's entire system of new biological drug discovery and innovation.

Conclusion

The VC community supports the majority of revolutionary biologic drug discovery, thus the innovative biotech industry will be significantly adversely affected by biosimilars legislation which does not adequately incentivize continued investment in this sector. Lack of adequate data exclusivity to ensure a reasonable return on investment means that venture capital funds cannot invest with confidence in promising biotech opportunities. This is a perverse result and cannot be what Congress intends with biosimilars legislation.

The NVCA has strongly supported the principle of a biosimilars approval system to reduce excessive costs of biologic drugs, particularly arising from inflated earnings streams extending far beyond the reasonable expectations of market exclusivity. However, we must also avoid disincentivizing investment in the development of revolutionary and innovative new biologic drugs. NVCA believes that a 12 year data exclusivity provision will accomplish both goals.

Mr. JOHNSON. Thank you, sir.

Last, but not least, Ms. Rea—Mr. McNeely. I am sorry.

Mr. McNeely, please proceed.

TESTIMONY OF LARRY McNEELY, HEALTHCARE REFORM ADVOCATE, U.S. PUBLIC INTEREST RESEARCH GROUPS (USPIRG), WASHINGTON, DC

Mr. MCNEELY. Not last, but perhaps least. We will see. I suppose you will judge.

Thank you very much, Mr. Chairman, Mr. Ranking Member, and to Members of the Committee, for the opportunity and really the honor to testify here today.

My name is Larry McNeely. I am the health care advocate for USPIRG, U.S. Public Interest Research Group. USPIRG is a federation of State-based public interest research groups. It is a nonprofit, nonpartisan public interest advocacy organization.

I think much has been made about the truly miraculous results of some of these new biologic drugs, and I think, you know, that is a value that we all hold. But the one thing that hasn't changed with these new, more complex biologic drugs we are here to discuss, the laws of economics haven't changed. It is still true that those with the monopoly are going to continue to fight to keep that monopoly, whether it is in the marketplace or in the halls of public policy.

Now, I suppose the Members of this Committee and Congress have a balancing act to strike here, to reward those who invested in the innovator drugs, the pioneer drugs, and also to encourage competition. And to give you that balance, I would like to actually return to where we started today, with the cancer biologic drug Herceptin.

Approved by the Food and Drug Administration in 1998, this amazing medication, produced by Genentech, helps women fight off a particularly tough form of breast cancer. I believe it is related to the protein HER2.

Herceptin has made a serious difference in that fight. Its use increases the disease-free survival rates of this type of breast cancer by 12 percent. And it did cost its maker—well, I say on average biologics like this cost their makers $1.2 million to bring a drug to market. And, frankly, with that kind of risk, Genentech should, the maker of the drug, should profit for bringing a product to market that saves lives.

But there is a serious danger in conferring too much intellectual property protection. In Herceptin's case, every year the drug manufacturer benefits from high monopoly prices conferred by exclusivity will cost patients both in dollars and in lives. Herceptin's high monopoly prices make it less likely and more expensive for insurers to cover it, and thus fewer patients with breast cancer have access to this life-saving medicine.

Herceptin's patent protections, the legal mechanism that protects intellectual property in most industries, expired in 2005, but Genentech continues to enjoy effective monopoly pricing power. They certainly made the most of it, charging $48,000 a year wholesale for their Herceptin treatment.

So, how should a law strike a balance between access and future innovation on one hand and the manufacturer's need to profit from its investment in a great product? Rather than looking at research from one industry group or another, to fine the right balance, we examined an independent source, the Federal Trade Commission's

report on follow-on biological drug competition. The report found that the patent system has a proven record of protecting and stimulating biotechnology innovation. In fact, they found in some ways biologic patents are stronger than chemical drug patents. In summary, FTC found that the pioneer biologic drug manufacturers can earn significant revenues many years after follow-on biologic entry, obviating the need for the 12- and 14-year exclusivity period. It is far too long.

Finally, USPIRG's recommendations. The Hatch-Waxman Act established the generic drug program at FDA for chemical drugs and conferred patent extensions and 5 years exclusivity—forgive me.

It makes sense to learn from those successes. USPIRG believes that an approach such as that included in the Promoting Innovation and Access to Lifesaving Medicine Act of 2009 represents the best option before Congress today.

Mr. Chairman, we need a strong, vibrant markets for biologic drugs in this country, but we need markets that drive innovation, not those that reward monopoly.

Thank you for the opportunity to testify.

[The prepared statement of Mr. McNeely follows:]

PREPARED STATEMENT OF LARRY MCNEELY

TESTIMONY

By Larry McNeely, Health Care Advocate
U.S. Public Interest Research Group
Before the Courts and Competion Sub-Committee
House Judiciary Committee
U.S. House of Representatives
July 14, 2009

U.S. PIRG, the federation of state Public Interest Research Groups, is a non-profit, non-partisan public interest advocacy organization. U.S. PIRG's mission is to deliver persistent, result-oriented public interest activism that protects our health, encourages a fair, sustainable economy, and fosters responsive, democratic government. We uncover threats to public health and well-being and fight to end them, using the time-tested tools of investigative research, media exposés, grassroots organizing, advocacy and litigation.

In recent years, medical and pharmaceutical science has produced a new, powerful class of medicines, known as biologic drugs. Rather than a chemical admixture like most drugs on the market, these medicines are developed using biological materials and processes. Often, biologics can only be manufactured using very expensive, state of the art processes.

This new class of drugs has already offered hope to millions of patients suffering from previously untreated diseases. Yet because they were excluded from the procedures to incentivize generic versions of prescription drugs contained in the 1984 Hatch Waxman legislation these already expensive drugs are rendered more expensive. As health care costs skyrocket and biologic drugs gain a greater share of the pharmaceutical market, many now advocate for a pathway to create generic diseases. Opponents suggest that such a pathway would stifle innovation within this vibrant business sector and slow invention of new biologic medicines.

In our view, the best way to understand how to best incentivize innovation and balance other policy goals is to look at an example. Consider the cancer biologic drug Herceptin. Approved by the FDA on September 25th 1998, this amazing medication, produced by the biotech firm Genentech, helps women fight off a particularly tough form of breast cancer that is positive for the protein HER2.

Herceptin has made a serious difference. Its use increases the disease-free survival rates of this type of breast cancer by 12%.[i] Doctors estimate that it can save 7000 women from relapse in a year.[ii]

On average it costs $1.2 billion to take a biologic drug to market, and companies like Genentech should be rewarded for that investment. Genentech should profit from bringing a product to market that saves lives. In fact, they have recouped their development costs and much more, earning $5.5 billion from 2003-2008 alone.[iii]

But there's a catch. Herceptin's patent protections, the legal mechanism that protects intellectual property in most industries, expired in 2005. The available evidence, namely Genentech's enormous annual profits, suggests that the patents on the drug provided an

ample incentive for the important research that Genentech did on this drug. Yet today, without a pathway for follow-on biologics, Genentech continues to enjoy monopoly pricing power. They have certainly made the most of it, charging $48,000 a year wholesale for the Herceptin treatment.[iv] Some reports have indicated that some consumers paying twice that amount or more.[v] But under current law, it's unlikely that a generic company will introduce a cheaper version of the drug anytime soon, and Genentech recognizes that.

Intellectual property protection is important. The success that Herceptin brought Genentech will encourage other manufacturers to make the long-term investments needed to produce the drugs that can vanquish cancer and other diseases.

All the available evidence is that the patent system provides adequate protection for innovator biologics and provides an adequate incentive to raise capital for investments everywhere in the world. I recognize that the biotech companies argue that 14 years of exclusivity is necessary for them to invest in these products. But it is obviously in their interest to get the maximum amount of exclusivity to maximize their profits. Thus it is important to look to an independent source to evaluate the validity of the biotech industry's argument that 14 years is essential to create a sufficient incentive for investing in these products. A recent report by the Federal Trade Commission provides a very helpful evaluation. As you know the FTC is an independent federal regulatory agency. It does not always side with the generic or brand companies. Recently it has vigorously argued against patent settlements, a position which the generic companies vigorously dispute.

The FTC studied the issue of generic biologics and issued a comprehensive report in June 2009, *Emerging Health Care Issues: Follow-on Biologic Drug Competition.* In its report the FTC examined the question of whether the existing patent system provides adequate intellectual property protection to biologics. It found that "The patent system has a proven record of protecting and stimulating biotechnology innovation." (p. 35)

Interestingly, the FTC concluded that in some ways biologics patents are stronger than patents on chemical drugs. It stated that "pioneer biologic drugs are covered by more and varied patents than small-molecule branded products, including manufacturing and technology platform patents." (p. 26) Thus the FTC stated that "there is no evidence that patents claiming a biologic drug product have been designed around more frequently than those claiming small-molecule products." (p. 26; see p. 36) In summary, the FTC found that the pioneer biologic drug manufacturer can continue to earn significant revenues many years after FOB entry. (p. 26).

The FTC's conclusions are important because chemical treatments have flourished without the 12 or 14 years of exclusivity that the biologics manufacturers are demanding. Under the Hatch-Waxman legislation, enacted 25 years ago, chemical drug manufacturers are entitled to only 5 years of exclusivity. Because patents almost always run longer than 5 years, the purpose and effect of this exclusivity is to provide market protection for the unusual products for which patents have expired or which have less than 5 years of patent

protection remaining. For most chemical drugs, it is the patent system which provides the basic intellectual property protection.

The basic compromise that led to the enactment of Hatch-Waxman was not the 5 years of exclusivity. Instead the brand companies demanded and received patent extensions to compensate patent time lost as a result of the FDA drug approval process, which includes both the time needed to test the drugs and the time the FDA takes to approve products. Under Hatch-Waxman, companies are eligible for a patent extension of up to 5 years as long as the extension does not extend patents to more than 14 years. Importantly, these patent extensions already apply to biologics. Thus, even though Hatch-Waxman did not establish a generic program for biologics, it did give biologic innovators the same patent extensions that it gave to the chemical brands.

Hatch-Waxman has been a tremendous success. It gave the medical research industry a sufficient incentive to innovate and it established a safe and effective generic drug program.

But there is a serious danger to conferring too much intellectual property protection. In the case of a drug like Herceptin, every year the drug's manufacturer benefits from the high monopoly prices conferred by exclusivity will cost patients both in dollars, and in lives. Herceptin's high monopoly prices make it less likely and more expensive for insurers to cover it. And thus, fewer patients with breast cancer have access to this life-saving medicine.

It is also significant that every year that Herceptin is enjoying monopoly profits is one more year that Genentech has no overriding incentive to develop additional products. Instead Genentech's principal incentive is to preserve the market for its most profitable drugs, including Herceptin.

Rewarding yesterday's innovation too much can prolong the day that we see the next life saving biologic drug. By granting additional protection to biologic products, above and beyond the manufacturer's patent, we not only keep the drug expensive and out of reach of many Americans. We strip away the incentives to develop the next generation of life-saving drugs.

What is true of Herceptin is even more true of other biologic blockbuster drugs:

US PIRG's Recommendations

In determining where to strike the balance on this issue: we encourage you to keep focused on three important considerations:

- the affordability of these drugs to consumers across the country;
- the impact of your actions on the efficiency of the American economy; and
- the incentives you're creating for innovation for the next generation of life-saving drugs.

The original Hatch-Waxman legislation successfully addressed all these priorities, and it makes sense to learn from those successes. U.S. PIRG believes that an approach such as that included in the Access to Life Saving Medicine Act of 2009 sponsored by Representative Henry Waxman and Senator Chuck Schumer represents the best option before Congress today. This bill is modeled on the Hatch-Waxman Act, which established the generic drug program at FDA for chemical drugs and which conferred the patent extensions and the five-years exclusivity described above.

Evaluation of the Alternatives

Several alternatives to this approaches have been advanced. These approaches would combine longer periods of exclusivity for generic biologic drugs with additional steps to protect the original manufacturer of the pioneer drugs.

Proponents of more protection for pioneer drugs claim that biologics are different from chemical drugs. They argue that the investments needed in sophisticated manufacturing and development of biologics would render patents or even Hatch/Waxman style 5 year exclusivity periods inadequate.

In fact, if their position was true, we should first consider extending protection to industries who face the greatest cost of capital. But that would mean providing monopoly power to investing in several industries with higher capital costs long before we got around to biotechnology. These dubious arguments serve primarily to defend and preserve the monopoly position enjoyed by a few powerful manufacturers.

It's no wonder recent Federal Trade Commission argues clearly that a short exclusivity period strikes a better balance. They find that "

> *The potential harm posed by such a period [if 12-14 years] is that firms will direct scarce R&D dollars toward developing low-risk clinical and safety data for drug products with proven mechanisms of action rather than toward new inventions to address unmet medical needs. Thus, a new 12- to 14-year exclusivity period imperils the efficiency benefits of a FOB approval process in the first place, and it risks over-investment in well-tilled areas.*[vi]

So when it comes to encouraging innovation, we can only conclude that the industry is selling a cure that's worse than the disease. Fundamentally, the choice before Congress this year is whether to reward yesterday's life saving innovation or tomorrow's.

We need strong vibrant markets for biologic drugs in this country. But we need markets that drive innovation not those that reward monopoly. We urge you to make the right choice.

Thanks you for the opportunity to testify. I would be happy to answer any questions.

[i] MSNBC Health, *Drug Found Effective Against Early Breast Cancer,* October 2005
[ii] Ibid.
[iii] AARP Public Policy Institute, *Biologics in Perspective: The Case for Generic Biologic Drugs,* May 2009
[iv] MSNBC Health, *Drug Found Effective Against Early Breast Cancer,* October 2005
[v] The Assertive Cancer Patient, *The True Cost of Herceptin,* March 2007
[vi] Federal Trade Commision, *Emerging Health Care Issues: Follow-on Biologic Drug Competition*, June 2009.

Mr. JOHNSON. Thank you, Mr. McNeely.

Last, but not least, Ms. Rea. Please.

TESTIMONY OF TERESA STANEK REA, PRESIDENT, AMERICAN INTELLECTUAL PROPERTY LAW ASSOCIATION (AIPLA), WASHINGTON, DC

Ms. REA. Thank you. Mr. Chairman, Mr. Ranking Memberand Members of the Subcommittee, I am Teresa Stanek Rea, the president of the American Intellectual Property Law Association.

For purposes of my testimony today, I represent the AIPLA, and I am not speaking on behalf of my firm or any firm clients. I am pleased to have the opportunity to present the views of the AIPLA at this hearing.

As outlined in my biography, I have spent a good portion of my legal career working with patents related to biotechnology and pharmaceutical chemistry. I am also a registered pharmacist in the State of Michigan and have worked for many years as a hospital pharmacist. I think that this experience provides me with a unique perspective to discuss the issues before the Subcommittee today.

AIPLA believes that should Congress create an abbreviated regulatory approval process for a follow-on biological product, it is essential that such a process contain a patent enforcement mechanism that preserves the value of intellectual property by including five specific provisions.

First, a timely and confidential information exchange between patent owners and the biologic follow-on companies.

Second, a streamlined, efficient litigation mechanism that encourages prompt resolution of patent infringement claims.

Third, a corresponding opportunity for a follow-on product applicant to seek declaratory judgment.

Fourth, procedures which apply the existing law of venue.

And, five, have all remedies available to both parties, including damages and injunctive relief.

The development of a new pharmaceutical or biological drug product is both expensive and unpredictable. Pharmaceutical and biotech companies depend on patents to protect their innovations and to provide some expectation that they can recoup their investments in high-risk research and costly clinical trials.

The value of a patent is undermined if there is no effective mechanism to enforce it.

With the Hatch-Waxman Act, Congress recognized the critical role of patents by creating a mechanism by which an innovator could enforce its patent before a generic product obtains FDA approval and is launched into the marketplace. The pending bills in the House attempt to develop procedures parallel to the Hatch-Waxman Act. They include mechanisms for prelaunch patent dispute resolution, which is the primary focus of my testimony today.

If there were no procedures, or ones adopted were inefficient, this may undermine the value of valid patent rights and potentially cause an unnecessary drain on the resources of all parties as well as the judiciary. With these thoughts in mind, I would like to share some specific observations regarding the patent dispute resolution procedures proposed in the two bills.

We believe that H.R. 1548 would encourage efficient, streamlined prelaunch patent litigation that would cover the follow-on product and employ procedures that would be less subject to gamesmanship and abuse.

This bill addresses the need for an exchange of information concerning the follow-on product to allow a preliminary infringement analysis. The notice and certification provisions in H.R. 1548 would limit the patents that may be challenged to those which the patent holder believes are infringed by the follow-on product.

This bill would also allow the follow-on applicant to bring a declaratory judgment action if an infringement suit is not filed on a timely basis.

Conversely, H.R. 1427 has the potential to weaken the value of biotechnology patents by limiting the ability of the referenced product holder to assert its patents prior to market launch of a follow-on product.

We believe that the bill lacks sufficient mechanisms for referenced product holders or third-party patent owners, such as universities, to obtain access to product and manufacturing information necessary to determine whether there is a good-faith basis for asserting an infringement claim.

At the same time, H.R. 1427 would appear to expand declaratory judgment jurisdiction to create opportunities for interested parties to challenge patents which may not cover either the referenced product or the planned follow-on biotech product.

Lastly, the patent notification procedure in H.R. 1427 includes ambiguous standards with severe penalties that may encourage additional patent challenges and create uncertainty in subsequent intellectual property transactions and litigation.

Mr. Chairman, I appreciate the opportunity to present these views, and I look forward to any questions the Subcommittee may have concerning the observations and comments that I have presented.

Thank you.

[The prepared statement of Ms. Rea follows:]

PREPARED STATEMENT OF TERESA STANEK REA

AMERICAN INTELLECTUAL PROPERTY LAW ASSOCIATION
241 18th Street, South, Suite 700, Arlington, VA 22202 Phone: 703.415.0780 – Fax: 703.415.0786 – www.aipla.org

STATEMENT OF

TERESA STANEK REA

PRESIDENT

AMERICAN INTELLECTUAL PROPERTY LAW ASSOCIATION

BEFORE THE

SUBCOMMITTEE ON COURTS AND COMPETITION POLICY

COMMITTEE ON THE JUDICIARY

UNITED STATES HOUSE OF REPRESENTATIVES

HEARING ON

"BIOLOGICS AND BIOSIMILARS: BALANCING INCENTIVES FOR INNOVATION"

JULY 14, 2009

Mr. Chairman and Members of the Subcommittee,

I am pleased to have the opportunity to present the views of the American Intellectual Property Law Association (AIPLA) at this hearing on "Biologics and Biosimilars: Balancing Incentives for Innovation." Let me first express our appreciation for your interest in this very important topic.

AIPLA is a national bar association of more than 16,000 members engaged in private and corporate practice, in government service, and in the academic community. AIPLA represents a wide and diverse spectrum of individuals, companies and institutions involved directly or indirectly in the practice of patent, trademark, copyright, and unfair competition law, as well as other fields of law affecting intellectual property. Our members represent both owners and users of intellectual property, and therefore have a keen interest in an efficient and smoothly functioning patent system.

As outlined in my biography, I have spent a good portion of my legal career working with patents related to biotechnology, pharmaceutical chemistry, medical devices, immunology, and specialty chemicals, as well as polymers and nanotechnology. I am also a registered pharmacist in the State of Michigan and worked for years as a hospital pharmacist. I believe that this experience provides me with a unique perspective to discuss the issues before the Subcommittee today.

AIPLA believes that, should Congress create an abbreviated regulatory approval process for a "follow-on" biological product, it is essential that such a process contain a patent enforcement mechanism that preserves the value of intellectual property. Such a regime should include:

1. a timely and confidential information exchange sufficient to allow the reference product holder and third-party patent holders to determine whether they have a good faith basis to assert a patent infringement claim;
2. a streamlined, efficient litigation scheme that encourages resolution of patent infringement claims by the reference product holder as well as by third-party patent holders before FDA approval of the follow-on product;
3. a corresponding opportunity for a follow-on product applicant to seek a declaratory judgment of non-infringement, invalidity or unenforceability as to patents that it believes in good faith may be asserted against the follow-on product, if the patent holder does not bring a timely infringement action before product launch;
4. procedures that apply the existing law of venue; and
5. all available remedies, including damages and injunctive relief, should patent infringement be found.

General Background

Patent rights play an important role in promoting and protecting biotechnology innovation, and the available enforcement mechanisms for these rights can significantly affect patent value and the ability to obtain investment for further research. In addition to creating an abbreviated regulatory approval pathway for biologics, the pending bills (H.R. 1548 and H.R. 1427) would create a mechanism for pre-launch patent dispute resolution. It is this mechanism that is the primary concern of AIPLA and the primary focus of this testimony. AIPLA submits that the patent dispute resolution mechanism should operate prior to FDA approval of the biosimilar product and should not unduly create additional rules that increase the cost and complexity of litigation or otherwise undermine the value of valid patent rights in biotechnology inventions.

The U.S. patent system stimulates technological innovation by providing legal protection to inventions and by disseminating useful technical information on which others can build. In essence, patents fuel research and development, which is particularly true in the biotechnology and pharmaceutical industries. The fact that the biotechnology and pharmaceutical industries rely

more heavily on patent protection than any other industry was recognized by the Federal Trade Commission in its 2003 Report entitled, "To Promote Innovation: The Proper Balance of Competition and Patent Law and Policy."

The development of a new pharmaceutical or biological drug product is also very expensive and unpredictable. Pharmaceutical and biotech companies depend on patent protection to protect their innovations and to provide some expectation that they can recoup their investments in high-risk research and costly clinical trials. This reliance on patent protection arises long before a product is available to patients. Much of the early biotechnology research is conducted in academic institutions or in small technology firms that then seek to license to larger entities for the next, more costly, stage of research. Often, there are several transfers of rights for this purpose, and the availability of enforceable patent rights can determine the value of these transactions and the availability of any additional investments. In essence, the value of a patent is the right to exclude competitors from practicing the claimed invention for the life of the patent. Today, that generally means 20 years from the date when the patent application was filed. The value of a patent is undermined if there is no effective mechanism to enforce the patent and keep others from infringing that patent during its life.

Without question, an abbreviated regulatory approval pathway for biological drugs needs an effective pre-launch mechanism for resolving patent disputes to provide certainty as to the effect of patent rights to both biosimilar manufacturers and innovators. Without such a mechanism, patent disputes in this area would strain the federal judiciary by requiring -- in preliminary injunction proceedings – resolution of the complex legal and scientific questions involved with each biosimilar product launch. Those circumstances would require quick decisions

on claims of patent infringement and invalidity in a pressurized context and without the benefit of a complete evidentiary record.

As explained below, AIPLA believes that H.R. 1548 achieves the objective of establishing an effective pre-launch mechanism for resolving patent disputes, and avoids many of the concerns raised by H.R. 1427.

Hatch-Waxman Model. Congress expressly recognized the critical role of patents in fostering innovation and the need to resolve patent disputes before FDA marketing approval in 1984 when it enacted the Drug Price Competition and Patent Term Restoration Act, commonly known as the "Hatch-Waxman Act."

As a first step, the Hatch-Waxman Act requires a reference product holder to list all patents which cover the reference product in the FDA's Orange Book.[1] Unless the generics manufacturer agrees to defer launch until after the expiration of a listed patent, the reference product holder is given statutory authorization to file a patent infringement action to enforce any of the listed patents prior to the FDA's approval of the generic manufacturer's abbreviated new drug application. When such an infringement action is commenced, FDA approval of the generic product is stayed for 30 months to allow for resolution of patent disputes before market launch of the generic product.

[1] Consistent with the prevailing view of stakeholders that there should be no "Orange Book" equivalent in the follow-on context, neither bill would establish any sort of registry requiring the reference product holder to identify patents covering the reference product or its methods of manufacture. The "Orange Book" procedure was created by the Hatch-Waxman Act for small molecule compounds. Under 21 U.S.C. § 355(b)(1), the reference product sponsor must list all patents which claim the drug or method of using the drug with respect to which a claim of patent infringement could reasonably be asserted if an unlicensed person engaged in the manufacture, use or sale of the drug. Because there is no "Orange Book" equivalent, there is a need for information exchange sufficient to allow patent holders to determine whether the biosimilar product or its method of manufacture may be infringing their patents.

In other words, when it authorized a regulatory pathway for generics, Congress at the same time created a statutory mechanism permitting developers of innovative drugs to quickly resolve patent disputes, and developers of innovative biologic drugs should be able to do the same.

Need for Patent Dispute Mechanism. The specific procedures of the patent dispute mechanism which have been proposed deserve careful consideration. In addition to undermining the value of valid patent rights, inefficient or ineffective procedures will cause an unnecessary drain on the resources of the judiciary and will increase costs to the parties. Indeed, recent initiatives to reform the patent law have been driven in part by the spiraling cost and complexity associated with enforcing patent rights.

AIPLA conducts a nationwide survey of our members every two years on the cost of patent litigation. In 2007, we reported that the median cost of a patent infringement suit was $1,600,000, if $1 million to $25 million was at risk. The cost rises significantly as the stakes increase. The median average cost of a patent infringement case involving more than $25 million dollars was about $5,500,000. Patent law is a complex, dynamic field of law, and the technologies at issue in these patent litigation suits have become increasingly sophisticated. Patent litigation places a significant burden on the federal judiciary, which by and large relies on generalist judges and lay juries.

For these reasons, care should be taken to ensure that the proposed patent dispute resolution procedures do not impose additional burdens on litigants or otherwise increase the complexity and uncertainty of enforcing these patents. Doing so would only exacerbate the problems that the ongoing patent law reform efforts aim to address.

With these thoughts in mind, I would like to share AIPLA's analysis of the patent dispute resolution procedures proposed in H.R. 1548 and H.R. 1427.

I. H.R. 1548's Patent Enforcement Provisions.

Information Exchange Provisions. H.R. 1548 would provide a reasonable, balanced procedure to exchange information. The reference product holder would be entitled to access to the follow-on product's abbreviated application as well as information about the product and its method of manufacture. Third-party patent holders would be entitled to notice of the abbreviated application filing, with the right to request information. The bill would require that all such information be treated as confidential by the recipients. Reference product holders and third-party patent holders could then conduct informed analysis about whether their patents cover the follow-on product and its method of manufacture. In order to begin enforcement proceedings before market launch, they must provide the basis for their infringement contentions to the follow-on applicant.

Scope of Pre-Market Launch Patent Litigation. Under H.R. 1548, the patents available for litigation would be limited to those patents that the reference product holder or third-party patent holder identifies as "covering" the follow-on product. This scope is much narrower than the categories of patents that may be challenged under H.R. 1427, and is consistent with declaratory judgment law and the requirements of Article III of the Constitution.

Opportunity for At-Risk Launch of Follow-On Product. H.R. 1548 would provide a balanced approach for interested parties to initiate suit before FDA approval, although in some situations the bill may not sufficiently protect the interests of a follow-on applicant seeking resolution of patent issues before FDA approval and launch. In particular, the bill would give the reference product holder and/or patent holder the opportunity to bring an infringement action within 60 days of receiving the patent certification from the follow-on applicant. If no suit is

brought within this time frame, then the FDA's approval of the follow-on product may not be precluded on patent grounds. However, there is still the possibility that a "late" patent infringement proceeding could be brought and a preliminary injunction could be obtained to preclude market launch of the follow-on product, despite FDA approval.

H.R. 1548 would also provide the follow-on applicant the opportunity to bring a declaratory judgment action, in the event that the reference product holder or patent holder fails to bring suit within the 60-day period. However, the bill does not allow such an action to be brought until 3 years before expiration of the reference product's data exclusivity period. The assumption that a patent infringement litigation can be resolved in 3 years may not necessarily hold true. If patent reform legislation passes allowing interlocutory appeal of claim construction rulings, we can expect that a hard-fought patent litigation will not be completed within 3 years. We therefore recommend that this particular section of H.R. 1548 be revisited in the event that the patent law reform efforts succeed.

Venue of the Pre-Launch Litigation. Unlike H.R. 1427, H.R. 1548 does not attempt to alter the law of venue. As a result, the courts would have discretion to transfer and consolidate pre-launch lawsuits as appropriate. We believe this is a better approach than a blanket rule allowing a particular category of litigant to make the final determination of venue.

Multiplicity of Litigation and the Abuse of Litigation Process. Under H.R. 1548, there is the possibility for multiple litigations brought separately by the reference product holder and third-party patent holders.[2] For example, because the third-party patent holder has more time to provide its patent list to the follow-on applicant than the reference product holder has, it is

[2] There is also the possibility that a patent issues or the reference product holder in-licenses a patent after the initial certification process, whereupon the reference product holder or third-party patent owner could begin another lawsuit to enforce that "new" patent.

possible that the follow-on applicant could face separate lawsuits initiated at different times by each third-party patent holder. However, jurisdiction over the follow-on applicant would likely be limited because the follow-on applicant would not yet be marketing an approved product. Moreover, under the existing venue law, the follow-on applicant could move to transfer and consolidate patent infringement actions, if it chose to do so.

Effect on Third Party Patent Owners. H.R. 1548 has several provisions that recognize and attempt to balance the interests of third-party patent owners, including the requirement of notice that the follow-on application has been filed. The bill includes a procedure that would allow the third-party patent owner(s) to gain confidential access to information about the follow-on product, and a pre-launch litigation process that would allow a third-party patent owner to enforce its patent before FDA approval. The bill also includes a time-limit requirement if a third-party patent owner wishes to enforce the patent for the purpose of delaying FDA approval until after the expiration of the patent in suit. The bill would further create a mechanism by which a follow-on applicant may bring a declaratory judgment action.

II. H.R. 1427's Patent Enforcement Provisions

Information Request Provisions. H.R. 1427 would create an information request process that would allow any party to request that the reference product holder provide a list of "all those patents owned by, licensed to, or otherwise under the control of, the holder of the approved application that the holder believes in good faith relate to the reference product."

Importantly, the bill does not define "relate to," but expressly includes "patents that claim the approved biological product, any formulation of such product, any method of using such product, or any method or process that can be used to manufacture such product or component,

regardless of whether that method or process is used to manufacture the reference product." This standard would require more than just an identification of patents owned or controlled by the reference product holder that cover the reference product. It would seem to require the reference product holder to review its entire patent portfolio, as well as all patents it has in-licensed for any purpose, to determine whether those patents "relate to" the reference product. In practice, this obligation would become most onerous with respect to methods that "can be used to manufacture" the reference product. This disclosure obligation would continue for 2 years after the date of the request, and may be extended by a subsequent request by the follow-on applicant.

The bill also includes forfeiture provisions directed against patent holders. If a "relevant patent" that "should have been disclosed" was not disclosed as required, then the owner of the patent or licensee of the patent may ***never*** sue for infringement of that patent. In effect, the patent would lose all value. This forfeiture provision would create uncertainty for all parties involved, harsh consequences for third-party patent owners who license their patents to others developing commercial products, and increased likelihood of complex, expensive litigation – all of which discourage continued investment in biomedical research and development.[3]

---

[3] Given the high stakes involved in the potential forfeiture of the right to enforce a patent, the ambiguity of the phrase "relate to" would likely create an entirely new unenforceability defense that would parallel the inequitable conduct defense in terms of the amount of discovery required. Accused infringers would be encouraged to seek discovery from every entity that controlled the patent over time, including third parties, in an attempt to make an argument that the patent should have been disclosed in response to a patent notice request provision. In addition to extensive fact discovery, including inquiries into the subjective intent of reference product holder employees, each party would hire one or more experts to address the question of whether the patented process "relates to" the reference product. Would the inquiry be whether one of ordinary skill in the art believed that the patent process "related" to the reference product at any time during the 2-year obligation to list period? What if the process was "obvious to try" but no one had done so? To complicate matters, the use of the phrase "in good faith" suggests that the inquiry is the state of mind of the patent owner during the 2-year time period. In this context, which employees' state of mind is/are relevant? Does the belief of a single scientist employed by the reference product holder that the patented process could have been used to make the reference product at a lab bench constitute such "good faith"? This subjective standard would create a new unenforceability defense, similar to the often maligned inequitable conduct defense, but with even less certainty about how the inquiry should be performed.

Moreover, because the forfeiture provision apparently attaches to the patent itself, rather than limiting the enforcement right of the particular reference product holder or licensor with respect to the particular proposed follow-on product, it could have profound implications in ***all*** litigation involving biotechnology patents, not just the pre-launch provided by H.R. 1427, as well as in all transactions involving the sale or license of biotechnology patents. Any party against whom a biotechnology-related patent was asserted could request discovery of all communications with follow-on applicants by any owner or licensee of the patent at issue as well as discovery directed to the "good faith belief" of the owner or licensee during the obligation-to-list period, regardless of whether the owner or licensee is a party to this litigation. In addition, potential purchasers or licensees in transactions involving biotech patents would be forced to engage in time-consuming and expensive diligence to determine whether the patent(s) involved in the transaction may be rendered valueless by this new form of unenforceability defense.

At the same time, H.R. 1427 does not provide the reference product holder with *any* access to information to determine whether the follow-on product likely infringes any of the reference product holder's patents. The reference product holder who receives a patent statement from a follow-on applicant, which may represent that the applicant does not infringe, must sue for infringement of its patents within a specified and very limited time period or else forfeit its opportunity to obtain injunctive relief. Yet, the reference product holder has no ability under the terms of the bill to obtain information sufficient to provide a good faith basis to make infringement allegations under Rule 11 of the Federal Rules of Civil Procedure. The reference product holder may ultimately determine, after expensive discovery and the intervention of the courts, that there is no infringement. This would be a waste of court and party resources.

Scope of Pre-Market Launch Patent Litigation. Under H.R. 1427's patent enforcement procedures, the follow-on applicant would have the ability to determine which and how many patents owned or licensed by the reference product holder would be litigated before follow-on product launch. The follow-on applicant's patent notice must provide a detailed statement of the factual and legal bases for the applicant's belief that the ***cited*** patents are invalid, are unenforceable, ***or*** will not be infringed by sale of the follow-on product. However, the bill does not require the follow-on applicant to include such notice for all the patents identified by the reference product holder, nor does it require the follow-on applicant to request patent information at all. Only the patents included in the follow-on applicant's patent notification are subject to litigation before the follow-on product launch.

Indeed, H.R. 1427 would amend 35 U.S.C. § 271(e) to define the follow-on applicant's patent notice as an act of infringement only as to a patent identified in that notice. The reference product holder must then bring suit within 45 days of receiving this patent notification. Failure to do so would limit the patent holder's available remedies to a "reasonable royalty." This is neither an equitable nor efficient method of identifying patents for resolution before launch. The patent owner would lack any certainty concerning whether relevant patents can be enforced before the launch of the follow-on product.

Significantly, the follow-on applicant may identify patent(s) that it would like to challenge *for any reason*, regardless of whether there is a colorable argument that the follow-on product would infringe the patent. For example, the follow-on applicant could send a notice challenging the validity of any patent listed by the reference product holder as "relating to" the reference product, even if the patent does not cover the proposed follow-on product. The follow-on applicant's notice could state that the patent will not be infringed and is invalid. If the reference

product holder agrees that the patent is not infringed on the basis of the information provided, it would lack any basis to sue. However, the follow-on applicant could still seek a declaratory judgment that the patent is invalid, in the hope of obtaining freedom to practice the patent with respect to other products or operations. This provision is counter to declaratory judgment standards, which require an actual case or controversy, may violate Article III of the U.S. Constitution, and could burden the federal judiciary with needless patent cases.

Opportunity for At-Risk Launch of Follow-On Product. Under H.R. 1427, pre-launch litigation of any patent is entirely within the control of the follow-on applicant, despite patents held by the reference product owner that cover the follow-on product or its method of manufacture. For example, under paragraph (18)(B), a follow-on applicant *may*, at any time after submitting its application, provide "patent notification," which serves as the trigger for pre-launch litigation.[4] However, nothing in H.R. 1427 would require the follow-on applicant to trigger the pre-litigation process before launch of its follow-on product. The bill expressly recognizes the "discretion of applicants" and provides that an applicant is not required by this bill, nor can it be required by court order or otherwise, to initiate the patent notification or litigation procedures under paragraph (18).

In effect, H.R. 1427 would enable the follow-on applicant to pursue an "at risk" launch, *i.e.*, launch without resolution of infringement of *any* patents owned or licensed by the reference product holder. Unlike under the Hatch-Waxman Act, which provides for an automatic 30-month stay of approval when an infringement suit is brought, the reference product holder would be

[4] The first step in the litigation process is the "Patent Notification" step, under which the follow-on applicant provides notice to the reference product holder and, in certain circumstances, the third-party patent owner (if that patent owner was previously identified in an optional information exchange between the reference product holder and the follow-on applicant). Within 45 days of receiving notice, the reference product holder or third-party patent owner may bring an infringement action. As noted above, failure to bring suit in 45 days results in a forfeiture of the right to injunctive relief and limits damages to a "reasonable royalty."

limited to seeking preliminary injunctive relief through the courts. This likely will impose a significant burden on the federal court system to consider and quickly make preliminary injunctive relief determinations. Such determinations will require an analysis of the likelihood of success on the merits of the patent infringement claim as well as the invalidity and unenforceability defenses asserted in connection with each patent in suit. In addition, whatever the district court decides, the decision would be immediately appealable to the Federal Circuit.

If the reference product holder does not obtain a preliminary injunction preventing launch, once the product is available and being administered to patients, the follow-on applicant likely would argue, even if the patent is found to be valid and infringed, that the Supreme Court's decision of *eBay Inc. v. MercExchange, L.L.C.* requires trial courts to consider the effect on the public health of removing a drug from the marketplace. Unless the newly approved follow-on product is determined to be "interchangeable" with the previously reference product by the FDA, which is unlikely in the near term, the follow-on applicant likely would argue that the public would be harmed by the removal of the follow-on product from the market because, due to lack of substitutability, the patients taking the follow-on product cannot simply switch to the licensed product if the follow-on product is removed from the market. This mechanism, with no stay of approval during litigation and no ability of the patent holder to resolve a patent dispute in advance of product launch, would undermine the value of patents covering the reference product.

Venue of Pre-Launch Litigation. H.R. 1427's venue provisions appear to give follow-on applicants an unfettered ability to transfer infringement cases away from the forum chosen by the reference product holder (and third-party patent owner) into whatever district the follow-on applicant prefers, allowing for forum shopping and strategic separation of related cases that could otherwise be consolidated to maximize efficient use of judicial resources. The venue provision

would amend 28 U.S.C. § 1404 to allow the follow-on applicant who has been sued for infringement to move to transfer the action to any other jurisdiction in which venue is proper. The proposed amendment further provides that, in ruling on any motion to transfer, "the greatest weight shall be given to . . . the interest in identifying a district court in which the case will be adjudicated expeditiously . . . [and] the strong public interest in obtaining prompt judicial resolution . . . ." This provision would constrain the district court's discretion to consider other traditional factors such as the convenience of the witnesses and parties, and the interests of justice, which would otherwise be relevant to such transfer motions under 28 U.S.C. § 1404.

Multiplicity of Litigation. H.R. 1427 appears to neither limit nor streamline the pre-launch litigation process. Because there is no streamlined process requiring a review and certification of all relevant patents at one time, one possible consequence is that there would be multiple litigations pending at the same time. For example, the follow-on applicant could make a strategic decision to "divide and conquer," sending patent notices to the reference product holder and third-party patent holders in a seriatim manner. Because of the requirement that a patent holder or reference product holder must bring suit within 45 days of receiving that notice, there could be separate, serial proceedings over a lengthy period of time. It is unclear whether, even if the cases were all brought over time against the follow-on applicant in the same district, those cases could be consolidated as related cases. Indeed, under the bill's venue provision, the follow-on applicant could decide to move to transfer to another jurisdiction and the district courts appear to have no discretion to override the follow-on applicant's decision, even if the patents in suit were related. In sum, these provisions would create opportunities for strategic use of multiple, separate lawsuits that would result in an inefficient use of judicial resources and cause undue diversion of the resources of the reference product holders and third-party patent holders.

Effect on Third Party Patent Holders. The complexity of the proposed process increases when patents owned by third parties are involved. This is often the case with patents covering biotechnology products, which may have originated in academic research and been licensed to the reference product holder. Correspondingly, the burdens on these third parties, who may have limited resources to engage in litigation, are greatly increased. For example, there is no absolute requirement that the follow-on applicant send its patent statement to third-party patent owners. If the follow-on applicant has not requested information from the reference product holder in advance of sending a "patent notification" to the reference product holder, then the follow-on applicant can list a patent that the reference product holder has non-exclusively licensed from a third-party, yet the follow-on applicant has no obligation to send a notice to the patent owner/licensor. Because the patent owner would not have received notice from the follow-on applicant, it would not have the right to sue under the patent enforcement litigation provisions of this bill. However, under the Federal Circuit's standing law requirements, the patent owner may be a necessary party without whom the reference product holder could not bring an infringement action. As a result, both the reference product holder and the patent owner could be deprived of any remedy for infringement other than a reasonable royalty, *i.e.*, no injunctive relief and no recovery of lost profits.

H.R. 1427's patent enforcement procedures could create significant problems for third party patent holders, many of whom are universities, research organizations or small biotechnology companies with little or no resources available for litigation. The follow-on applicant could use a combination of seriatim proceedings and venue changes to put pressure on third-party patent owners with limited budgets. The follow-on applicant could, through the "patent statement" procedure, bring separate lawsuits at different times on different patents. This

would multiply the burden of discovery: university inventors, who are research scientists and medical doctors, could be forced to engage in time-consuming and duplicative document production and depositions in each case. These cases may be pending in different jurisdictions, far from the university, adding to the expense and burden on the researchers' time.

In addition, the forfeiture provision's potential effect on third-party patent owners is troubling. Many biotechnology products are covered by patents originally developed and licensed by universities and research institutions. Under H.R. 1427, a reference product holder that is a non-exclusive licensee of a university patent covering platform biotechnology could forfeit the university's right to enforce the patent against any party, even if the university never received the follow-on applicant's patent notification statement, and even if the reference product holder is not using the licensed method in its reference product or for any purpose. In short, as a result of actions or omissions of its non-exclusive licensee, the university could in effect forfeit all of its patent rights and lose its entire royalty stream. The university's other non-exclusive licensees could then stop paying royalties to the university on the ground that the patent has been rendered unenforceable. Moreover, there is a strong argument that, since the request for information is directed only to the reference product holder (and not third-party patent owners), forfeiture of the owner's right to enforce the patent based upon the reference product holder's failure to list the patent would violate the patent owner's constitutional right of due process.

Conclusion

In our view, the patent enforcement provisions of the H.R. 1427 would likely weaken the value of biotechnology patents by severely limiting the ability of the reference product holder to assert its patents prior to market launch of a follow-on product. The bill lacks sufficient

mechanism for reference product holders or third-party patent owners to obtain access to product and manufacturing information necessary to determine whether they have a good-faith basis for asserting an infringement claim. At the same time, the bill would expand declaratory judgment jurisdiction to create opportunities for interested parties to challenge patents which may not cover either the reference product or the planned follow-on biologic product. The patent notification procedure includes ambiguous standards with severe penalties that would encourage additional patent challenges and create uncertainty in subsequent intellectual property litigation and transactions. Moreover, the ambiguous standards and expanded declaratory judgment jurisdiction in the bill would create opportunity for abuse of the patent litigation system that would waste judicial resources and unduly burden third-party patent owners.

By contrast, H.R. 1548 would encourage efficient, streamlined pre-launch patent litigation involving patents that may cover the follow-on product, employing procedures that would be less subject to gamesmanship and abuse. The bill addresses the need for an exchange of information about the follow-on product to conduct a preliminary infringement assessment by the reference product holders and third-party patent owners. The bill's notice/certification provisions would limit the patents that may be challenged to those which the patent holder believes are infringed by the follow-on product. The bill would allow the follow-on applicant to bring a declaratory judgment action on any of the patents identified by the reference product holder or a third-party patent holder if an infringement suit is not filed on a timely basis.

I wish to thank the Subcommittee for the opportunity to present these views and I look forward to any questions that you may have concerning the observations and comments that have been presented.

Mr. JOHNSON. Thank you, Ms. Rea.

And at this time, I will commence with my questions.

Mr. Leicher and Mr. Kushan, in the Hatch-Waxman Act data exclusivity and patents work together to provide guaranteed market

exclusivity for about 7.5 years. After that period, continued market exclusivity is contingent solely on the strength of the patents.

Why wouldn't a similar system work in the biosimilar context?

Mr. LEICHER. We believe a similar system would work in the biosimilar and biogeneric context. Maybe it is worth taking a step back for a moment because there has been a use of the word biosimilar but not biogeneric this afternoon. We discussed this at the FTC as well. One of the things we believe Momenta is doing and many other biologics companies will begin to do over the next several years is develop the technology, and it's really the next generation of biologics, to characterize what happens in a cell after a protein is created from its gene, is understanding the black box that exists today in biologics manufacturing that's often referred to as post-translational events.

I don't want to get too detailed, but that's what we have done at Momenta with the work with Heparin. We believe that once you are able to use this new technology, you are going to be able to characterize proteins and biologics with the same kind of specificity that one sees today with drugs. And that's what we have done in the heparin world.

And so it's important to distinguish the two pathways. And the reason I bring that up is, I am very concerned, and we are very concerned, that if we adopt a law for the next 25 years, we are going to put in place a roof on the advancement of science. We need to have the pathway so that there's a reason for venture capitalists to invest in biotech companies to actually develop this new technology. And if we limit the world to biosimilars, we are going to fall behind in the global race in the biotech industry.

Mr. Kushan. Thank you, Mr. Chairman.

It's a very good question. The context for this debate, really is, when you center on Hatch-Waxman is, what is the expectation of the innovator regarding the time between the launch of the innovator drug and the time the generic competition begins? And that, in the Hatch-Waxman system, is predicated on the strength and the certainty that patent rights in that product will deliver.

So when you are thinking, from an investment and pre-innovation points of view, the Hatch-Waxman system is designed to provide, you know, the period that the patent will deliver for exclusivity.

When you look at the statistics, that period is around 12 to 14 years at this point. So for small-molecule drugs, you are seeing generic competition start 12 to 14 years.

Now, the big difference when you shift over into the biosimilar environment is that there's a loophole that has been created. And that loophole is simply, unlike Hatch-Waxman, where it is prohibited to do this, a biosimilar manufacturer can essentially skirt the patent rights but then get the benefit of the clinical data to get on to the market much faster.

And it's that character of the biosimilar product that creates the risk that is answered and addressed by a data exclusivity period that essentially provides a backstop for the patent rights.

Now, one important perspective on this, I think Representative Eshoo pointed to this, if you have the system work as it has been designed, if you have it work as the FTC hopes it would work,

where patents are delivering their intended purpose of 12 years or so of effective protection against biosimilar competition, then data exclusivity that is co-extensive with that period has no impact because the patents are working the way they should.

The concern that is driving the call for a stronger data exclusivity period is precisely the uncertainty that exists that we can, as innovators, know that our patent rights will give us that protection, and that's essentially the major difference. You have in the Hatch-Waxman system, the ability to kind of get around the patents. You are similar enough, but not so similar to not rely on the clinical data.

Mr. JOHNSON. Thank you.

Mr. Brill, you suggest that 10 percent is the right value for the cost of capital.

And Mr. Lasersohn, you suggest the figure should be closer to 20 percent.

Can you both briefly explain this concept of the "cost of capital" and how you came up with different numbers and how they should affect data exclusivity?

Mr. BRILL. Thank you. The cost of capital is, without question, an important component into the calculation that investors would make when looking forward at a potential investment in a biologic. And it's also an important component into the modeling work that I have done, the FTC has done, and Henry Grabowski, a professor at Duke University, has done.

The difference between 10, 11 or 12.5, which are cost-of-capital estimates that I use in my modeling, and higher numbers, such as the 20 percent figure that was cited earlier, has to do with where in the process that cost of capital applies.

Without question, the hurdle rates in venture capital are significantly higher than they are in later-stage development of biotech, but that's only one stage of the process. The proper cost-of-capital rate to consider is the average across the entire development process of a biologic drug. The cost of capital is very expensive at the beginning, but as a product develops and moves forward through the system, the risks decline and the cost of capital declines as well.

So it may be expensive at the beginning to get funding, but many of our biologic drugs are provided by enormously large corporations that have access to equity markets as well as sophisticated debt markets, and cost of capital later in the process is much lower, thereby reducing the average cost of capital.

Mr. LASERSOHN. I think the simplest way to think about this is, there are two key points. The first is cost of capital is equivalent to going to a bank and borrowing money at 10 percent. If you borrow money from a bank at 10 percent and invest it at 9 percent, you will be bankrupt.

If you invest it at 11 percent, you will have positive cash flow. And so the rate of return that you need to make on an investment is related to what your cost of capital is.

The problem with Mr. Brill's analysis is that, in fact, we have a chain of development that starts from universities, goes to the venture capital community, and then later goes to large pharmaceutical companies.

If you break that chain at any point, if at any point in the cost of capital, the return on capital doesn't meet the requirements of whoever is supplying capital at that point, in particular, at that early linking of the chain, the chain is broken, and nothing gets developed; nothing ends up in the hands of large pharmaceutical companies.

So that is really the key, the point that we are trying to make. If that chain is broken, which it indeed will be, if we have a data exclusivity, for example, if, in fact, our exclusivity is much less than what we think it needs to be, for example, under Hatch-Waxman, of 12 years, that chain will be broken, and there will be nothing left for the large pharmaceutical companies to buy and invest in because we will not have invested in them.

Mr. JOHNSON. Thank you both.

Thank you, Mr. Lasersohn.

We have got one vote on the House floor in about 10 or 11 minutes. So what we will do is have a brief recess so we can go over there and take care of that business, and we will be back quickly in about 15 or 20 minutes. Thank you.

So we will stand in recess.

[Recess.]

Mr. JOHNSON. We are back in session, and Mr. McNeely is coming back; correct? I see some papers there.

All right, what I would like to do is, Ms. Rea, I would like to ask you a question.

You indicate that H.R. 1427 permits biosimilar makers to launch their products at risk. And if they do, is there not the potential for treble damages if a patent has been found valid and infringed? And isn't this a substantial enough risk to keep biosimilar products off the market until their patent has expired?

Ms. REA. I can't speak on behalf of all generic follow-on biologic companies, but the opportunity to launch at risk is rarely undertaken by most generic companies at this time.

Business certainty is something that everyone wants, whether you are the patent holder or you are the follow-on biologic applicant. Yes, if there is litigation, there is the potential for treble damages. You run a potential risk that maybe the payment of treble damages—- it may be difficult to pay treble damages, depending on the economics of any particular company. So even if a patent holder succeeded in litigation and obtained treble damages, the likelihood of recovery is not something that would be guaranteed.

Mr. JOHNSON. Okay. Thank you.

Last, I would like to ask Mr. McNeely, most analysts, Mr. McNeely, believe that biosimilar market entry will only result in modest price increases. And, if so, how much would consumers and the Federal Government really save?

Furthermore, will these savings be worth any uncertainty we may cause in the biotechnology company financing?

Mr. MCNEELY. Mr. Chairman, thank you for the question.

I would say that, especially given the value that the current market is putting on these high-tech biologic medicines, that, in fact, there is quite a bit to be saved. If, I believe the FTC's number was, if you will correct me, 10 to 30 percent reduction in prices due to—or 10 to 30 percent market penetration if there is a generic compet-

itor, and that that, one, would not have the effect of the generic competitors that now consume about—take about 70 percent of the chemical market when they come in.

But the reality is, when you are talking about a drug like Herceptin, with $48,000 a year wholesale and we have seen reports of a lot more being charged to consumers, every little bit helps, and it helps a great deal in that respect.

I am sorry, can you repeat your second question, Mr. Chairman?

Mr. JOHNSON. Yes, I can. Will the savings that would be generated be worth any uncertainty we may cause in the biotechnology financing?

Mr. MCNEELY. Sir, the biotech industry, while made up of small firms, certainly, is an extensive industry and a large industry, an important one. The reality is that the benefits of enhanced innovation that would come through a pathway, along the lines of what Hatch-Waxman did for chemical drugs, could actually benefit the industry as a whole over the long term and certainly would benefit consumers.

Mr. JOHNSON. All right.

And, Mr. Brill, would you respond to that part of the question?

Mr. BRILL. Thank you. I wanted to comment on the potential for cost savings from a competitive market for biologics.

As was noted, the FTC and as well the Congressional Budget Office have made estimates of how much prices will decline. And it is far less than it does, than the price declines and the savings per drug that we see in small-molecule drugs.

In aggregate, the savings will be quite substantial. It could be billions of dollars a year for the Federal Government and an equal amount for private payers. But because the prices won't collapse to the same extent they do for small molecules, that means that there are still opportunities for the innovator drugs to earn profits. They have a very large initial expense from developing this drug, over a billion dollars to bring a drug to market initially.

We need a structure that ensures they can earn back profits to cover that expense. What's different in this market is that, even after we have generic entry, we will still have an opportunity for the innovator drug to make enough profit to help pay off that fixed, that sunk cost, that fixed cost. That is one of the differences in the dynamics of the market.

It doesn't mean that there won't be savings, but there is a tradeoff between the price decline effects and data exclusivity. So the less the prices are expected to decline, the less important it is, or, rather, the shorter duration of data exclusivity that we can have.

Mr. JOHNSON. Thank you.

Mr. Lasersohn.

Mr. LASERSOHN. Thank you, Mr. Chairman.

I would just like to respond. I, with respect to the issue that increased generic or FOB competition, or that those competitors will be innovators, is something I have to admit I have heard over and over again, and I don't understand.

It is absolutely the case that the FOB companies will produce price reductions, which may benefit consumers, but they have never been innovators. And I don't think they are suggesting, in

fact, none of the ones I talked to suggest there are going be innovators in developing new drugs.

That is my first point. Innovation will continue to come from branded, innovative, small entrepreneurial VC-backed companies.

The second point is that the FTC's analysis was based, on what the effect of competition would be, it was based on many assumptions, which I have to say, I don't understand. One critical assumption is that their cost of entry would be very, very high, and that it is much higher than generic drugs, small molecules, and that they would have to make that return back. And this was in part based on the idea that they would have to spend $100 million or $200 million building plants to manufacture these drugs, which I can tell you is just not the case.

I mean literally this morning we were approached, our firm was approached, by the Chinese-Taiwanese government with an offer to subsidize us to the tune of $50 million to build a bioreactor that could be accessed by the biotechnology, biosimilar industry. In essence, many governments around the world are going to build these plants essentially for nothing at their nickel. This is already happening in Singapore, Taiwan, Japan and in China.

And the biosimilar companies are not going to have spend that kind of money. As a result, they are not going to have to make that money back, which means that they have much greater flexibility to reduce prices, far beyond what the FTC has assumed.

So our group, the venture capital community, has looked at this very, very carefully. And we simply don't agree with that conclusion.

Mr. JOHNSON. Thank you, sir.

Mr. Leicher, did you have something you wanted to add also?

Mr. LEICHER. Yes, I just would like to comment, and that is, as I noted earlier, we really probably just disagree with the comment that the follow-on biologics industry is not an innovative industry. In fact, that is exactly what we are doing at Momenta and, we believe, at other companies.

And that that data exclusivity actually works against that innovation, both on the brand side and on the innovator side. Let me just take a minute to say how. If you set up an excessively lengthy data exclusivity period, it is great from an investor point of view because it allows you to invest in lower-risk development activities, and that is what is being talked about when people are saying biosimilars have a patent loophole.

If you invest in developing the second, third, and fourth version of an existing mechanism of action, all the hard science to discover the mechanism of action has already occurred. And what you are doing is essentially a drug development program, and that is a much lower-risk product. And you are not developing a new cure.

And that was the beauty of Hatch-Waxman. What Hatch-Waxman did was it said to the brand industry, stick to your knitting, go out there and find new cures and get strong patent rights that lets you get the exclusivity you need.

And it said to the generic industry, apply your science to find out how to make generic copies so that they can deliver affordable products that perform what the maturing biotech products today should be able to do in years to come.

And if we are shortsighted enough, and this is what concerns us, to pass a law that assumes that we are only going to have biosimilars and assumes that it is not possible to advance this science, then we are going to make ourselves captive to what is happening in China because they will move ahead of us, and we will be competing with China.

If we build our technology base in the United States and actually own the science here in our biotech industry for innovative biogeneric products, we really create an opportunity that keeps us ahead of the rest of the world.

Mr. JOHNSON. This has turned into a spirited debate.

I don't want us to take this too far. And I see a second round has been requested, but the water—I don't want to go near the water.

So I am thinking probably now would be a good time to turn it over to the Ranking Member, Mr. Coble.

Mr. COBLE. Thank you, Mr. Chairman.

And I thank the witnesses for appearing today.

Mr. Brill, you mentioned it was costly and difficult to produce. It is indeed costly and difficult to produce. I don't know that the average person appreciates this, but if a chemical pharmaceutical company brings a state-of-the-art drug to market, it is going to incur a cost of about $800 million, give or take, give or take a dollar or two. It costs even more for a biotech firm to do the same thing in excess of a billion dollars. So you are talking about a whole lot of money, a heap of money as they say down home.

Mr. Kushan, let me—strike that. I was going to get into the 12 versus 7 years, but I think that has pretty well been plowed through.

Mr. Kushan, you don't endorse the findings of the 2009 FTC study on biosimilar drug competition. Explain briefly, if you will, why the study, in your opinion is flawed.

And did you and other representatives of the innovator industry attempt to contribute to the study?

Mr. KUSHAN. I will take the second half of that question first. We did, I mean, a number of companies, both biosimilar companies and innovator companies and a lot of different people spoke to the FTC and the process they were in. And it was a little bit surprising they didn't listen to any of us when they came up with a number of their assumptions that they then built a series of recommendations on.

I think one of the things we take away from their report is that they believe, because patents will deliver 12-plus years of market security before biosimilars come on to the market, that justifies not providing any special data exclusivity period.

And so that is the foundation of kind of why they—why they are saying, we don't need to create this data exclusivity period of 12 years.

When I look at that, and then you kind of dig down into why they think there is no problem with patents, that is where I think the problems arise. They have looked at the patent standards in kind of an abstract way that doesn't reflect what actually happens in the patent office.

One of the big issues we have flagged was that what we see in our current practices under current patent law standards is that, if a company does a research on a protein and you put that in a patent application and you send it to the patent office, the patent office will say, well, you can have that protein as your patent claim.

And then you go back and forth, and you try to stretch out your claim to cover variations from this protein that you actually did your research on, and the PTO pushes back.

And what that process ends up doing is giving you a relatively small number of alterations covered by a typical protein patent claim.

Now, the FTC looked at the standards, and they said, oh, well, we think you can get variations up to 30 percent of the reference sequence. And that is where, they heard so many different people, practitioners, talking to them and saying this is not what is happening; we are seeing numbers in the 98, 95 percent as a common one. And they just disregarded that.

I think the other thing they failed to do was to really understand the impact of the loophole that we have been talking about today. What they said, again, their assumption, we don't need data exclusivity periods up to 12 years, is resting on the assumption that these patents are going to be protecting us.

The design of the systems, the biosimilar systems, is they are being designed now to allow the proteins to change, the biosimilar to be different enough from the reference protein so that you don't have to infringe the patents, but you can still get the benefit of the clinical data that supported the innovator.

And that is the hole that I think they didn't see that was communicated to them, and that is where I think our ultimate disappointment sits.

Mr. COBLE. Thank you, sir. I need to move along to meet the 5-minute rule.

Ms. Rea, what is the best way to resolve a patent dispute in a world that includes biosimilar competition?

Ms. REA. The best way to resolve the patent dispute in a world that involves biosimilar competition?

Mr. COBLE. Yes.

Ms. REA. I think that it is critical to have timely and confidential information exchange between all of the parties, prelaunch, in advance of any FDA approval of the drug product. You need a streamlined efficient litigation mechanism to make sure that everything can be resolved in an efficient manner.

We need things like declaratory judgment, actions being available to the follow-on applicant. I think our existing law of venue would be very good. And I would like all remedies to be available to both parties whether it is in terms of damages or injunctive relief.

Mr. COBLE. Thank you.

Mr. Chairman, if I may, one more question.

Mr. Lasersohn, there are two competing bills, as we all know, that would create a pathway for biosimilars, the Waxman bill and the Eshoo bill. The economy, as we all know, is shaky now at best with unemployment hovering at around 10 percent. In light of

these economic conditions, Mr. Lasersohn, is one bill more likely to be a job loser as opposed to a job creator?

Mr. LASERSOHN. Well, obviously, a very difficult question.

We do support Representative Eshoo's bill that has a 12-year date exclusivity period in it. We believe that that is the most reasonable compromise, which is, of course, what this is, between the interest of consumers for low prices versus innovation.

As it affects jobs, the biotechnology industry does employ significant numbers of people. And our company specifically employs hundreds of thousands of people; that is our venture-backed biotechnology start-up companies. And our view is that data exclusivity of much less than 12 years will jeopardize continued investments.

So I would have to say that Ms. Eshoo's bill is more likely to protect the jobs than the alternative Waxman legislation.

Mr. COBLE. Thank you all.

Mr. Chairman, I yield back.

Mr. JOHNSON. Thank you, Mr. Coble.

Mr. Issa is ready to proceed.

Mr. ISSA. Thank you, Mr. Chairman.

I would like to ask unanimous consent that three submissions be put in the record. The first one is the California Healthcare Institute's position. California Healthcare Institute represents more than 250 of my constituent companies.

[The information referred to follows:]

Statement of the
California Healthcare Institute (CHI)

Submitted to the
U.S. House of Representatives
Subcommittee on the Courts aud Competition Policy

Hearing ou:
Biologics and Biosimilars: Balancing Inceutives for Innovation

Tuesday, July 14, 2009

The California Healthcare Institute (CHI) appreciates the opportunity to present our views on the issue of biologics and biosimilars for this important hearing.

CHI represents more than 250 of the state's leading biotechnology, pharmaceutical, and medical technology companies, venture capital firms, and premier academic research institutes and universities. CHI's mission is to identify and advocate for policies to promote biomedical research, development and innovation in California. The California life sciences industry, employing over 270,000 workers, is responsible for medical breakthroughs that are improving and extending the lives of millions in the United States and around the world.

While focused on the development of the next generation of innovative medicines, we understand that the increasing cost of health care is a growing burden for private-sector and government budgets. In the long term, competition among biosimilar products is likely to yield savings within the U.S. healthcare system. Considering the complexity of large molecule product development and manufacturing, CHI believes that it is possible to develop a successful, science-based FOBs approval pathway. This pathway must employ the best science to make sure that products are safe for patients, encourage price competition among manufacturers, and provide ample incentives and intellectual property protections to encourage continued private-sector investment in the next generation of breakthroughs.

CHI has endorsed H.R. 1548, the Pathway for Biosimilars Act, introduced by Representatives Anna Eshoo (D-CA), Jay Inslee (D-WA), and Joe Barton (R-TX) as best reflecting these important principles.

Follow-On Biologics: Enhancing Development of New Biologics Introduction

The term "biologics" refers to a broad range of therapeutic biological products, typically large, complicated molecules produced by biological processes.[1] The introduction of biologics has greatly affected the treatment of a wide array of diseases, including cancer, arthritis and autoimmune diseases and holds great promise for future therapeutics. However, these therapeutic agents can be very expensive. To address the expense of biologics and provide access to consumers, Congress is considering legislation that would create an approval pathway for biosimilars, or Follow-On Biologics ("FOB") – products that are claimed to have similar properties to existing biologics. FOBs are thus analogous to the generic version of a traditional chemical pharmaceutical. However, biologics are produced by culturing living cells as compared to traditional "small molecule" pharmaceuticals that are synthesized chemically. As such, an FOB could never be identical to the existing biologic it attempts to copy.

The development of biologics requires input of large amounts of time and money for the initial development and the lengthy clinical trials required to bring the product to market. Without a system to protect the investments necessary to develop biologics, companies and universities may be averse to inventing and commercializing new biologics. A traditional mechanism for protection of intellectual property (IP) has been the patent system. However, patents covering biologics are typically more limited in scope than those granted for traditional pharmaceuticals and seem insufficient to protect the full scope of investment by biologics innovators. To foster development of emerging biologics, an FOB regulatory approval system put in place by Congress should provide sufficient protection to provide strong incentives for biologics innovators to invest time and money into developing biologics. It is this regulatory system that will provide for the avenue for continued innovation in critical future therapies while also providing for increased price competition.

Approval of Generic Drugs

The Hatch-Waxman Act provides for a regulatory approval scheme for generic versions of innovators' pharmaceuticals, which are typically small molecules, produced chemically to be exact copies of the approved drug.[2] When filing an Abbreviated New Drug Application (ANDA), the applicant must show that the generic version of a pharmaceutical has both pharmaceutical equivalence – same active ingredients, strength, and dosage form – as well as bio-equivalence to the innovator pharmaceutical.[3] Upon such showings, the ANDA applicant is permitted to rely upon the safety and efficacy testing performed by the innovator producer. The Hatch-Waxman Act provides for five

[1] Section 351(i) of the Public Health Service Act (PHS Act) defines a biological product as "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound."
[2] 21 U.S.C. 505(j)
[3] 21 C.F.R. §314.92

years of data exclusivity [4] following approval of an innovator's drug,[5] during which time the Food and Drug Administration (FDA) will not allow an ANDA applicant to rely on an innovator's clinical efficacy and safety data. This regulatory scheme was designed for small molecules, as is clear from the requirement that a generic product must have the same active ingredient as the innovator's product – something that is not possible with biologics.

Currently, most biologics are regulated through the Public Health Service Act, which does not provide for an abbreviated application process such as that for small molecules under the Hatch-Waxman Act. Thus, there is no equivalent for the approval of an FOB as a "generic" version of a biologic. Multiple bills have been introduced in Congress to provide such a regulatory approval process.[6] While each bill differs in the particulars, most bills recognize the need for different treatment of biologics from the Hatch-Waxman scheme.

As a consequence of the differences between small molecule drugs and biologics, two key issues have surfaced for any follow-on biologics legislation: 1) what showings are necessary to establish similarity to the biologic to permit use of the FOB instead of the approved biologic (interchangeability and/or biosimilarity), and 2) for what period of time is the FOB not permitted to use the data that was generated by the innovator to gain FDA approval of the biologic (period of data exclusivity).

Biosimilarity

Generics of small molecule drugs are exact chemical duplicates of the approved innovative pharmaceutical. However, it is unlikely that a manufacturer of an FOB will be able to produce an identical active ingredient to an approved biologic due to the complexity of biologics and the resulting changes in the biologics stemming from innate differences between the cells and growth conditions utilized to produce biologics. Indeed, biologics such as proteins are variable and complex and are difficult to consistently manufacture. Because of these difficulties, an FOB manufacturer attempting to produce an FOB identical to an approved biologic would be unable to do so.[7] Thus, a major difference between the proposed legislation and the Hatch-Waxman Act is that FOBs, unlike generic small molecule drugs, need only show "biosimilarity," not complete identity with the innovator's biologic. For a biosimilar, small differences are likely to exist in properties such as pharmacokinetics, pharmacodynamics, and immunogenicity profile. Exactly what showings will be required – how similar the FOB must be to the approved biologic, and whether or what clinical trials will be necessary to

[4] The period of time during which a generic / FOB manufacturer may not refer to the pre-clinical and clinical trial data of the originator, usually beginning after approval of the innovator's product. Under Article 39.3 of the TRIPs Agreement, data exclusivity is considered an intellectual property right

[5] This period may be shortened to four years if a Paragraph IV certification is filed.

[6] These bills include: 1) the "Access to Life Saving Medicine Act" (S. 726 and H.R. 1427); 2) "The Pathway for Biosimilars Act" (H.R. 1548).

[7] Woodcock, "Follow-On Protein Products," 2007 (statement before the Committee on Oversight and Government Reform, U.S. House of Representatives) available at http://www.fda.gov/ola/2007/protein32607.html.

establish biosimilarity, safety and approval of interchangeability – is an issue to be resolved. Because the FOB and innovator's product will not be identical, they will not be "interchangeable" or will not be substitutable one for the other without the approval of a physician, at least initially.

The difference between "biosimilarity" in the proposed FOBs approval legislation and chemical identity under the Hatch-Waxman regulatory scheme, affects the ability of innovators to fully protect investments using the patent system. Because an FOB would not be identical to the approved biologic and need only show biosimilarity, an FOB would have significant latitude for slight molecular changes that would retain "biosimilarity" but fall outside the scope of the patents covering the approved biologic. The more dissimilar the FOB is to the innovator's biologic, the less likely that patent infringement could be proven. The large size of biologics increases the likelihood that an FOB will contain a difference that would preclude a finding of infringement. For example, if an innovator's patent claims cover a protein with a particular amino acid sequence, numerous changes could be made to that sequence while retaining biological equivalence or biosimilarity, but could avoid infringement of the innovator's patent.[8]

Patent Protection for Biologics

As with many areas of innovation, patent protection for biologics is important for fostering investments in the research and development of potentially life-saving biopharmaceuticals. However, a number of factors diminish the ability of patents to provide a level of coverage adequate to ensure continued investment in and development of the critically important biological pharmaceuticals. One factor is that the patent protection currently being afforded to biologics has become limited in scope and challenging to obtain. Additionally, the length of enforceability after lengthy prosecution before the United States Patent and Trademark Office (USPTO) and FDA approval can significantly reduce the time for recouping development costs. Another factor is that the patent enforcement provisions of the Waxman biosimilars legislation bill would undermine the value of biologics patents that are obtained.

Limited Patent Scope

Although biologics can potentially be protected by a multitude of patents covering products, methods of making the biologics, and methods of using the biologics, claims to the precise biologics have become increasingly narrower. Patent claims to small molecules frequently can cover a particular molecule and a large genus encompassing that molecule, thus providing protection for the drug and numerous variants. Such broad genus claims typically are not available for biopharmaceuticals, and an innovator may

[8] The Doctrine of Equivalents, which allows for a finding of infringement where an accused product does not literally infringe the claims, but comprises only minor deviations has been strongly curtailed by the Supreme Court and the Court of Appeals for the Federal Circuit. *See, e.g., Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 535 U.S. 722 (2002) (holding that narrowing a claim for reasons related to patentability causes the patentee to lose equivalents to the limitation narrowed, except those unforeseen at the time of the amendment).

need multiple patents to cover a fraction of the scope available for small molecules. In a typical prosecution at the USPTO, a broad genus claim to a biologic will be narrowed to a more limited genus or species by restriction and/or rejection as being too broad and failing to provide an adequate disclosure to support the claims to the broad genus. In order to obtain some protection for the biologic, applicants will often accept quite narrow claims and then refile continuations or divisionals to prosecute broader claims or claims drawn to another aspect of the invention. The amendment to narrow the claims may surrender the broader concepts and reduce or eliminate the ability of patentee to later assert during litigation that a biosimilar or close equivalent infringes the claims.

These differences in scope of protection between small molecules and biologics result from the application of the patent laws as interpreted by the courts and the examination practices in the USPTO, including restriction or limitation of the claims to a single claimed invention. In many cases, a biotechnology invention includes a protein, the DNA encoding the protein, the cloned protein and a monoclonal antibody which binds to the protein. However, through restriction of claims, the USPTO usually permits the coverage of only one of these facets of the innovation per patent, thus resulting in multiple patents if the innovator wishes to cover each facet. Additionally, unlike small molecules, typically the innovator is not able to claim a genus consisting of a large number of molecules within any of these groups. This result arises from court interpretations of the law concerning written description[9] and enablement,[10] and the amount of disclosure necessary to support the claims. While these rejections are being applied by the examiners in the USPTO more frequently in all technologies, they are applied routinely and stringently in biotechnology.

One reason for this may be that biologics are often claimed in terms of function, while small molecules are claimed as a structure. For example, a claim might be directed to an isolated DNA that encodes a polypeptide with at least 85% amino acid identity to sequence X, wherein the polypeptide has activity Y. Such a claim will be rejected by the USPTO as lacking adequate written description of the genus unless there is significant disclosure concerning a structure-function relationship between the necessary structure of the variations of sequence X which still retain the function or activity Y. Thus, without sometimes extensive additional experimentation and examples of specific changes that may be made to the amino acid sequence or detailed explanations of the structures necessary for the functions and those areas of the sequence which may be changed, the applicant will be limited to a narrow scope of disclosed sequences. In contrast, a small molecule is frequently claimed as a genus chemical formula with numerous variations of substituents on the core chemical structure with the USPTO raising written description or enablement concerns much less often. Thus, patent claims

[9] To satisfy the written description requirement of 35 U.S.C. §112, first paragraph, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention at the time of filing the patent application.
[10] 35 U.S.C. § 112, first paragraph requires that a patent application describe the invention in such terms that one skilled in the art can make and use the claimed invention, thereby insuring that the invention is communicated to the public in a meaningful way.

for biologics with limited scope provide limited protection for innovators and may allow opportunities for avoiding infringement.

Length of Enforceability

Several factors play a role in diminishing the period of patent enforceability for biotech patents. These factors include: (1) evolutionary development of biologics and the 20-year patent term, (2) significant prosecution time for patent allowance, and (3) FDA approval time. In biotechnology, it is common for the original innovations to occur in academia and subsequent developments to occur with a company licensing the patent(s) obtained by the university. For example, the original patent may disclose a protein or biomarker associated with a disease, the DNA encoding the protein, and cloning of the protein. The company licensing the foundation patents or another larger company may then develop advances on the original innovation, such as specific antibodies to the protein for therapy of the disease. During this period of development, the 20-year patent term is running from the original patent filing. For subsequent evolution and development of treatment of other indications or improvements, a new patent term may exist.

It often takes a considerable amount of time to prosecute an application to allowance, sometimes requiring a number of continuation applications to reach agreement with the examiner as to allowable subject matter. As noted above, the application of the enablement and written description rejections against the claims necessitates extensive arguments and often evidentiary showings to establish patentability. This takes considerable amounts of time, all while the clock is ticking on the patent term.

Also, for both biologics and small molecules, significant time is required for all of the analyses and clinical trials required for FDA approval. While it is possible to recover up to 5 years of patent term for these regulatory delays, there may not be an adequate period to recoup the costs of the research and development of the biologic. The cost of performing the research and development necessary to produce a biopharmaceutical is very high. One analysis has estimated that the total out of pocket expenses for preclinical and clinical trial periods for a new biological entity range from $1.24 to $1.33 billion.[11] Additionally, the period from initial discovery of a biological disease target through discovery and testing of a biologic to approval by the FDA can take decades. One well-described instance of this lengthy period involves the biopharmaceutical Avastin®. From the initial discovery of Avastin's® target (vascular endothelial growth factor) to the approval of Avastin® by the FDA, fifteen years elapsed.[12] As a consequence even with the patent term extension provision of up to five years, patents may be inadequate to provide the necessary period of exclusivity needed to incentivize investment in this area.

[11] Capitalized costs adjusted for inflation over time. DiMasi and Grabowski, "The Cost of Biopharmaceutical R&D: Is Biotech Different?" *Managerial and Decision Econs.*, 28: 469-479 (2007).
[12] Flanagan, "Avastatin's Progression" *Bio Century*, 14(11): A1-A5 (2006).

Patent Enforcement

Currently, there are legislative proposals for developing an FOB regulatory scheme, including proposals by Representatives Waxman and Eshoo. These bills differ in some particulars, including several aspects that may affect patent value. One such aspect is the time period during which the FDA could accept abbreviated applications – under the Waxman bill an application could be filed at any time, whereas under the Eshoo bill, an application could be filed only after four years have passed since the innovator product was approved. Another aspect is the length of time for data exclusivity – the Waxman bill provides a period of 3 or 5 years and the Eshoo bill provides for 12 years. Other aspects include provisions for multiple indications – the Waxman bill would allow use of the FOB for all indications even if the FOB applicant sought approval for one indication, whereas the Eshoo bill would require approval for all indications – and would require product nomenclature. While each of these differences affect the potential value of patents held or licensed by the innovator, the differences in the patent enforcement provisions of the two bills would result in drastically different effects on such value.

The Waxman bill's patent enforcement provisions are skewed in favor of the FOB applicant and would allow an FOB applicant, or prospective applicant, to request patent information from the innovator as to all patents owned or licensed which the innovator "believes in good faith relate to the reference product." Any patent erroneously not listed in response is thereafter unenforceable against anyone, even if the patent is held by a third party – in effect, the patent loses all value. Unfortunately, the Waxman bill does not define what the term "relate to" means. Furthermore, under the Waxman bill, the FOB applicant would determine, based on the listing by the innovator, which and how many of the patents would be litigated. Thus, under the bill's provisions, the FOB applicant could challenge a listed patent for any reason, even if that patent would not actually block the FOB. The Waxman bill also allows an FOB applicant to serially respond to the innovator, potentially resulting in multiple patent suits. Timing of litigation (i.e., pre-launch litigation) and venue would also be entirely under the control of the FOB applicant. Such a system, far from streamlining and simplifying the litigation process, would allow for excessive gamesmanship on the part of an FOB applicant. Additionally, potential abuse of the Waxman enforcement procedures could create serious problems for third-party patent holders – such as universities and small biotech companies – who could lose all rights in their patents and, thus, lose an important research revenue stream.

In contrast, the Eshoo bill provides that those patents held or licensed by the innovator which would be available for a declaratory judgment action would be limited to those identified by the innovator or third-party patent owner as covering the FOB. A determination of which patents "cover" an FOB would be determined by the innovator or the third-party after analysis of the abbreviated application, information about the product and it's method of manufacture. All such information would be treated as confidential and the analysis would be provided to the FOB applicant. The innovator and/or third-party would have 60 days to file suit. If no suit is filed, then the applicant could file a declaratory judgment action, if there are three years or less remaining in the approved

product's exclusivity period. In short, the Eshoo bill more strongly recognizes the importance of maintaining patent rights.

Encouraging investment in innovators

In order to foster investments in the discovery and development of new biologics, biotechnology companies must have some certainty that innovative biologics they produce will yield a return on initial investments, including costs and some profit. Currently, most U.S. biotechnology companies are small start-up companies that do not have a product on the market and thus have little or no revenue stream. In a recent survey of small biotech firms conducted by the Biotechnology Industry Organization, 65% of the companies had fewer than fifty employees and 40% had revenues less than $150,000.[13] For many such companies, their intellectual property – in the form of patents or data exclusivity – is the only asset of real value. Such companies rely heavily on venture capital investments to produce the innovative biopharmaceuticals that are the cutting edge of medical treatment. Often eventually acquired by a larger company, these small companies have become the source of the important biologic pharmaceuticals and innovation.

To provide incentives for companies and their venture capital financers to engage in such high-risk new biologic development, it is necessary for there to be some certainty of return on investments. In other words, a biosimilars regulatory scheme needs to supply some certainty regarding the protection provided by the innovator's patents and, potentially, further safeguards. Without sufficient patent protection and reasonable patent enforcement for innovators, FOB producers will be able to establish biosimilarity, rely on the innovator's data for FDA approval, and avoid infringing the innovator's patents. Such results would lead to fewer investments in new biologics because of the lengthy time that it takes to get a biologic approved after the initial discovery is made and the staggering costs of developing biologics.[14]

Conclusion

The cost of cutting-edge biopharmaceuticals can be prohibitive for some patients. To address this concern, Congress is considering developing a regulatory scheme to allow for the approval of "generic" biopharmaceuticals, more accurately known as biosimilars or follow-on biologics. While the need exists to lower patient costs and provide more people with access to biopharmaceuticals, it is also important to protect the investments of time and money by innovators so that new biologics, and new uses for existing biologics, continue to be discovered and developed. The patent system may not provide sufficient protection to these innovators because of limitations on scope and

[13] Available at http://www.bio.org/healthcare/followonbkg/FOBSMarket_exclusivity_20070926.pdf

[14] Expenditures in excess of one billion dollars on average must be made for new biologic development, despite the fact that biologics have a lower probability of success in Phase III trials, higher discovery and pre-clinical expenditures, and longer clinical development times than traditional small molecule pharmaceuticals. Grabowski, "Data Exclusivity for New Biological Entities," June 2007; available at http://www.econ.duke.edu/Papers/PDF/DataExclusivityWorkingPaper.pdf.

length of patent coverage for biologics. Furthermore, the ability of an FOB to gain FDA approval if it is only "biosimilar" further compounds the likelihood that an innovator's patents will not adequately protect its investments. Additionally, one of the legislative proposals for a regulatory scheme for follow-on biologics would provide the opportunity for litigation gamesmanship and undermine future investments and likelihood that an innovator will invest time and money into developing new biologics. Without adequate protection of investment through patents and/or data exclusivity, which CHI believes is best provided through H.R. 1548, fewer new biologics will be developed, effectively cutting off access to such innovations for all persons, undermining the initial concern of Congress in developing an FOB regulatory scheme.

Mr. ISSA. Secondly, I would like to ask unanimous consent that an article from bloomberg.com—thank you.

[The information referred to follows:]

Biocon Agrees to Develop Generic Biologics for Mylan (Update1)
Share | Email | Print | A A A

By Simeon Bennett and Tuhin Kar

June 29 (Bloomberg) -- Biocon Ltd., India's biggest biotechnology company, signed an agreement with Mylan Inc. to develop, make and market generic biologic drugs.

Mylan will get exclusive marketing rights for the treatments in the U.S., Canada, Japan, Australia, New Zealand and the European Union through a "profit-sharing agreement" with Biocon, Bangalore-based Biocon said in a statement. Both companies will sell the drugs in other markets worldwide. Financial terms weren't disclosed.

Biologics are made from living cells such as human proteins and hamster ovaries, and are more complex, difficult to make and more expensive than traditional pharmaceuticals, which consist of comparatively simple chemical compounds. The Obama administration said June 25 brand-name biologics should face competition from cheaper copies in the U.S. after seven years.

"Through this partnership we hope to deliver high-quality, affordable biogeneric antibodies and biologics, thereby addressing a critical need to lower spiraling health-care costs in both the developed and emerging economies," Kiran Mazumdar- Shaw, Biocon's managing director, said in the statement.

Americans spend more than $60 billion a year on biologic drugs to treat cancer, rheumatoid arthritis and other serious illnesses at a cost of as much as $200,000 for each medicine, Ernst & Young estimates. Sales of generic biotech drugs in emerging markets may grow by 20 percent each year for the next five years from about $1.5 billion now, Biocon said.

To contact the reporter on this story: Simeon Bennett in Singapore at sbennett9@bloomberg.net; Tuhin Kar at tkar1@bloomberg.net

Last Updated: June 29, 2009 01:34 EDT

Mr. JOHNSON. Without objection, those two.

Mr. ISSA. The first and second.

And then the third one is simply a table of estimates that I am relying on for the return rate on pharmaceutical and R&D investments, the 15-year, if you will, basis.

Mr. JOHNSON. Without objection.

[Mr. Issa subsequently decided not to submit this material for the record.]

Mr. ISSA. I thank the Chairman.

I would like to take a slightly different tack in my questions, because I am concerned about the future of patents as well as the future of bio follow-ons.

So, Mr. Kushan, if I could start with you, from BIO's standpoint, assume for a moment that contract or, sorry, patent historical sanctity went away and you had zero patent protection.

In the BIO-type developments, these large complex proteins of molecules, wouldn't it be possible to protect in perpetuity, or nearly in perpetuity, using complex series of trade secrets? In other words, if we failed to protect through patent, isn't it certainly possible that the bargain that we have enjoyed for decades of, you tell all, you make a duplicatable product; we agreed to a limited period, a defined limited period; and, when exhausted, or as it is exhausting, generics come on?

Isn't that one of the risks if we don't get it right in either one of these pieces of legislation?

Mr. KUSHAN. You are correct in several respects. The historical trend of restricting patent protection has been to push innovators to kind of keep their innovations secret. And that will have impacts on things like manufacturing technology or the ways that we make proteins, the way we enhance their properties. There are a lot of things that in kind of the business of making our products that will probably be hit by that kind of a practice.

The other, you know, the molecule patents and things like that, as a practical matter, we won't be able to use trade secrets to protect because they will be publicly known and in circulation. And how you use them to treat new diseases, obviously, those procedures will be publically known.

I think one general point to appreciate about the biotech industry; this industry grew out of the university community, and there is a cultural bias against keeping things confidential. It is hard for me to quantitate this, but if you had a discussion with a scientist, telling him not to publish something, so you could file a patent application, you will know what I mean.

There is just a real culture of disclosure, which I think ultimately has helped our industry.

Mr. ISSA. And I appreciate that, although that is a culture of disclosure at our universities. That is not true in China, is it?

Mr. KUSHAN. No. I think what my comment is really focused on just the practice, and it is also against a backdrop of having that patent protection available.

Mr. ISSA. Ms. Rea, when you look at the history of patents and the benefits versus those countries who either don't respect or don't have them, in general, isn't ultimately the trade secret route the only thing you could advise a client if they could not get a strong and durable patent?

Ms. REA. It if it was impossible to get a strong and valid patent——

Mr. ISSA. I like the term durable, because valid doesn't keep them from ripping you off.

Ms. REA. Okay, durable patent. I agree trade secrets would be the only alternative.

But, in this day and age, it is difficult to maintain things as trade secrets with the very mobile work force we have today. But I guess you could do sequences of trade secrets in difference places, and thereby, unless somebody could put all the pieces of the puzzle together——

Mr. ISSA. Everybody but the CIA manages to keep at least some secrets.

Mr. Brill, biosimilar, from a standpoint, this is a Committee that cares about patent. Our hook for today's legislation is our constitutional obligation for patents.

But aren't we inherently heading toward, if we are not careful, similarity being defined as close enough, but you take your chances on the medical similarity actually not causing a problem? Isn't that inherently the problem? If the entire technology string of both the patented item and all of the know how involved, if that isn't passed on in some transparent way, aren't we essentially going to end up with, as I held up a couple of years ago in committee, a Rothschild wine being replaced by Mogen David?

Mr. JOHNSON. And before you respond, I will say, Mr. Issa, that Ms. Eshoo was here earlier, and she would have appreciated your comment about the CIA.

Mr. ISSA. You know, everybody except Mr. Waxman did. He cringed when I held up these various California wines and said, not all California wines are created equal, but they are all California wines.

Mr. BRILL. Thank you, Congressman.

I may know more about wine than I know about some of the scientific aspects of the complexity of developing biologics.

Mr. ISSA. If you know enough to know that there is such a thing as a Cabernet and something that you cook with, but they are both called Cabernet, then you probably know about some of my concerns.

Mr. BRILL. And I think that the scientific issues are important given the significantly greater degrees of complexity for the products that we are talking about here.

With regard to the importance of ensuring that we have the intellectual property protection, I would echo a similar comment from Mr. Kushan, which is that the data exclusivity period can help ensure that protection. But I would also add that there is a period of which that protection is excessive and that the key here is to balance these factors.

Mr. ISSA. And just one last question that hasn't been asked, if I could, Mr. Chairman.

It is not currently in either bill, but if this Committee wanted to find a fair compromise between the bills, if we provided, for example, Ms. Eshoo's period, but strengthened or, let me rephrase that, but made a bargain that in order to take advantage of it, you must have exhausted all of your, if you will, similar patent claims so that small changes, incremental changes, the bar would rise at the patent office, and to get that protection, you essentially forego later patents still in the process.

Now whether we set that at 2 years or 30 years, really it doesn't matter. Is that something that any of you foresee being part of the bargain, meaning, if I am going to give you 15 years from the day your product is approved, can I expect that your continuations that are still coming and—Ms. Rea, you are laughing, because you know how many of those sometimes are stacked up behind, is that, in fact, part of the bargain that, if you will, if you get something extraordinary separate from the normal patent period, this Com-

mittee may have to consider whether or not that is a terminal disclaimer, so to speak, of some or all of your claims?

I am not proposing it. I am just asking about it.

Ms. REA. I do not think that it is a good idea. But, even so, to change the entire patent office and how all patent applications are followed, just to try to come out with a compromise in this area in the manner that you suggested, I think is not viable and would be difficult to implement and is not appropriate. Our patent system has existed the way it has for 220 years. It has worked well. I think it is why innovation drives our economy and we are where we are today.

So I don't think a compromise on the order that you suggested would be viable. Thank you.

Mr. ISSA. And by the way, I hope you feel the same on the patent reform that we are wrestling with in this Congress, but I know you might not be quite with us on that.

Yes, sir.

Mr. LASERSOHN. I just wanted to add that there is, in fact, a provision that relates to this and these bills would have to do with the idea of evergreening.

In other words, what is entitled to data exclusivity, to additional data exclusivity, and in fact, it is very restricted. They really are new drugs, new indications. It is not just tweaking this and tweaking that or a slightly different root of administration. So that had—in particular, in the Senate bill, that was looked at very, very carefully. And I think a very reasonable balance was struck there.

Mr. ISSA. Yes, sir. You are the last one, because the Chairman will cut me off.

Mr. KUSHAN. Thank you, I will try to be quick.

I think that approach would be a very bad approach for the way the biotechnology industry innovates today because you shouldn't think of biotechnology innovation as being limited to making new proteins that become blockbuster drugs. It is a whole environment, you know, of innovation that has a lot of opportunities at various levels.

That issue should not be a problem. What happens typically is that innovations will be incremental. They will have limited protections, and you can work around them, such as manufacturing techniques. And I think that is essentially the self-solving problem for those later issuing patents.

Mr. ISSA. Thank you all for clearing that up.

Thank you, Mr. Chairman.

Mr. SHERMAN. [Presiding.] I will now recognize the gentlelady from Texas.

Ms. JACKSON LEE. Thank you very much, Mr. Chairman.

And I want to thank Chairman Johnson for doing a real good balancing act. I think we have a team that can represent the issues that have been expressed by the Eshoo bill and the Waxman-Hatch bill very well.

Let me anecdotally say that this Judiciary Committee room seems to be the bastion or the holding place for tensions between disparate but very important issues. For those of you who are aware of something called the Performance Rights Act, H.R. 848, you would believe on the surface that the legislation is all about

pop artists and maybe reflecting on the man in the mirror, and against radio stations.

But, Mr. Chairman, as you well know, we have worked for a very long time to recognize that both of those entities are needed and that they are working together and coming together to resolve how you would best effectuate a response to the art and talent of a performance artist, and as well, how would you respond to championing radio stations which provide an important and powerful service?

But the record is clear, for those of us who are supporting that legislation, that we want to strike a balance. Now we have come full circle on questions that you are concerned about, which are represented in the legislation by a very dear colleague, Congresswoman Eshoo, and, as well, interesting points that are being made by the Waxman bill as well.

So my interest is to find that balance. I think we did it well, as you well know, that we were working on patent reform. And there was this whole tension on how you account for the work that has been put into patent, and how do you, in essence, assess the monetary value of a patent? How do you determine that a patent has not been copied, using layman's terms? So we have had that challenge here in Judiciary, and I think we have clearly worked through it.

For that reason, let me try to raise these questions quickly.

The National Venture Capital Association asserts that, without 12 to 14 years, the cost of capital will drive away venture capital investment from biotech and derail innovation.

Mr. Leicher, would you tell me whether that is correct as we look at this effort to balance? Would we drive venture capital away, which is, the big pharmaceuticals might make that argument?

Mr. LASERSOHN. Yes, is the short answer. And the question is, how much? Our view is that, at the extreme that the FTC took, for example, where there would be no data exclusivity and the ability for a, quote,generic biosimilar to be introduced the day after a new drug was approved, that that would have a devastating impact.

At 12 years, we believe we can manage it. That is what we have under Hatch-Waxman. We have lived with it. Obviously, some investments are not being made because of that under Hatch-Waxman, but we have learned to live with 12 years.

And at 7 years, the models, for example, Mr. Brill's model, other models that we have run when we used the real cost of capital of the innovation sector of this industry, which is the venture, the small entrepreneurial venture-backed sector, relatively few drugs can break even.

It doesn't mean there might not be some investment continuing in the most extraordinary breakthroughs, but the volume of that investment activity will clearly decline substantially even at 7 years.

Ms. JACKSON LEE. Mr. Leicher, why don't you give me an answer on that question? Remember, you are talking to someone who really does believe we can get into a room and address this question that brings balance to what we are all trying to do, but let me not put words in your mouth.

Mr. LEICHER. Thank you for the opportunity.

And let me start with the first basic point, and it was a point that was brought up earlier that I think there is some disagreement on the panel, and that is the notion that there is a patent loophole.

I actually believe that if we engage Mr. Kushan to file patents for us on some of our novel products in the biologic space, I have no doubt they would be strong, effective, and work as long as we were operating at the novel end of developing new mechanisms of action that really provide new cures. And we would be able to get patents that cover not just the product, which is what he was talking about earlier, but patents covering portions of the product, patents covering the biologic pathway, patents that would cover the whole range of biologic activity that could provide a lot of exclusivity and well more than—potentially more than 12 years in the experience of biologics.

And what I think everyone is missing is, if we provide an excessive exclusivity period, we are going to create a huge incentive for the biotech industry to derisk their portfolios, because now, without having to innovate, without having to get patents, you can get a product developed and, by virtue of getting it approved by the FDA, guarantee 12, maybe 14 years of exclusivity.

Ms. JACKSON LEE. And that kills innovation?

Mr. LEICHER. I think it kills innovation.

Ms. JACKSON LEE. What about investment?

Mr. LEICHER. I think it would hurt—it might not kill investment. What it might do—but let's talk about that over the long term. It is a little puzzling to me, in 2009, you know, in the year that GM declared bankruptcy and perhaps declared bankruptcy because it stopped innovating in the 1990's and focused on high-margin SUVs as opposed to innovative cars—and I am concerned, having lived in biotech for 20 years, that we are going to push biotech from the innovative scale and the leadership in the world to the non-innovative scale.

And if you step back from a historical point of view, look at what it was——

Mr. SHERMAN. We thank you for your answer.

Ms. JACKSON LEE. Thank you, Mr. Chairman.

We may have to revisit this again.

Thank you very much. I will look forward to visiting with you.

Mr. SHERMAN. Without objection, I will enter into the record a Bloomberg article about Mylan's recent deal with India's biggest biotechnology company for the development, production, and marketing of biosimilars.

[The information referred to follows:]

Rep. Sherman Submission for the Record for the July 14, 2009 Courts and Competition Policy Subcommittee Hearing on "Biologics & Biosimilars - Balancing Incentives for Innovation"

Biocon Agrees to Develop Generic Biologics for Mylan

By Simeon Bennett and Tuhin Kar

June 29 (Bloomberg) -- Biocon Ltd., India's biggest biotechnology company, signed an agreement with Mylan Inc. to develop, make and market generic biologic drugs.

Mylan will get exclusive marketing rights for the treatments in the U.S., Canada, Japan, Australia, New Zealand and the European Union through a "profit-sharing agreement" with Biocon, Bangalore-based Biocon said in a statement. Both companies will sell the drugs in other markets worldwide. Financial terms weren't disclosed.

Biologics are made from living cells such as human proteins and hamster ovaries, and are more complex, difficult to make and more expensive than traditional pharmaceuticals, which consist of comparatively simple chemical compounds. The Obama administration said June 25 brand-name biologics should face competition from cheaper copies in the U.S. after seven years.

"Through this partnership we hope to deliver high-quality, affordable biogeneric antibodies and biologics, thereby addressing a critical need to lower spiraling health-care costs in both the developed and emerging economies," Kiran Mazumdar- Shaw, Biocon's managing director, said in the statement.

Americans spend more than $60 billion a year on biologic drugs to treat cancer, rheumatoid arthritis and other serious illnesses at a cost of as much as $200,000 for each medicine, Ernst & Young estimates. Sales of generic biotech drugs in emerging markets may grow by 20 percent each year for the next five years from about $1.5 billion now, Biocon said.

Mr. SHERMAN. By contrast, the innovative biotechnology industry is uniquely American, and most of its companies are based in the United States. In fact, most of them are based in our best State, California.

As the U.S. is struggling with the highest unemployment numbers in recent memory, now is not exactly the right time for Congress to be taking actions that would imperil future jobs in the United States.

Mr. Lasersohn, I realize a similar question was asked, I just wasn't here for the answer. And, actually, before I ask that question, I will start with an observation.

There has been talk about the biotechnology industry being able to recover its sunk costs on a particular drug. And if they can't recover their sunk costs on that drug, obviously, there will be no more innovation. I think this massively understates the situation, because the vast majority of drugs are—the vast majority of drug development projects are failures.

And even when they lead to success, they may be outmarketed by some other cure for that disease. So unless an innovator is able to recover double, triple or quadruple its sunk costs on the successful drug, we can basically pack up this industry and say we are not going to have any more innovation.

Now, Mr. Lasersohn, I think that venture capital is the lifeblood of this industry, particularly some of the smaller and newer firms, and there is no denying that a lot of that investment is based on strong patent laws.

In your view, is data exclusivity absolutely critical for the continuing development of biotech products, and, if so, how long should that period of exclusivity be?

Mr. LASERSOHN. The easy part of the answer is, yes, I do think it is necessary. The hard part is, how long? I guess we believe that 12 years is something that we have learned to live with. Our best guide here is Hatch-Waxman, small-molecule development has continued to exist under Hatch-Waxman.

When we run our analysis of our cost of capital, making exactly the point that you have just made, Mr. Chairman, that we must recover all of the losses that we also take on drugs, 12 years appears to give us a reasonable chance to break even.

I might just add one other thing about data exclusivity. I think there is a real misunderstanding. It is not market exclusivity. This doesn't prevent anybody from competing at all. It just means that they can't free-ride on the data produced by the innovator.

Mr. SHERMAN. They can't copy the innovator's product or infringe on the innovator's patent and use their data. They can just go out and perhaps develop an entirely different way of curing that same disease.

Mr. LASERSOHN. Or agreeing to clinical trials.

Mr. SHERMAN. Yes.

Mr. LASERSOHN. And if we did, and the other key point is that the data exclusivity is merely a backstop for the patents. The question to ask yourself is, what if the FTC is wrong in their analysis? I mean, they are just speculating about what's going to happen with all of the patent laws. I mean, what if they are wrong? If they are wrong, and we don't have data exclusivity, and they just turn out to be wrong about how good these patents really are, we are in deep trouble.

If, on the other hand, we have data exclusivity, it doesn't add anything more to the 12 years that the FTC is saying we should have. It simply ensures that we actually get it. It is just an insurance system.

Mr. SHERMAN. Mr. Leicher, as I understand my good friend Congressman Waxman's bill or Chairman Waxman's bill, the bill pre-

vents a patent holder from getting an infringed patent off the market even after a court has found the patent is valid, the patent is enforceable, and the patent has been infringed. And it does so if the suit was not initiated within the narrow window determined by the infringer.

Now how does this compare with all other litigation in America, and particularly patent litigation? Would this impose upon the biotech industry a patent-minus as compared to every other kind of patent that is issued?

Mr. LEICHER. I don't believe it would impose a patent-minus. I think there is a trade-off in the Waxman approach versus the current Orange Book approach in the current Hatch-Waxman statute. The trade-off is, because we have a complex web of biologics patents that are often embracing the pathway and the biology, it requires more of a process of identification, and it is not as susceptible to an Orange Book, which was the criticism raised by some in developing the bills.

There is an opportunity to the bring the suit, and we don't see that as an issue. It actually provides an opportunity to clear patents that are invalid, and move forward with some innovative biogenerics.

Mr. SHERMAN. Let me hear from somebody from the biotechnology industry. I believe Mr. Kushan is raising his hand, and I believe he will be our last speaker.

Mr. KUSHAN. Yes. I think I can say, obliterating a patent right is a patent minus. The procedures that they have laid out essentially result in a loss of the patent right. And whether you call it a limitation on the recovery or just a lack of ability to enforce it, hinging that kind of a sanction on an administrative error is unprecedented in U.S. law.

And I think it is important to also appreciate, this will change patent rights in a way that I think go against our international obligation. We are not supposed to make patent rights in biotech weaker compared to patent rights in other areas.

Mr. SHERMAN. So if we pass this kind of law, other countries could question all U.S. patents, and industries not even realizing we having a hearing today could be subject to lawsuits in other countries saying, well, the United States is in violation of the internationally accepted rule that patents come in one flavor, one level of strength, if you will.

So there are a lot of people not here who could be hurt by that.

Mr. Brill.

Mr. BRILL. Yes. If I could just very quickly address the comment about the sunk costs, the fixed costs, and the modeling, and as well the differences between the industries.

Mr. SHERMAN. If you can do it in 30 seconds.

Mr. BRILL. Okay. Very quickly, the costs assumed for bringing a biologic to market, generally discussed to be over $1 billion, that number includes the cost of failure, not just the cost of the successful drug.

The modeling that I have done, that Professor Grabowski has done, BIO has done, all includes the cost of that failure. In addition, that modeling work also assumes that the only protection provided is the data exclusivity. The models that the FTC, that

Grabowski and I have all used, do not model the existence of the patent. It is a very conservative assumption in that regard.

Mr. SHERMAN. Yes, although, it would be hard to figure out why we would try to protect a patent one way but not protect it another way; it would be an odd policy for us to say, well, we want to encourage copying and we want to prevent copying both on the same bill.

I would also point out that I believe the Waxman bill has limits on the forum in which the suit can be brought. And this Committee gets bills limiting where plaintiffs can bring lawsuits all the time, and 99 percent of those proposals this Committee does not adopt.

I don't know if we have ever adopted anything quite as strict as Congressman Waxman's bill.

With that, I would like to—and at the same time, I want to voice again not only my affection but my incredible respect for Chairman Waxman and his knowledge of health care and pharmaceuticals in particular.

I would like to thank all witnesses for their testimony today.

Without objection, Members will have 5 legislative days to submit additional questions which we will forward to the witnesses and ask that you answer promptly in writing and that will be made—your answers and the questions, of course, will be made part of the record.

Without objection, the record will remain open for 5 legislative days for the submission of any additional materials.

With that, we stand adjourned. I would like to talk to the witnesses, but I have got to rush off to the floor. Thank you.

[Whereupon, at 4:30 p.m., the Subcommittee was adjourned.]

APPENDIX

Material Submitted for the Hearing Record

RESPONSE TO POST-HEARING QUESTIONS FROM BRUCE A. LEICHER, SENIOR VICE PRESIDENT AND GENERAL COUNSEL, MOMENTA PHARMACEUTICALS, INC., CAMBRIDGE, MA

Bruce A. Leicher
Sr. VP and General Counsel
(617)395-2786

July 21, 2009

By Email

The Honorable Hank Johnson
Chairman
Subcommittee on Courts and Competition Policy
1133 Longworth House Office Building
Washington, DC 20515

Re: Biologics and Biosimilars: Balancing Incentives for Innovation

Dear Mr. Chairman:

On behalf of Momenta Pharmaceuticals, Inc., thank you for the opportunity to participate in the Subcommittee hearing Tuesday, July 14, 2009. The follow-on biologics legislation under consideration will set the stage for the next generation of biotechnology research, and for this reason alone is critical to the future of our biotechnology industry. The particular legislation will determine whether we will choose a course that provides affordability and access and encourages and sustains innovation by brand and biogeneric companies alike or, alternatively, choose a course that preserves the status quo: unchallenged monopolies for branded biologics, limited patient access to potentially life-saving therapies, and increased barriers to entry for emerging biotechnology companies. We are confident that after careful examination, the Subcommittee will support the approach of the Waxman-Deal legislation, and we appreciate the opportunity to provide balance to this debate.

As counsel to an emerging biotechnology company with both brand and biogeneric development programs, I am concerned that the Biotechnology Industry Organization ("BIO") is not representing the best interests of research and development stage biotechnology companies. More importantly, BIO is not representing the best interests of the patients that await the discovery of new products and cures by these companies. BIO claims that 12-14 years data exclusivity is necessary to promote innovation. To the contrary, short term investment in biotechnology companies may be preserved by this approach, but investment in innovation as well as long term competitiveness and innovation will be sacrificed.[1] These same arguments were made in

[1] Smaller research and development biotechnology companies today are facing substantial funding hurdles unseen the past 15 years. Pharmaceutical companies and large biotech companies are focused on acquiring late stage so-called "Phase 3" products and venture capitalists are investing substantially less today in companies that cannot provide an extraordinary return in a reasonable timeframe. The consequence, as reported this Spring by Capital IQ, a research arm of Standard and Poors are that approximately 45% of development stage biotechnology companies have less than one years' cash in reserve. This is not a

675 WEST KENDALL STREET CAMBRIDGE, MA 02142 T: 617.491.9700 F: 617.621.0431 WWW.MOMENTAPHARMA.COM

1984 by the pharmaceutical industry at the time Hatch-Waxman was proposed. As noted by the FTC, the pharmaceutical industry did not suffer but was spurred on to innovate the next generation of cures. Rather than experience a decline in innovation, investment in early stage innovative research flourished, including substantial investment in high risk projects in the biotechnology industry that launched the first generation of recombinant proteins. All of this investment relied principally on patents to provide extraordinary return for extraordinarily risky discovery research and development.

The teaching of Hatch-Waxman is that the sieve of patent driven exclusivity motivates research and development and long term industrial competitiveness as it selects for survival of the fittest[2]. My testimony sets forth the basis for this view, and these supplemental comments will answer a number of statements made by counsel for BIO and by the representative from the National Venture Capital Association ("NVCA").

1. Biogenerics, not only Biosimilars, are possible and will drive investment in safety enhancing research as well as novel development of new cures.

Supporters of the Eshoo-Barton bill have asserted by implication that the science of biologics has achieved its end game[3], that biosimilars[4] are all that are possible, and

---

sustainable position, and this is forcing companies to discontinue high risk, high reward programs in favor of low risk, short term reward projects that may not take advantage of their unique capabilities and scientific expertise.

[2] The fear of the unknown was raised at the hearing regarding changes to the current law. While that makes for interesting rhetoric, that is a debater's point and needs to be supported by substance. Is our objective to give in to our fears rather than display the courage to let science drive future investment? We think not, and that the FDA is best suited to evaluate applications based on real data, not hypothetical study, to apply rigorous standards and to assure safety and efficacy of biogenerics and biosimilars as provided for in the Waxman-Deal and Senate HELP bills.

[3] The discovery, development and launch of biotech products (e.g., EPO, HER2 antibodies, anti-TNF antibodies, recombinant factor VIII) demonstrates the power of biotechnology and the strength patent rights provide for the brand company. The novelty of each product led to strong patent rights, substantial long term exclusivity, and extraordinary rewards. Yet, significant diseases remain in search of a cure. HIV, many cancers, neurological disorders, and many autoimmune disorders, to name a few, are at best "managed" or "kept in check", and at worst remain unresponsive to therapy or treated with biologics with challenging side effects and safety profiles. While we understand the genes that encode these biologics, we have much to learn and discover about their structure, their glycosolation (their unique "carbohydrate" backbone) and the relationship of their structure to their biological function. Research into the structure and function of these types of products offers the opportunity to understand why they may perform or not perform as well as understand and characterize existing products to develop biogenerics or design new more efficacious biologics with improved efficacy and safety profiles. It also offers the opportunity to design both novel and biogeneric products that may have lower immunogenic potential or to design manufacturing processes that make biogeneric versions of existing products.

[4] We differentiate, as does the FTC, between "biosimilars" and "biogenerics". We use "biogenerics" to refer to interchangeable generic biologics that have been sufficiently characterized or studied to be interchangeable and substitutable, and "biosimilars" refer to follow-on biologics that are similar in therapeutic use but not interchangeable and substitutable.

that biogenerics are at best theoretically possible[5]. This is a very troubling assumption for a science based industry; particularly because legislative policy will impact research and development for the next 25 years and result in a law that effectively enacts a freeze on scientific advancement. We should reach for the moon at a time when we need research most to reduce health care costs while discovering new cures. As noted in our testimony, Momenta Pharmaceuticals has already thoroughly characterized low molecular weight heparin, a biologic-like drug that is made in cells and has the same complexity as biologics in terms of understanding its structure, its potential for immunogenicity and its variability. It was similarly asserted that this type of scientific analysis was not possible by the brand manufacturer, in part, because, as they asserted, they have not been able to thoroughly characterize their own product. Momenta was able to finance and partner this program because there was an ANDA abbreviated pathway for approval of the generic product; making it an attractive investment for a high risk venture. The same incentives should be available for biogenerics so that the same breakthroughs can be made as we better understand biologics to make them safer, better and more affordable.

Because Momenta Pharmaceuticals was able to thoroughly characterize heparin, it was also able to apply its tools to assist MIT and other academic centers in a collaboration with the FDA to identify the contaminant in Chinese Heparin. A task the brand manufacturers assert was not possible. The approach we used is very similar, if not the same, as the process we are developing to characterize brand biologics (and subsequently better understand, perhaps even better than the brand company, structure and structure-function relationships, in order to develop both biogeneric and potentially improved novel therapies). This activity demonstrates the quality and safety enhancing potential of having a law that promotes the development of biogenerics. If the Eshoo-Barton language is enacted, we expect that we and others will not have an opportunity to use science and technology to compete with the larger branded biopharmaceutical companies and that our funding potential along with other biogeneric competitors could be seriously impacted.

Based on the progress we have made to date and continue to make on a daily basis, we are confident that biogenerics are possible in the not too distant future, and that if a pathway is made available, investors will finance the development of technology to create biogenerics and achieve the dual purposes of Hatch-Waxman: make mature biologics affordable as biogenerics and encourage extraordinary returns for extraordinary risk for novel drug discovery and the invention of patentable new cures.

2. <u>BIO's arguments regarding patent rights are misleading because they assume biogenerics are not possible, and fail to mention that (a) the purported narrowness of biologic patent rights relate more to the non-innovative nature of the inventions at issue and (b) the complex web available for patenting biologic intellectual property more than makes up for any possible uncertainty of biologic product patent claims.</u>

[5] We do find it curious that when the brand industry builds new manufacturing facilities, it asserts, without necessarily thoroughly characterizing its biologics, that clinical trials or thorough characterization are not necessary for using the new facility.

If one assumes that only biosimilars are available (i.e., that it is not possible to thoroughly characterize a biologic) then one can better put in context BIO's arguments. Essentially, BIO argues first that biogenerics are either impossible or second that they are only theoretically possible. BIO's argument that the products are only biosimilar, and not the same, do not apply to biogenerics because, by definition, they will be the same. As a result the patents would be just as broad and as strong (and probably stronger in the aggregate) than they would be with regard to novel small molecule drugs. The major reason biologics patents would potentially be narrower is if, as is the case with a small molecule, they are a 2nd, 3rd or 4th version of an existing mechanism of action, and the novelty of the claims are already taken by the patent claims of the first biologic in the relevant mechanism of action class. This is not a flaw in the patent system. Rather it is the fuel that encourages funding or early stage research for discovering and developing new cures or mechanisms of action by brand companies, and assigns through this incentive to biogeneric companies a reason to develop "me-too" biogenerics when the pioneer's patents expire.

Next BIO argues that patents today are somehow narrower than they used to be and they will not provide protection against biosimilars, even if they are a formidable defense against biogenerics. This argument sets aside, without addressing, the complex web of biotechnology patent rights available to protect biologics cited in my testimony. Not only are patents sought covering the biologic itself (which were the only so-called narrow patent rights cited at the Hearing), but patents are generally pursued that cover much of the biology, including its structure-function relationship in medicine or in manufacturing, formulation, or dosing. As a result, today, biologic exclusivity during brand life generally exceeds drug exclusivity during brand life as a result of these more complex biologic patent rights. As the FTC found, there is no evidence to suggest that this will be any different with the entry of biosimilars or biogenerics.

3. Excessive Data Exclusivity will promote incremental, non-innovative research and development and starve the Biotechnology industry of high risk capital to fund early stage research into cures for critical unmet needs.

Notably, the most vocal proponents of Eshoo-Barton assert that in the absence of 12 years data exclusivity, innovation will be stifled. This is not only a myth, but it turns reality on its head. Patents have precisely the opposite effect. By providing protection for innovative new inventions, one incents the industry to invent new cures, to invent new technology, and to find patentable methods for enhancing safety and efficacy. An extended data exclusivity period in the form of an "invisible hand" will encourage biotechnology companies to focus more on rapid approval of biologics based on existing mechanisms of action. It will discourage innovating new cures and studying new mechanisms of action or new innovative manufacturing or dosing methods which require more time and more risk. We agree with the NVCA study, biotechnology companies should earn extraordinary returns for extraordinary risk. Strong patents will reward extraordinary risk, narrow or weak patents reward non-innovative, incremental research and development. The NVCA by arguing for 12 years data exclusivity is not irrational;

who would not seek to earn extraordinary pharmaceutical returns for approval of incremental, "me-too" products?

4. Eshoo-Barton is the real "patent-minus" bill; Waxman-Deal encourages inventions and the use of patents to drive future competitiveness.

A question that came up during the hearing that I may not have fully addressed related to the perception that the Waxman-Deal bill is a "patent minus" bill. I was puzzled by the question because of my experience in biologics patent litigation. Biologics patent litigation is very different than small molecule drug patent litigation. Since the start of the biotechnology industry, brand companies have aggressively challenged biologics patent rights, and some would argue more aggressively than the alleged future behavior of biogeneric and biosimilar companies. For example, Amgen challenged the homogeneous EPO patent filed by Genetics Institute in order to launch EPO, and Genentech challenged competing tPA patent rights and patent rights to the next generation tpA in order to launch its products. Both Amgen and Genentech believed they were acting property in pursuing this strategy and no one asserted that their efforts to seek to remove patents as "patent minus".

Similarly, Genzyme led a group of biologics companies in challenging the Axel patent rights held by Columbia University relating to a generic process for manufacturing recombinant proteins, and Lilly challenged the biologic patent rights obtained by Ariad Pharmaceuticals that allegedly covered the use of the NFK-B biologic pathway to treat disease (a biologic pathway that is implicated in many existing biopharmaceuticals). Lilly's counsel noted after one hearing that the filing of that patent was the equivalent of someone filing a patent today to patent gravity. Similarly, Pfizer and its predecessor, Pharmacia, challenged the University of Rochester's pathway patent covering the biologic pathway regulated by its drug Celebrex. These are but a few examples.

Challenges to patents are not "patent minus" but an integral part of patent law and an essential check and balance provided by federal judicial system. They are pursued by brand and generic companies alike. The right to challenge does not change the legal principal that patents are presumed valid, but puts into the hands of federal judges and juries, the right to resolve objectively, for both brand and biogeneric companies alike, questions about whether improvidently granted patents are valid, not infringed or unenforceable. To assume this is "patent minus" means we assume that courts are biased or our federal bench is not capable of this task. The law should be balanced and afford both brand and biogeneric companies the opportunity to clear inappropriate patents from the landscape so that competition results in affordable products.

It is also worth noting that unlike the generic drug marketplace, where the cost of development is relatively low and the barrier to filing an ANDA triggering Hatch-Waxman litigation may allow for a level of litigation risk taking that some consider put patents at risk, the opposite is true with regard to biologics. As noted by the FTC, the cost of developing a biosimilar or a biogeneric could require investments of $50-$100 million in development expense (or perhaps more) and may involve a filing with the FDA that is as comprehensive as a novel application in order to demonstrate thorough

characterization of a biogeneric or similarity of a biosimilar[6]. This is not as some may suggest the "copying" of a brand product, but rather the design and engineering of a copy based on innovation, scientific research and better understanding of the brand biologic – much as Momenta has done with low molecular weight heparin. This is important because it would not be profitable to embark on the development process to file a biosimilar or biogeneric application if one did not have a relatively high certainty of success that the brand patents were expiring and/or that any remaining patents were improvidently granted and could be cleared. The result is one should expect the courts will be in a good position to hear cases fairly, and as they have for the brand industry, consider and rule on cases with due respect for the validity of patents. To establish a barrier to entry that makes it more difficult for biogeneric or biosimilar companies to clear patents than for the drug industry under Hatch-Waxman is unbalanced and unwarranted. This is why the Eshoo-Barton patent process provisions which delay and make the process unreasonably burdensome should be rejected.

A related question concerned the strict filing deadline under Waxman-Deal. Filing deadlines are a customary part of most judicial proceedings, and follow strict notice rules. Patent term extension requires that one meet a filing deadline, as does the filing of a patent prior to publication or marketing of a patent invention or any statute with a statute of limitations. The filing deadline in the Waxman-Deal bill parallels that provided in the time tested Hatch-Waxman law. The Eshoo Barton bill delays the opportunity to initiate clearance of an inappropriate patent, in an unbiased judicial forum, until 3 years before the end of the data exclusivity period. Because this is longer than the expected time for completion of the litigation, it further extends an excessive exclusivity period and is designed not to protect valid patents, but to protect both valid and invalid patents. This means consumers are being asked to pay for the cost of excessive exclusivity.

The timing for initiating patent clearance and bringing suit under Waxman-Deal was also questioned because it might somehow render our patent system unenforceable in the international community. At present, in Europe, there is already a system for any person to file an opposition to a patent granted by the European patent office without the need to file or launch a product. In addition, numerous countries like Germany also permit the filing of nullity actions in court seeking to invalidate patents that are improvidently granted. All Waxman-Deal proposes is to allow for early resolution of allegedly improvident patents at a time that is early enough to reach resolution prior to expiration of data exclusivity. More importantly, one can only initiate the process after the FDA accepts for filing the abbreviated application, which is a very significant hurdle; particularly given the substantial characterization needed for biogenerics and the requirement of clinical trials for biosimilars and the investment noted above. These are major research and development programs and offer the savings that result from not having to conduct unnecessary clinical trials or the discovery research to re-prove the mechanism of action.

---

[6] As noted in our testimony, we believe the FDA should have discretion to consider abbreviated applications and should use care to set a high burden for demonstrating thorough characterization. Notably, we understand Congresswoman Eshoo agrees with this position by endorsing the discretionary language in the Senate HELP bill.

A biogeneric or biosimilar applicant would not undertake an investment of that magnitude unless it believed that the patent rights were improvidently granted or unenforceable. The risk is too high. Thus the laws of investment risk will protect valid patents. This is much more like the decisions of Amgen, Genentech, Genzyme and brand biotech companies deciding whether to invest in innovation and factoring in the risk of patent clearance for a novel biologic. The alternative would be to launch at risk, which would defeat the whole purpose of a follow-on biologics pathway by raising prices to brand levels– particularly because of the presumption of patent validity. That is why Hatch-Waxman and now Waxman-Deal offers a patent clearance process that can occur in advance of product launch. Eshoo-Barton does not.

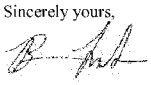
Finally, there was a suggestion made in the discussion at the hearings that somehow the Waxman-Deal legislation would impair University licensing opportunities. There is little basis for this assumption in the biologics area. Momenta is a technology spin out from MIT and licenses important characterization patent rights from MIT for which we anticipate MIT will earn significant return as it should. As we proceed with development of biogenerics, we intend to license rights from Universities and third parties as would any other biotechnology company that builds its business through technology innovation. Our only need to clear patents, if the need exists at all, would be to clear patents like the ones that have been routinely challenged by brand companies today because they have been improvidently granted.

Summary

The Waxman-Deal legislation offers the best opportunity to finance and promote real innovation by both brand and biogeneric companies alike. The former would react as large pharmaceutical companies did in 1984, and seek to discover new patentable cures to fill their pipelines. This would in turn stimulate investment in biotech companies through collaborations and license agreements. At the same time biogeneric and biosimilar companies would focus investment on the technology needed to deliver affordable and safe biogenerics and biosimilars. By using the patent system to reward these investments, we all benefit. By creating legislative barriers to scientific advancement, we sow the seeds for the decline of the biotechnology industry as the rest of the world invests in science and leave patients in need as our precious and scarce research and development funds are allocated to lower risk, high reward projects. We have the opportunity to continue our leadership in this field, and we urge you to support Waxman-Deal to further this goal.

Please let us know if there is any way we can help bring further balance and an alternative perspective to this discussion. We are absolutely committed at Momenta to the ideal of increasing patient access to safe and effective therapies through rigorous scientific innovation. We would be pleased to meet or speak with you or your staff at your convenience.

Sincerely yours,



Bruce A. Leicher
Senior Vice President and General Counsel

Cc: Eric Garduno

RESPONSE TO POST-HEARING QUESTIONS FROM ALEX M. BRILL, RESEARCH FELLOW, AMERICAN ENTERPRISE INSTITUTE (AEI), WASHINGTON, DC

American Enterprise Institute for Public Policy Research

Alex M. Brill
Research Fellow
American Enterprise Institute
1150 Seventeenth St., NW
Washington, DC 20036

March 8, 2010

Committee on the Judiciary
Subcommittee on Courts and Competition Policy
B-352 Rayburn House Office Building
Washington, DC 20515

Response to Representative Bob Goodlatte's questions following the July 14, 2009, hearing concerning "Biologics and Biosimilars: Balancing Incentives for Innovation." To be included in the final record.

1. *What is the harm in long periods of exclusivity in your view?*

Long periods of data exclusivity allow excessive monopolies for brand name pharmaceuticals, resulting in government-granted pricing power beyond a useful period of time. Exclusivity is not in itself harmful. In fact, allowing a *reasonable* period of time for a company to profit from the product it funded through all stages of research and development is essential for encouraging innovation in pharmacology. Without eventual competition, however, drug prices remain excessively high—both for beneficiaries and for government. The result will be that patients have more limited access to medicines. Research I have conducted indicates that seven years of exclusivity is a sufficient period of time for biologic drugs so that innovator drug companies earn economic rents sufficient to induce innovation.

This research applies solely to appropriate exclusivity periods for biologic drugs, not small-molecule drugs governed by the Hatch-Waxman Act. It should be noted that the expected market dynamics for follow-on biologic drugs and small-molecule drugs are likely very different. The Federal Trade Commission, the Congressional Budget Office, and others have projected that biologics, generally far more expensive than small-molecule drugs, will experience significantly less drastic price declines resulting from the market entrance of generic competition on a percentage basis. However, the dollar price decline is likely far greater.

2. *Do long periods of exclusivity lead to more innovation?*

Patents are intended to create incentives for innovators by giving them exclusive rights—and thus exclusive profits—for a limited time. Pharmaceuticals are awarded an additional period of exclusivity at the time of product launch to further ensure adequate incentives for innovation. But a fixed-length, excessive period of government-granted market exclusivity (monopoly) necessarily stifles innovation by removing the incentive of drug manufacturers to develop better products or develop improvements to existing products.

Encouraging further innovation and improvements to an existing drug is possible by structuring a tiered exclusivity period that extends for (and only for) truly novel and substantial improvements to a product. The proper period of additional exclusivity should be relatively brief—180 days to a year.

○