



## Biogenerics:

What They Are, Why They Are Important, and Their Economic Value  
to  
Taxpayers and Consumers

by

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CAGW was founded in 1984 by J. Peter Grace and nationally-syndicated columnist Jack Anderson to build public support for implementation of the Grace Commission recommendations and other waste-cutting proposals. Since its inception, CAGW has been at the forefront of the fight for efficiency, economy, and accountability in government.

CAGW has more than 1.2 million members and supporters nationwide. Since 1986, CAGW and its members have helped save taxpayers more than \$944 billion. CAGW publishes special reports, its official newspaper *Government WasteWatch*, and the monthly newsletter *Wastewatcher* to scrutinize government waste and educate citizens on what they can do to stop it. CAGW's publications and experts are featured regularly in television, radio, print, and Internet media.

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## **Executive Summary**

Washington is encountering a legislative battle this year concerning a new type of therapy – generic forms of biotech drugs. Biotechnology means using microorganisms, such as bacteria or yeasts, or other substances from live organisms to manufacture specific products such as drugs or foods.

Biologic products represent an ever-increasing component of prescription pharmaceutical spending in the United States, with sales growing at approximately 17 percent annually to about \$38 billion in 2006. Yet there is currently no regulatory process for approving generic versions of these products. The absence of such a regulatory approval process for biogenerics artificially extends patent protection to brand name biologics. This leads to reduced incentives to discover and develop new brand biologic products and prevents competition that would lower biologic drug costs, as competition has done with traditional (chemical) pharmaceutical products.

“The Access to Life-Saving Medicines Act,” H.R. 1038/S. 623 introduced respectively by Rep. Henry Waxman (D-Calif.), and Senator Charles Schumer (D-N.Y.) would create a path leading to such an approval process. This analysis conservatively estimates that were such a process to exist and were it to lead to competition with brand name biologics from FDA-approved biogenerics, \$43.2 billion in economy-wide savings could be realized during the period 2011-2020.

## **Introduction**

There is a legislative battle on the horizon in Washington, D.C. that will affect the cost of drugs paid for personally and through tax dollars in government-run programs such as Medicare and Medicaid. This conflict will involve Congress, the Food and Drug Administration (FDA), biotechnology companies and the special class of drugs they innovate called biologics, generic drug manufacturers, and whether patients will have access to generic versions of biologics in the near future.

This new type of drug that Congress will likely address this year is being called many things: generic biologics, biosimilars, follow-on biologics, follow-on protein products, and biogenerics. Citizens Against Government Waste (CAGW) is taking a closer look at biogenerics, why they are important, what kind of savings a generic form of these special drugs could produce, and why the outcome of this debate is important to taxpayers and consumers.

## **Generic Drugs and Biologic Therapies – A Review**

Just about everyone who takes a prescription medication is familiar with a generic drug. According to the FDA, “a generic drug is a copy that is the same as a brand name drug in dosage, safety, strength, how it is taken, quality, performance and intended use.”<sup>1</sup> Generic drugs are substituted for the brand name drug everyday.

CAGW has long been supportive of a vibrant generic drug market. The organization has spoken out against brand name companies trying to use government as a tool to interfere with the marketplace and restrict patients’ access to generic pharmaceuticals. In a 1998 report, *David v. Goliath*, CAGW detailed how some brand name companies were lobbying state legislatures to pass laws that would limit access to a special category of drugs – narrow therapeutic index (NTI) drugs – in an effort to stifle generic versions from being dispensed by pharmacists. A NTI drug has a small therapeutic range: take too little, the patient doesn’t get the desired effect; take too much, the patient can suffer serious harm. While a brand name company may have claimed limiting access to a generic NTI drug was important for safety reasons, the real reasons for their position were facing competition for the first time and/or the imminent expiration of their patent.

The generic drugs that Americans are familiar with today came about because of a landmark law enacted in 1984 called the Drug Price Competition and Patent Restoration Act, more commonly called the Hatch-Waxman Act. It amended the Federal Food, Drug, and Cosmetic (FD&C) Act, which oversees the marketing approval process for pharmaceuticals. It created the Abbreviated New Drug Application (ANDA) process that allowed generic companies to demonstrate their drug was bioequivalent with the brand name drug without having to conduct lengthy and duplicative safety and effectiveness clinical trials on patients.

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<sup>1</sup> Food and Drug Administration, “Generic Drugs: Questions and Answers,” Web site accessed April 9, 2007, [http://www.fda.gov/cder/consumerinfo/generics\\_q&a.htm#whatare](http://www.fda.gov/cder/consumerinfo/generics_q&a.htm#whatare).

Congress's goal in passing this legislation was to balance the financial needs of brand name and generic drug companies. The law had to create an environment that would encourage research and the development of new, therapeutic and life-saving drugs, while at the same time produce an efficient process for manufacturing safe generic drugs.

Twenty-three years later, many policy and industry experts agree the law did what it was intended to do. Generic drugs are available soon after patent expiration, at much lower prices than the brand name drugs, while investment in research and development continues to grow in the pharmaceutical industry.<sup>2</sup>

One of the fastest growth areas in the pharmaceutical industry are biotechnology drugs, which grew at an average rate of 17 percent over the past two years, greater than any other sector of the pharmaceutical market. Right now, there are many biologics in the approval pipeline and it has been projected that 50 percent of drugs approved for the marketplace in 2010 will be the result of biotechnology.<sup>3</sup>

The Biotechnology Industry Organization (BIO), the trade association that represents biotechnology companies, notes that the word biotechnology comes from bio – the use of biological processes, and technology – to solve problems or make useful products. BIO points out that biological processes have been used for thousands of years to produce many products and commodities such as hardier crops, farm animals, and clothing. Using single celled organisms to make something isn't really new either. For example, man has used microorganisms to make many food products such as cheese and bread, and to preserve dairy products, for 6,000 years.

But during the 1960s and 1970s, the understanding of biology research reached a point where the smallest parts of organisms could be used – molecules such as DNA – to produce a product or develop a process. Therefore, today the term biotechnology means using cellular and biomolecular processes to develop better foods or discover miraculous cures.<sup>4</sup>

It is difficult to simply describe a biologic product, as it has many facets. This report focuses only on therapy-related biotech products. The FDA's Center for Biologics regulates most therapy-related biologics. Their definition includes vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or they may be living entities such as cells and tissues.<sup>5</sup> More simply, a biologic therapy is made from a living organism and can come from a human, an animal, or a microorganism.

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<sup>2</sup> Congressional Research Service, "Follow-On Biologics: Intellectual Property and Innovation Issues," March 5, 2007, p. CRS-4.

<sup>3</sup> Ibid, p. CRS-1.

<sup>4</sup> Debbie Strickland, "Guide to Biotechnology 2007," BIO, Washington, D.C., p. 1.

<sup>5</sup> Food and Drug Administration, Center for Biologics, "Frequently Asked Questions," Web site accessed April 9, 2007, <http://www.fda.gov/cber/faq.htm#3>.

The first biotech therapy approved by the FDA, recombinant human insulin, occurred in 1982 and was produced by Genentech and Eli Lilly.<sup>6</sup> Recombinant DNA (rDNA) occurs when a new DNA structure is formed by combining DNA segments from at least two other organisms. The insulin product, Humulin, is produced by using a non-disease, laboratory-produced bacteria, *Escherichia coli* (*E. coli*), that is genetically altered by adding the human gene for insulin production.<sup>7</sup> The gene essentially tells the *E. coli* to produce human insulin, and it does. As the *E. coli* rapidly re-produces, it acts like a miniature factory and creates more human insulin. Eventually, the insulin is separated from the *E. coli*, packaged, and marketed for use by diabetics.

Thousands of companies are conducting similar biotech processes and making new therapies today. According to BIO, there were 1,415 biotech companies in the United States in 2005. Their sales amounted to \$32.1 billion in 2005, compared to \$9.3 billion 10 years ago. Currently, there are 400 biotech drug products and vaccines in clinical trials targeting some 200 diseases. Biotechnology has created more than 200 new therapies and vaccines, many of which have treated diseases such as diabetes, HIV/AIDS, and autoimmune disorders.<sup>8</sup>

Some examples of biologic drugs are:

- Epogen, a product made by Amgen, which stimulates bone marrow to produce red blood cells. It is used to treat anemia in patients that has been caused by chronic renal failure or other reasons such as chemotherapy and HIV.
- Genotropin, a product made by Pfizer, which is used to treat growth hormone deficiency.
- Humalog, an insulin product made by Eli Lilly, which is used in diabetes treatment.
- Pulmozyme, a product made by Genentech, which is used with other treatments in cystic fibrosis patients to improve lung function.

Many patents on biotech therapies have expired or are due to expire. For example, the patent on Genotropin expired in 2004 and Humalog's patent is due to expire in 2013.<sup>9</sup> Epogen patents expired in 2004 in the European Union and are believed to expire in the U.S. by 2015.<sup>10</sup> According to the Generic Pharmaceutical Association

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<sup>6</sup> Strickland, p. 2.

<sup>7</sup> Eli Lilly, "Information for Patient, Humulin®," web accessed April 12, 2007, <http://pi.lilly.com/us/humulin-r-ppi.pdf>.

<sup>8</sup> Strickland, pp. 2-3.

<sup>9</sup> Steve Miller, MD and Jonah Houts, "Potential Savings of Biogenerics in the United States," *Express Scripts*, February 2007, pp. 4-6.

<sup>10</sup> Citigroup, "A Global 'Generic Biologics' Guidebook," November 6, 2006, p. 16.

(GPhA), some \$10 billion worth of biopharmaceutical drugs are expected to come off patent by 2011. Some of these drugs can cost an individual \$10,000 per year.<sup>11</sup>

### **Biologics + Generics = Biogenerics**

As biologics patents expire, the generic versions are not yet being developed, unlike what occurs for chemically-based drugs. A few drugs have been approved through the abbreviated pathway found in the Hatch-Waxman Act including Hylanex, GlucaGen, and Omnitrope. While the manufacturers were required to provide new scientific data for their products, the FDA also relied on the information found in the past approvals of the brand name drugs. None of these drugs however, has been rated by the FDA to be therapeutically equivalent. In other words, they are not substitutable for the brand name drug.<sup>12</sup>

Biologic therapies, for the most part, are licensed under the Public Health Service (PHS) Act, not the FD&C Act, and therefore do not fall under the Hatch-Waxman Act that provides the mechanism for an ANDA process to bring a generic version of a biologic safely and quickly to the market.

There is also the understanding that a chemically-based drug is quite different from a biologic. In a March, 2007 hearing before the House Committee on Oversight and Government Reform on safe and affordable generic biotech drugs, FDA Deputy Commissioner and Chief Medical Officer Janet Woodcock, M.D. stated,

First, there is general recognition that the idea of *sameness*, as the term is used in the generic drug approval process under the Federal Food, Drug, and Cosmetic (FD&C) Act and applied to small molecules, will not usually be appropriate for more structurally complex molecules of the type generally licensed as biological products under the Public Health Service (PHS) Act. Additionally, as a related matter, there are clearly scientific challenges involved in determining that a molecule that is not the same as an approved or licensed version is nevertheless similar enough that the Agency's conclusions about the safety and effectiveness of the approved or licensed version could be relied on to support approval of the follow-on product.<sup>13</sup>

The FDA therefore believes that, while it will be more challenging, it will be possible to create a process to develop safe and effective biogenerics. In fact, the Europeans have already done so for the less complex biologics. The European Medicines Agency (EMA) has written guidelines for therapies that contain insulin, somatropin (human growth hormone), granulocytic-colony stimulating factor, and erythropoietin.

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<sup>11</sup> "GPhA Hails Omnitrope Approval as Significant First Step in Opening Door to Biopharmaceutical Sales for U.S. Consumers," GPhA press release, May 31, 2006.

<sup>12</sup> Statement of Janet Woodcock, M.D., Deputy Commissioner, Chief Medical Officer, Food and Drug Administration, before the Committee on Oversight and Government Reform, United States House of Representatives, "Follow-On Protein Products," March 26, 2007, pp. 14-15, Web accessed April 13, 2007, <http://oversight.house.gov/documents/20070326104056-22106.pdf>.

<sup>13</sup> Ibid, p.1.

Except for interferon-alpha, the EMEA is not addressing the more complex proteins until they gauge the experience with the less complex ones.<sup>14</sup>

With Europe leading the way to find pathways to produce generic versions of biologics, policy makers in Washington are clamoring for similar initiatives. Studies have shown that patients, insurance companies, and taxpayers could save billions if generic versions of biotech drugs were allowed on the market. Express Scripts (a pharmacy benefit manager) showed a potential savings of \$71 billion over 10 years, while Engel & Novitt, LLP (a law firm that specializes in health issues) found that there would be \$14.1 billion savings over 10 years in Medicare alone.<sup>15</sup>

### Biogenics – An Economic View

This study determined that the market for *existing* biologics would grow from \$38 billion in 2006 to approximately \$55 billion in 2020; new discoveries would make the biologics market far larger, but any new discoveries would face generic competition in a time frame well beyond the scope of this analysis.

Annual U.S. Biotech Sales  
2003-2005 – 2010 Projected - \$ in Billions



Sources: "Biotech Takes a Stronghold on Sales," *The Star-Ledger*, March 2, 2006; "2004 Year-End U.S. Prescription and Sales Information and Commentary," *IMS Health*, Web accessed April 19, 2005, [http://www.imshealth.com/ims/portal/front/articleC/0,2777,6599\\_18731\\_69890098,00.html](http://www.imshealth.com/ims/portal/front/articleC/0,2777,6599_18731_69890098,00.html).

In determining the potential savings from biogeneric competition, the analysis utilized price discount assumptions suggesting that biogeneric competition could generate savings of 10-25 percent in the initial year when compared to the brand biologic price, rising to a range of 25-47 percent in the fifth year of competition. (The biogeneric human growth hormone, Omnitrope, was introduced at a 20 percent discount to the brand

<sup>14</sup> Citigroup, p. 6.

<sup>15</sup> Miller, MD and Houts; Engel & Novitt, LLP, "Potential Savings That Might Be Realized by the Medicare Program From Enactment of Legislation Such As The Access To Life-Saving Medicine Act (H.R. 6257/S. 4016) That Establishes A New cBLA Pathway For Follow-On Biologics," January 2, 2007.

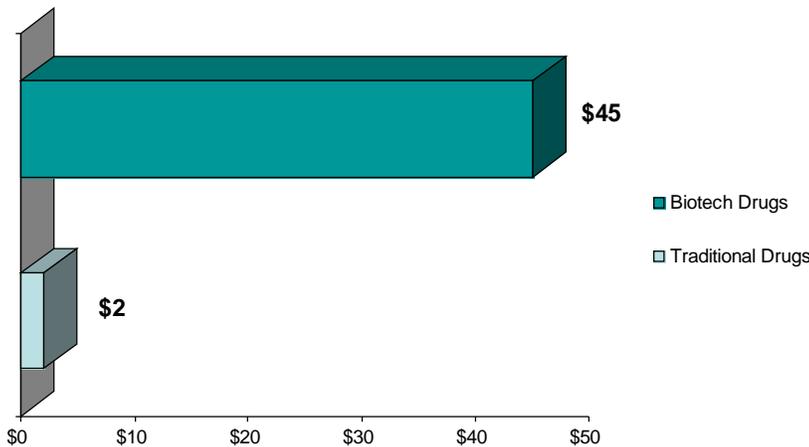
biologic product when approved in Europe.) The analysis also assumed that biogenics could capture market share of 3-10 percent in the first year of introduction, growing to 15-50 percent in the sixth year of competition.

As discussed, the regulatory approval process for the generic versions of most existing drugs is governed by the FD&C Act, which specifies how applications for such approvals shall be made. Specifically, it directs that applicants can seek approval for a generic drug by relying on FDA’s approval of the original (“brand”) drug being copied. The drugs eligible for this treatment primarily are chemical-based products.

But the vast majority of so-called biologics – drugs manufactured using biological, as opposed to chemical, processes – are licensed under the PHS Act, which does not specify a process for generic, or otherwise equivalent, biological products, and FDA has appeared to have concluded that the PHS Act does not authorize it to establish a generic drug approval pathway for these products. Thus, for most biologic drugs coming off patent, there is no process for certifying biogenics.

The FDA, in May 2006, made its first approval of a biogenic product – Sandoz’s Omnitrope, a generic version of Pfizer’s Genotropin, a human growth hormone, but only after Novartis, Sandoz’s parent company, filed a lawsuit against the FDA demanding resolution. (Growth hormone was one of the few biologics approved under the FD&C Act.) In addition, the FDA did not qualify Omnitrope as interchangeable with Genotropin. The FDA’s official policy is now to hold off on issuing new guidelines for further approvals.

### Average Cost Per Day Biopharmaceuticals vs Traditional Drugs



Source: Ben Hirschler, "FDA Rebuffs Novartis Over Delay to Biogenic Drug," Reuters News, November 15, 2005.

In response to these problems approving biogenic drugs, Rep. Henry Waxman introduced H.R. 1038, the Access to Life-Saving Medicine Act. Similar legislation,

S. 623 has been introduced in the Senate by Sen. Charles Schumer. These bills would direct the FDA to establish a path to regulatory approval for biologics comparable to the route available to conventional generic medicines, by allowing petitioners to establish a new product's equivalence to an existing one. For that reason, such products are referred to in this study as biogenerics. Were such a process to exist and were it to approve biogenerics, the resulting competition would drive down the price of many drugs and lead to substantial economy-wide savings, as now occurs with conventional generics.

The focus of this study is the effect that such competition would have in the market for biologics – it estimates the cost of not having that competition. Competition would have important effects because, as of this moment, the market for biologics is not competitive. Instead, most biologic products are still under patent, and those products that have expired patents are protected from direct competition indefinitely because there is no regulatory process to approve competing products.

A patent rewards innovators with a monopoly franchise on their innovation for a fixed, pre-determined period of time. The expiration of that patent allows competition to erode those monopoly profits and subjects the product to the discipline of the market.

The regulation of biogenerics should be seen in this context. The goal of regulation is to preserve the public health by providing strong assurance of the safety of medicines. It does so by weighing costs and benefits using all the available tools of science. The issue of the appropriate regulatory treatment for biogenerics from a scientific perspective is beyond the scope of this paper. From an economic perspective, however, the issue is this: the delay in specifying a regulatory approval process artificially extends the patent protection granted brand name biologics. This prevents competition from pushing down prices to consumers and pressuring firms to increase their research and development to produce new products that will replace lost sales or generate greater sales. This analysis estimates the size of those benefits by comparing a world in which there are no bioequivalent drugs to one in which there is a statutorily-based process for their entry into the market.

### **The Nature of Biogenerics**

Generic pharmaceutical products are identical at the molecular level to the brand name products for which they substitute – they are synthesized chemically to achieve this result. Biologics, in contrast, are produced from living organisms – this is their defining characteristic. Therefore, they cannot be duplicated with the same complete precision.

In the early days of biologic manufacture – insulin being the first and representative early biologic product – these substances were obtained by processing the organs of other species. But in the last twenty years, the availability of recombinant DNA technology has revolutionized the biologics manufacturing process. Today, a broad range of substances are produced by inducing a single-celled organism (such as bacteria or yeast) to produce the substance through genetic manipulation – be it insulin, growth

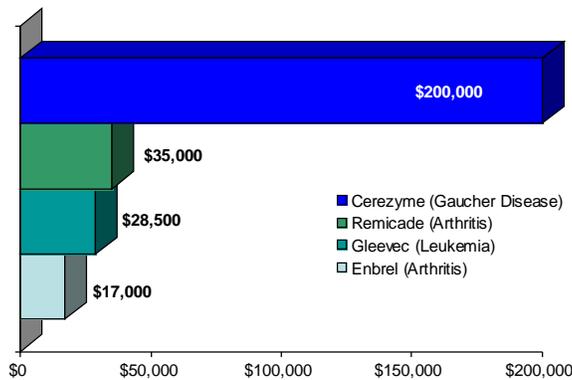
hormone, interferon, medicines for Gaucher’s disease or cystic fibrosis, or a wide range of other products.

A process based on genetic technology is complex and requires a great deal of control. When a brand name biologic producer changes its manufacturing plant, for example, it must carefully replicate its process. The regulatory issue, therefore, boils down to identifying what the salient characteristics of a biologic product are and defining the range over which they can be considered “the same” for therapeutic purposes. This same regulatory oversight can be used to ensure that a biogeneric version follows a careful process resulting in a well-characterized product.

The differences between conventional generic pharmaceuticals and biologics will also reveal themselves in the competitive marketplace in terms of both price discounting and market penetration (the market share won by biologics). On the one hand, since conventional and biologic branded products enjoy the same monopoly franchise, the introduction of generics could have comparable price and penetration in both types of products. But the process of obtaining regulatory approval is likely to be more costly for biologics, regardless of how it finally comes to rest. Moreover, given their greater complexity, the manufacturing costs of biologics, whether brand or equivalent, are likely to be higher, particularly when the substantial capital investments in the equipment required to produce biologics are considered. These upfront costs may also result in a smaller number of manufacturers competing for an individual biogeneric, which would reduce the level of competition when compared to the large number of manufacturers present in the current generic drug industry.

On the other hand, the prices of biologics are so high – dosages for diseases such as Gaucher’s or leukemia can run into the thousands or even tens of thousands of dollars each month – that there may be substantial room for price competition once the shield of patent protection is withdrawn.

Average Annual Cost  
Select Biopharmaceuticals

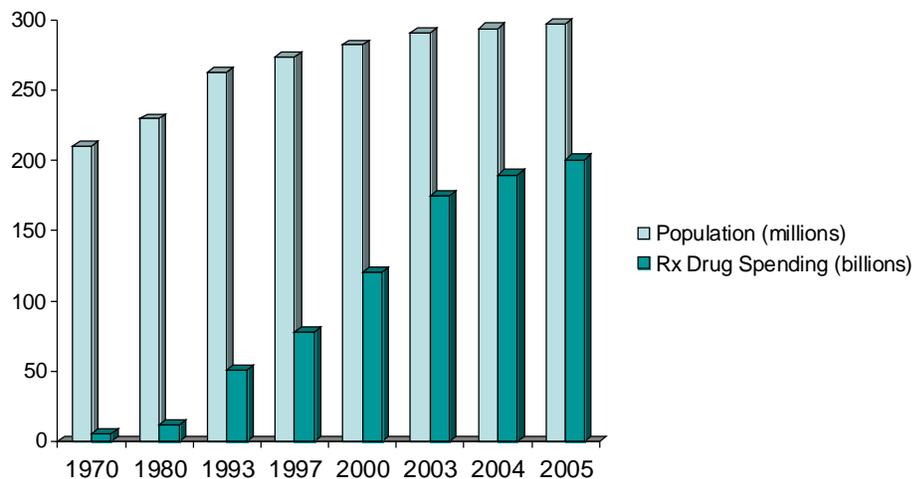


Sources: Linda Loyd, "Opening a Path for BiotechGenerics," *The Philadelphia Inquirer*, Sept. 19, 2006; Stephen Heuser, "Shire Drug Gets FDA Approval," *The Boston Globe*, July 25, 2006.

Market penetration of biologics is also probably going to be slower than for generic pharmaceuticals, as practitioners may initially require more time and evidence to view equivalent drugs for such life-saving treatments as chemotherapy with the same equanimity as generic substitutes for treatment of allergies or heartburn. On the other hand, most biologic substances are dispensed through treatment centers (for example, dialysis facilities, as opposed to the practitioner overseeing treatment) where purchasing managers and insurance companies may be more prepared to take into account the likely high cost-effectiveness of biogenerics.

## National Health Expenditures: Total Rx Drug Spending Compared to Population Growth

*Selected Years: 1970 – 2005*



Source: Aaron Catlin, Cathy Cowan, Stephen Heffler, Benjamin Washington, "TRENDS: National Health Spending In 2005: The Slowdown Continues," *Health Affairs*, Jan. 1, 2007.

### The Size of the Biologics Market

There are a number of estimates, but no definitive list, of the sales of biologic substances in today's market. For purposes of this analysis, estimates were collected from a variety of industry sources, compared for consistency, and a judgment made to define a base case volume of sales for 2006.<sup>16</sup>

In addition, for each of the brand biologics in this study, the same industry sources were reviewed to identify the year in which the basic patents relevant to that substance would expire in the United States.<sup>17</sup> In reality, whether or not a patent covers a

<sup>16</sup> Merrill Lynch, "Biogenerics: Big Opportunity, Small Threat," September 6, 2006, pp. 9-14; "How Drugs For Rare Diseases Became Lifeline For Companies," *Wall Street Journal*, November 15, 2005, p. A1; Citigroup, pp. 16-18 ; Peter Benesh, "Generic Threat Puts Biologic Firms on the Defensive," *Investor's Business Daily*, Oct. 16, 2006, p. A9.

<sup>17</sup> Citigroup, pp.16-18; CuraScript, "Specialty Pharmacy Management Guide and Trends Report 2004," June 2005, p. 6.

given product may involve information not available to the public and often will only be resolved after litigation. Ultimately, identifying a market entry date on products with large multiple patent profiles, especially given the likelihood of litigation, is an educated guess at best, even in the current generic drug system, let alone one that does not have an approval system in place. The estimates presented here represent the date that industry analysts believe the major patents for each substance would expire absent litigation. This is a conservative assumption that does not take into account generic challenges to patents that might bring products to market sooner should a process for approving biogenerics be instituted, just as they do in the generic industry now.

Table 1 presents the market size and patent expiration assumptions for the 25 leading biologic products in the U.S. market. These volumes are assumed to grow at a

Sales in Millions		
<b>Table 1</b>	<b>2006 (E) SALES</b>	<b>Patent Expiration</b>
<b>PRODUCT</b>		
Procrit/eprex – Epogen	\$3,320	2004
Aranesp	\$2,771	2010
Enbrel	\$2,645	2009
Epogen	\$2,489	2012
Neulasta	\$2,235	2015
Rituxan/Mabthera	\$2,057	2014
NeoRecormon/Epogin	\$1,830	2005
Avastin	\$1,809	2019
Remicade	\$1,800	2014
Herceptin	\$1,256	2013
Human insulin/related products	\$1,250	2004
Novolin	\$1,250	2005
Neupogen	\$1,200	2006
Avonex	\$1,033	2003
Humulin	\$1,000	2004
Synagis	\$920	2015
Genotropin	\$808	2008
Lantus	\$660	2009
Insulin analogues	\$536	2014
Byetta	\$450	2013
Norditropin	\$450	2004
Xolair	\$433	2018
Tarceva	\$402	2020
Humatrope	\$390	2003
Nutropin/Protropin	\$383	2009
Pegasys/Copegus	\$372	2019
All Other	\$4,240	

rate of 6 percent annually between now and 2011, at 3 percent from 2011 to 2016, and then be flat thereafter, unless specifically otherwise noted. In fact, the biologics market has doubled in the past four to five years, suggesting a much faster rate of growth, and the factors that drive it, including the aging of the population, speak to its ongoing growth. Some projections maintain that rate of growth over the next several years. But, at the same time, the growth in the overall biologics market depends to some extent on the introduction of new brand products. Any product introduced today, however, would likely enjoy patent protection for the duration of the period analyzed here (2011-2020), and is therefore not relevant.

Manufacturers of brand name biologics will certainly attempt to create and patent new extensions of existing drugs, prolonging their life and sales growth. But the growth rate of existing products will inevitably slow, as new products replace and improve upon them. The growth rates here are conservative, reflecting the reality of declining growth rates for existing medicines over time. Using these growth assumptions, the body of biologics under study here grows from about \$38 billion in 2006 to \$55 billion in 2020. In contrast, some analyses forecast a market for all biologics as large as \$60 billion in 2010.<sup>18</sup>

In a few instances, published reports or discussions with industry sources suggested alternative growth paths for individual products. Rebif, NovoSeven, and GonalF are projected to grow faster than 6 percent over the next five years. Alternatively, U.S. sales of products such as Humulin, Genotropin, or Pulmozyme are projected to decline or, at best, stay flat.

### **Price and Penetration Assumptions**

The price and penetration effects of conventional generics have been studied extensively. For example, the price discounts offered by conventional generic producers increase both over time and as the number of new generic entrants into the market increases. To some extent, these same patterns will be seen in the market for biogenerics. But at the same time, as noted above, the differences between conventional generics and biogenerics require special consideration.

The FDA and Congressional Budget Office (CBO) both employ a common set of assumptions regarding the price and penetration effects of conventional generics.<sup>19</sup> In order to maintain the conservative approach taken in this analysis, the assumption is made that price effects cannot be meaningfully higher, and penetration cannot be as extensive, as would be assumed for conventional generics.

The price and penetration assumptions used in this analysis are taken from an industry analysis performed by Merrill Lynch.<sup>20</sup> They are presented in Table 2 and

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<sup>18</sup> Citigroup.

<sup>19</sup> Congressional Budget Office, "How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry," U.S. Congress, Washington, D.C., July 1998.

<sup>20</sup> Merrill Lynch.

compared to the FDA/CBO assumptions for conventional generics. In the Merrill Lynch analysis, biogenerics are assumed to enter the market at a price 20 to 30 percent below those of brand biologics. As the number of generic competitors increases, the discount biogenerics offer rises to 40 to 50 percent. In this analysis, biogenerics are assumed to enter the market in the year *following* patent expiration at a discount of 20 percent and rising to 40 percent in the fifth year. Both of these assumptions are at the low end of the range suggested by Merrill Lynch.

For those individual cases that merit such treatment, there are calculated alternative “high” and “low” discounting scenarios, also shown in Table 2. The “low” discount assumption has prices falling 10 percent upon the inception of competition, with the discount rising to 25 percent in the fifth year. The “high” discounting assumption starts at 25 percent and rises to 47 percent in the fifth year. This 47 percent discount is the FDA/CBO assumption regarding the long-term, steady-state discount offered by conventional generics. Thus, only the most heavily discounted biogenerics offer the same discount as do the *average* conventional generic drug. While this reflects the special nature of biologics and biogenerics, it remains a very conservative assumption, particularly in light of the cost-minimizing pressure under which insurance companies, health care providers, and government-run programs will operate in the years ahead.

The “mid-range,” “high,” and “low” cases for the penetration of biogenerics are taken again from Merrill Lynch’s corresponding three cases for the drug erythropoietin (EPO). In the mid-range case, biogenerics capture 3 percent of the market in their first year, rising to 30 percent of the market in their sixth year. The “low” case has bioequivalent market share rising from 3 percent to 15 percent over the same 6 years, while the “high” case has market share rising from 10 percent in the first year to 50 percent after four years. Once again, a conservative assumption, as EPO is used to treat anemia resulting from chronic kidney disease, cancer, and chronic inflammatory diseases, such as Crohn’s disease and inflammatory bowel disease, and to manage the debilitating effects of chemotherapy or radiation treatment for cancer; it therefore may enjoy more brand loyalty among practitioners than do conventional (as opposed to biologic) brand medications.

The alternative price and penetration assumptions were not used frequently in this analysis. Insulin and human growth hormone products, for example, are assumed to have high penetration but low price discounts. This is because they are already the subject of some degree of competition among branded products. Thus, prices are already somewhat lower than they would have been without competition, and users are already familiar with the idea of different makers of the same product. It should be noted, however, that when Omnitrope, the human growth hormone biogeneric that was approved in Europe, entered the market shortly thereafter, it was priced 20 percent below its branded equivalents, a level more consistent with the mid-range assumption.

On the other hand, such specialty medications as Remicade (Crohn’s Disease) or Cerezyme (Gaucher’s Disease) may have greater discounts, given the very high prices now charged for these medicines.

**Table 2**

**MARKET PENETRATION ASSUMPTIONS**

	Target Year*	Year +1	Year +2	Year +3	Year +4	Year +5	Year +6
<b>Generics</b>	10.00%	46.25%	58.75%	70.00%	70.00%	70.00%	70.00%
<b>Low Range</b>	0.00%	3.00%	8.00%	11.00%	14.00%	15.00%	15.00%
<b>Mid-Range</b>	0.00%	3.00%	12.00%	20.00%	25.00%	28.00%	30.00%
<b>High Range</b>	0.00%	10.00%	15.00%	25.00%	50.00%	50.00%	50.00%

**PRICE DISCOUNT ASSUMPTIONS**

<b>Generics</b>	8.00%	35.00%	44.00%	47.00%	47.00%	47.00%	47.00%
<b>Low Range</b>	0.00%	10.00%	14.00%	18.00%	21.00%	25.00%	25.00%
<b>Mid-Range</b>	0.00%	20.00%	25.00%	30.00%	35.00%	40.00%	40.00%
<b>High Range</b>	0.00%	25.00%	31.00%	38.00%	43.00%	47.00%	47.00%

\* Year patent is assumed to expire

This analysis made several other assumptions. First, the growth rate in the demand for medicines is fixed, regardless of whether biogenerics enter the market. It may be the case that the price reductions triggered by biogenerics lead to improved drug coverage, but this is a benefit unrelated to price-driven consumer savings. Second, generic versions of biologic drugs for which the patent has already expired are not brought to market until 2009 and all other bioequivalent product introductions are made in the year *following* the expiration of all patents, beginning with those expiring in 2008. The assumption is also made that, absent a change in regulatory procedures, there would be no biogeneric drugs entering the U.S. market before 2020. Finally, the mark-ups on drug prices from distributors and pharmacies are unchanged when generics substitute for brand name drugs.

**Results**

This analysis focuses on the savings that would accrue economy-wide over the period 2011-2020; were the FDA to create a pathway for bioequivalent drugs, this is the likely time period over which substantial activity would begin to occur. Table 3 summarizes the results obtained in this analysis.



that bill. Congress could also consider biogenerics legislation as a stand alone bill. In any case, if a pathway for biogenerics does not become law this year, it is highly unlikely Congress would reconsider it again until after next year's Presidential election.

If Congress passes legislation, it should have clear standards to determine whether a generic biologic is comparable or not to the brand name, give the FDA the flexibility it needs to determine which tests are needed to ensure a biogeneric is safe and effective, and allow new technology and science to be utilized in its deliberation. At the same time, legislation has to provide mechanisms to establish a true abbreviated pathway and avoid a cumbersome system that prevents the FDA from making a timely decision. Finally, considering it will be more complicated and expensive to create a biogeneric as opposed to a chemically-based generic drug, Congress needs to avoid crafting legislation that may unintentionally raise barriers to generic competition such as unnecessary testing to ensure the brand name biologic and biogeneric are interchangeable or comparable, complicated procedures for determining patent disputes, and excessive measures to extend patents for brand name companies to compensate for the time spent on research and development.

The biotech industry is already vehemently opposed to any legislation that would bring biogenerics to the marketplace and is putting up a fight to stop Congress from legislating on this issue. Members of Congress will push back. House Oversight and Government Reform Committee Chairman Henry Waxman, said the following in a hearing on examining safe and affordable biogeneric drugs:

...the big brand name companies have gone beyond legitimate concern and have thrown up a defensive smoke screen around biologicals. They say there will be problems of safety, decreased innovation, and limited savings. When discussing creating generic competition, they say things like – and I quote:

*“[S]uch action may also save consumers a few dollars here and there, although that is by no means assured. But whatever short-term savings may be achieved will come at an enormous long-term cost to the public...Focusing solely upon short term lower prices – a ‘cheap drugs’ policy – will inevitably reduce research and hinder our public efforts.”*

These arguments have a familiar ring to them. That's because the words I just read were the formal testimony that the Pharmaceutical Manufacturers Association gave to the House in 1983 when they were opposing Hatch-Waxman.<sup>21</sup>

As the drug industry did in 1984, the biotech industry is heavily lobbying Congress and consumers on why generic versions should not be allowed on the market – citing safety reasons, biologics' complexity and sensitivity, and the difficulty in

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<sup>21</sup> Rep. Henry A. Waxman, Chairman, Committee on Oversight and Government Reform, Opening Statement, Hearing on Safe and Affordable Biotech Drugs – The Need for a Generic Pathway, March 26, 2007, p. 2., Web accessed April 17, 2007, <http://oversight.house.gov/documents/20070328111420-75473.pdf>.

manufacturing a therapy from lot to lot. However, biotech companies face these challenges every time they produce a new batch of a certain therapy. Generic companies will use sound science and technology to do the same thing.

Knowing that biogenerics are inevitable, the biotech industry will do whatever it can to delay an abbreviated pathway at the FDA. In fact, BIO President Jim Greenwood stated a delay “means a lot to the bottom line.”<sup>22</sup>

Some members of Congress are actively looking to force price controls on both the biotech and pharmaceutical industries to obtain lower prices. But price controls are a simplistic, shortsighted, and knee-jerk solution to achieving lower costs for needed drug therapies. Our nation provides most of the world’s new drugs and hundreds of thousands of jobs but if price controls are implemented, they will destroy our nation’s vibrant drug industry— just as price controls have done in Europe.<sup>23</sup>

A market-based approach is the proper solution to getting less expensive therapies in the marketplace while encouraging the development of new medicines at the same time. An accelerated pathway to bring biogenerics to the market that protects patients and balances the financial needs of brand name and generic drug companies, similar to Hatch-Waxman, is the way to accomplish this goal.

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<sup>22</sup> Neil Munro, “Lobbying and Law – Counting on Kennedy,” *National Journal*, April 7, 2007, p. 39.

<sup>23</sup> PhRMA, “What Goes into the Cost of Prescription Drugs,” June 2005, p. 11, Web site accessed April 27, 2007, [http://www.phrma.org/files/Cost\\_of\\_Prescription\\_Drugs.pdf](http://www.phrma.org/files/Cost_of_Prescription_Drugs.pdf).

## **Glossary**

**Allergens** – Allergenic extracts are injectable products that are manufactured from natural substances, such as molds, pollens, insect venoms, animal hair, and foods, known to elicit allergic reactions in susceptible individuals. These extracts are used for the diagnosis and treatment of allergic diseases such as "hay fever" or reactions to bee stings.

**Blood and blood components** – Blood, and its parts such as red cells, white cells, platelets, plasma, immunoglobulin, clotting factors etc., used for transfusion or for the manufacture of pharmaceuticals.

**Erythropoietin** – A hormone, produced by the kidneys, that stimulates red blood cell production.

**Insulin** – A hormone that lowers the level of glucose, a type of sugar, in the blood. When the body cannot produce or respond normally to insulin, diabetes is the result.

**Interferon** – A protein produced by white blood cells and other cells, which regulates the body's immune system. When there is a threat to the body, more interferon will be produced.

**Gene therapy** – Products that introduce genetic material into the body to replace faulty or missing genetic material, thus treating or curing a disease or abnormal medical condition.

**Granulocytic-colony Stimulating Factor** – A hormone that stimulates the production of neutrophils, a type of white blood cell. White blood cells fight infection in the body and are part of the immune system.

**Recombinant therapeutic proteins** – Proteins made from recombinant DNA technology, also called genetic engineering or gene splicing, a process that involves combining DNA segments from at least two other organisms.

**Somatic cells** – Generally, any cell in the body of an organism that is not a germline or sex determining cell.

**Somatropin** – A synthetic or naturally occurring growth hormone from the human pituitary gland.

**Tissues** – Human cells or tissue intended for implantation, transplantation, infusion, or transfer into a human recipient.

**Vaccines** – Microbial preparations of killed or modified microorganisms, such as a bacterium or a virus, which can stimulate an immune response in the body to prevent future infection with similar microorganisms. These preparations are usually delivered by injection.

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