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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

Thank you for the opportunity to participate in the November 21, 2008 Roundtable on Follow-On Biologic Drugs (Roundtable) at the Federal Trade Commission (the "FTC") and also for the additional opportunity to provide comments regarding the creation of an abbreviated regulatory approval pathway for biosimilars.[1]

These comments will focus on biosimilars exclusivities generally, and more specifically, on the appropriate amount of exclusivity for biosimilars.

INTRODUCTION

Biological drugs, which in contrast to chemical drugs are made from living things, account for some of the most important advances in medicine in recent years and are among the most expensive drugs on the market today. The Hatch-Waxman Act provided a pathway for generic chemical drugs, but not for most of these products. Since the patents on some biologic drugs have expired and others will expire during the next several years, Congress has been exploring biosimilars legislation to create a pathway for generic biologics, which could be approved with fewer studies and

[1] These comments will use the term "biosilmilars" in accordance with the recommendation made by the FTC during the Roundtable.

less expense. Competition from biosimilars will provide a market-based mechanism to reduce private and federal spending on biologics.

There are three critical elements to any effective legislation. If Congress fails to adequately address any element, the legislative will be unsuccessful because it will not create a viable pathway for biosimilars.

First, the biosimilars pathway should give FDA the discretion to adopt appropriate scientific requirements and procedures necessary to review and approve safe and effective biosimilar products. Just as the law does not mandate that the agency require specific tests for brand products, it should not require that any specific type of data be submitted to support a biosimilar application. For example, while it is expected that during the early years of any program FDA would generally require clinical studies prior to approving generic versions of biosimilar drugs, legislation requiring clinical studies in every case would cause unnecessary testing, expense and delay once the science develops to the point where safe and effective biosimilars can be approved without clinical data. Similarly, the legislation should not make the issuance of guidances or regulations a prerequisite to approval. FDA has tremendous flexibility when it comes to approving brand name biologics. There is no basis for being more restrictive here, particularly because FDA will have the benefit of data from brand biologics that it has already reviewed and approved. Although this issue is not one that the FTC is addressing, I raise it because it is critical to a biosimilars pathway.[2]

Second, the biosimilars pathway also should include a mechanism for the early resolution of patent disputes. Unless biosimilars legislation adequately addresses this issue, the innovator companies will often be able to extend their patents by the time required to resolve patent litigation. In addition, a biosimilars program should not permit the brand to sue on every patent prior to market entry. This is especially

[2] The approval of generic chemical drugs often is hampered by FDA's lack of resources, particularly since brand chemical drugs fall within FDA's successful user fee program. A biosimilars pathway will likely include user fees to ensure that generic biologics reach the market in a timely manner. Similarly, the approval of generic chemical drugs often is delayed by the filing of last minute citizen petitions by brand companies seeking to block approval. Congress, FDA and the generic drug industry have been discussing ways to address this problem, and the resolution of this issue also is critical to a successful biosimilars pathway.

important for biologics because, in contrast to chemical drugs, innovators often claim that 100 or more patents cover their products. Many of these are process patents, which are not a barrier to generic competition. While early resolution of the key brand patents is essential to an effective biosimilars program, any legislation should not permit brands to sue on every patent prior to market entry because this would overwhelm the generic competitor in patent litigation.

The mechanism in Hatch-Waxman that encourages early litigation of patents was largely successful until recent years, when some innovators have chosen not to initiate lawsuits prior to approval of the generic. All of the bills under consideration include provisions that their sponsors claim will address this issue, although some will not be effective as currently drafted. This also is not an issue that FTC is addressing, but it will be critical to any successful biosimilars legislation.

The third critical element to effective biosimilars legislation is striking the right balance with respect to intellectual property protection. Under current law, biologic companies obtain patents on their products, just as chemical drug companies obtain patents. Hatch-Waxman gave chemical *and biologic* companies the same five-year patent extension even though the Hatch-Waxman generic program applicable to chemical drugs does not apply to biologics. For chemical drugs, Hatch-Waxman also provided that where patent protection is unavailable or otherwise insufficient, companies can obtain five years of additional marketing exclusivity for new chemical entities (NCEs) or three years when the drug is not an NCE. The critical issue that must be addressed in any biosimilars legislation is whether something is needed in addition to what is currently available under patent law. These comments will address this question.

PATENT AND EXCLUSIVITY PROTECTION

Patent law grants chemical drug and biologic patent owners the right to exclude others from making, using and selling their patented drug or biologic.[3] Parties who engage in these acts without the permission of the patent owner may be sued for

[3] 35 U.S.C. § 271(a). *See also*, John R. Thomas, Pharmaceutical Patent Law at 6 (2005).

infringement.[4] Although patents are presumed valid, alleged infringers may assert that the patents on which they were sued are invalid or unenforceable.[5]

Exclusivity protection is separate from patent protection. It is a statutory bar to obtaining FDA approval and proceeding to market. This paper will use the term "exclusivity" to describe a type of exclusivity that bars approval and marketing of a drug or biologic that relies on another product's data to gain FDA approval. In other words, a second company may not rely on the approval of the earlier brand product or on the data submitted by that product's sponsor as a basis for obtaining approval to market an identical or similar product. There can also be a "filing moratorium" in connection with exclusivity. When a filing moratorium is in effect, an application for approval of a drug or biologic that relies on the brand approval or data cannot even be filed until the moratorium period has expired.[6]

Exclusivity typically runs simultaneously with patent protection. The protection afforded by exclusivity is in some ways weaker and in other ways stronger than patent protection. Exclusivity is weaker because it is just a bar to approval of a drug or biologic that relies on the prior approval of the brand product. If patent protection has expired, a manufacturer may obtain approval even while exclusivity is in effect by submitting an application with the full set of studies demonstrating safety and effectiveness. If a product is patented, then a generic competitor may not market that product regardless of FDA approval. Exclusivity is stronger than patent protection in that it is not subject to the usual patent challenges such as obviousness and inequitable conduct.

CURRENT PROTECTIONS AFFORDED TO BIOLOGICS

Drug and biologic patents have a life of 20 years from the date of first filing of the patent application.[7] Because the United States Patent Office typically takes about

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[4] 35 U.S.C. § 281.
[5] 35 U.S.C. § 282.
[6] The term "data exclusivity" also is sometimes used to describe exclusivity that bars even submission of an application that relies on protected data.
[7] 35 U.S.C. § 154. Prior to June 8, 1995, the effective date of the Uruguay Rounds Agreement, patents had 17 years of patent life from the date the patent was issued.

one year to issue a patent, the new patent term generally lasts 19 years from the date of issuance. Nevertheless, because patents usually are obtained before a drug has been studied and approved for marketing, the effective patent term of the product is usually significantly less than the 19 or 20 years afforded under the law.

In 1984, when Congress passed the Hatch-Waxman Act, it extended the patent life to compensate patent holders for time lost while developing their drugs and biologics and awaiting FDA approval. Under this law, drugs and biologics are eligible for a one-time patent extension of up to five years.[8] The extension period is calculated on the basis of length of time required to study and gain approval of the patented product. The total post approval, extended patent protection period may not exceed 14 years (*e.g.,* if there are still 12 years left on the patent post approval, the extension will be only two years; if there are 14 years left on the patent, no extension will be granted).[9] Biologics were included in the patent extensions even though an abbreviated pathway was not being created for biologics

In addition to the patent extensions, Hatch-Waxman also created exclusivity protection. These protections apply only to chemical drugs, not biologics. Under Hatch-Waxman, chemical drug products are eligible for five years of new drug product exclusivity (also called NCE or new chemical entity exclusivity), and three years of exclusivity for certain applications that include clinical data.[10]

With regard to the NCE exclusivity, if there is no patent protection, there is a filing moratorium of five years during which a generic application may not be submitted. Because it will take FDA one to two years to approve the generic, the brand's exclusivity is effectively extended by the review period. If the brand has a patent and the generic challenges the patent, the generic may not submit an application until four years after approval of the brand, and a timely patent suit by the brand will bar approval for 7 ½ years or until the patent litigation is resolved.[11]

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[8] 35 U.S.C. § 156.

[9] *Id.*

[10] 21 U.S.C. § § 355(c)(3)(E), (j)(5)(F); *see also* 21 C.F.R. § 314.108.

[11] 21 U.S.C. § 355(j)(5)(F). If the brand has a patent that is not challenged and the patent runs longer than the five years of NCE exclusivity, the exclusivity will expire before the patent and provide no additional market protection.

The three-year period of exclusivity is available for a product that is not an NCE (such as a new dosage form of the NCE) if new clinical data (other than bioavailability studies) is needed to obtain approval of the product.[12] This type of exclusivity delays approval rather than submission of an ANDA. Moreover, a generic may often be able to avoid the exclusivity by using the original formulation of the brand as the reference product.

As stated above, neither the five nor the three year exclusivity applies to biologics. There are, however, additional exclusivities that do apply to biologics. The first sponsor to gain approval of a drug or biologic product that qualifies for orphan designation will receive a seven-year period of marketing exclusivity.[13] This exclusivity applies only to the indication for which the drug or biologic has been designated and approved, permitting other applications for the same drug or biologic for a new use to be approved. The exclusivity applies broadly, however, to any application for the same drug or biologic, which is defined in the regulations generally to mean a drug that contains the same active moiety or the same principal molecular structural features for the same indication.[14] This means, in contrast to Hatch-Waxman exclusivity, that orphan drug exclusivity will block even the submission of a full NDA for the same product for the protected indication. The one exception is when the sponsor of a drug that is otherwise the same as one that already has orphan-drug approval for the same rare disease or condition can show that its drug is clinically superior.[15]

In addition, as part of the FDA Modernization Act of 1997, Congress created pediatric exclusivity, which awards an additional six months of exclusivity for conducting pediatric studies.[16] In order to qualify for the exclusivity, FDA must request a pediatric study, the study must be conducted in accordance with the request, and FDA must accept the study. Even if the study does not result in FDA

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[12] 21 U.S.C. § 355(j)(5)(F)(iv).
[13] 21 U.S.C. §§ 360bb, 360cc. An orphan drug is a drug for a disease or condition with a population of fewer than 200,000 persons.
[14] 21 C.F.R. § 316.3(b)(13).
[15] *Id.* *See also* 21 C.F.R. §§ 316.24, 316.25.
[16] 21 U.S.C. § 355A.

approving a pediatric indication, if it was conducted in accordance with the request, exclusivity will be granted.[17] Pediatric exclusivity attaches to any exclusivity and patent protection for any drug or biologic product containing the same active moiety as the drug or biologic studied and for which the party submitting the study holds the approved application.[18]

CURRENT LEGISLATIVE PROPOSALS

A number of the biosimilars bills propose to augment the current protections provided by patent law with provisions providing for exclusivity for biologics. The different bills take very different approaches.

H.R. 1038, The Access to Life-Saving Medicine Act (introduced in the House by Congressmen Waxman and Pallone and in the Senate by Senators Schumer and Clinton) provides for no exclusivity or intellectual property protection in addition to what is available under the patent laws, Hatch-Waxman and other provisions of the Food, Drug and Cosmetic Act.

S. 1695, The Biologics Price Competition and Innovation Act of 2007 (as marked up by the Senate HELP Committee), provides that no generic application may be filed for four years after the brand is approved and no generic biologic may be approved for 12 years after the brand is approved.

H.R. 1956, The Patient Protection and Innovative Biologics Medicines Act (introduced by Congressman Inslee), provides that no generic may be submitted before 12 years from the date the brand was approved and no generic may be approved before 14 years from the date the brand is approved. The exclusivity is extended to 15 years if FDA approves a new indication for which it finds a significant clinical benefit.

H.R. 5629, The Pathway for Biosimilars Act (introduced by Congresswoman Eshoo

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[17] 21 U.S.C. § 355A.
[18] 21 U.S.C. §§ 355A(a), (c).

and Congressman Barton), provides that no generic application may be submitted until the later of four years after the brand was approved or the date on which FDA begins the process of developing the guidance that the bill requires FDA to issue before approving a biosimilar. In addition, no generic may be approved for 12 years after the brand was approved. The Eshoo bill does not provide exclusivity for new indications, routes of administration, dosage form or strength. It does, however, provide for 14 years of exclusivity if during the first 8 years of the exclusivity the brand obtains approval of a medically significant new indication. This time can be increased to 14.5 years if the new indication is a pediatric indication.

With the exception of the Waxman bill, all of the bills currently introduced propose to give brand biologics more than twice (and in most cases almost three times) the exclusivity that Hatch-Waxman gave to chemical drugs. In addition, all of these bills currently appear to permit the brands to make minor changes to their product and obtain an additional 12-15 years of exclusivity. This strategy, referred to as "evergreening", creates the potential of a perpetual extension of market control. If exclusivity is going to be included in the law, it is essential that the law address the issue of whether a slight variation of the drug can get additional exclusivity. The Senate mark-up states that there is no exclusivity for a new indication, route of administration, dosage form or strength. Apparently even under this bill, however, the brand can get a full 12 years if it slightly changes the molecule, particularly if the sponsor can show some slight benefit, for example, improved safety or ease of administration. Hatch-Waxman addressed this issue for chemical drugs by making only new chemical entities eligible for five years of exclusivity. Under Hatch-Waxman, minor changes are at most eligible only for three years of exclusivity, which applies only to the change. The same approach should be taken with biologics.

THE BIOLOGIC INDUSTRY'S CLAIM FOR SIGNIFICANT EXCLUSIVITY

The Biotechnology Industry Organization (BIO), the trade association for the biologic drug companies, has argued that 14 years of exclusivity are necessary to create a sufficient incentive to innovation. This position is reflected in public

statements by BIO and its members[19] and in a number of the bills discussed above. The biologics industry is arguing that 14 years of exclusivity is needed to achieve the same protection afforded to chemical drugs under Hatch-Waxman. Specifically, BIO argues that chemical drugs are protected from generic competition for 13.5 years under Hatch-Waxman[20] and that brand biologics should get the same. The biologics industry asserts that their position is supported by an analysis described in a recent article entitled "Follow-on biologics: data exclusivity and the balance between innovation and competition," by Dr. Henry Grabowski, an economist from Duke University. [21]

According to Dr. Grabowski's analysis, 12.9 – 16.2 years is the "break even lifetime" – the point at which a firm recovers its R&D investment and earns a risk-adjusted rate of return. Dr. Grabowski appears to argue that brand biologic should be protected from competition until this time has passed.[22] Dr. Grabowski gets to the 12.9 – 16.2 year-number by examining prior analyses of the break-even lifetime for chemical drugs and conducting a break-even simulation for biologics. According to Dr. Grabowski, the break-even lifetime for a 1980-1984 portfolio of drugs is just over 16 years and for a 1990-1994 portfolio, 15 years. He further notes that the average period of market exclusivity for drugs from 1996-2005 is 12.5 – 15 years.[23]

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[19] *See e.g.,* BIO's Comments Re: Emerging Health Care Competition and Consumer Issues (September 30, 2008).

[20] I assume that BIO is referring to the period of time from approval to first generic approval, which is the effective intellectual property protection and could include patent protection and/or any other type of exclusivity.

[21] 7 Nature Reviews 479 (June 2008).

[22] In his conclusion, Dr. Grabowski states that "[w]hile the right to undertake patent challenges is an integral part of the US intellectual property system, entry through abbreviated filings should be delayed until the representative NBE has had an opportunity to earn risk-adjusted break-even returns." Dr. Grabowski appears to be saying that the generic should not be approved until the brand has earned "risk-adjusted break-even returns," which essentially is an exclusivity period as long as the break-even point exclusivity. 7 Nature Reviews at 487. Earlier in the article [p. 479] Dr. Grabowski goes even further and states that "[i]deally, data exclusivity would delay abbreviated filings and patent challenges until innovators have had an opportunity to earn a positive return." This appears to argue that there should be a filing moratorium equal to the 12.5-16.2 year break even period. Since the validity of a generic patent cannot be litigated until an abbreviated application is filed, at the earliest, Dr. Grabowski's contention amounts to an argument that the brands should not even have to face a patent challenge until they have received a return on their investment. So, for example, if he were proposing a 16-year exclusivity period, he actually would be proposing 16 years plus whatever time is needed to approve the generic or to litigate the patent, whichever is longer. This is assuming the generic does not want to launch its product at risk (and the generic usually does not). With 16 years of exclusivity, the innovator would be guaranteed a certain number of years on the market even if the innovators patents are weak. Blocking even the filing of an application unnecessarily protects what might otherwise be a weak patent. There is no basis for doing that.

[23] I assume that by "market exclusivity" Grabowski is referring to the period of time from approval to first generic

In a separate analysis of the costs of developing biologics, Dr. Grabowski calculates, using discount rates of 11.5% and 12.5%, that the break-even lifetimes for the mean biologic product are 12.9 and 16.2 years.[24]

The biologics industry's reliance on the current market protections afforded chemical drugs is both misleading and misplaced. It is misleading because Dr. Grabowski's average includes all drug products, even those that are not big sellers, for which there is little competition and presumably little incentive to challenge patents. When the analysis is limited to products with profits over $250 million, the segment of drugs for which there is likely to be the greatest interest in competition and for which there are the greatest potential savings, a different picture emerges. Table 1 (attached hereto) shows the effective patent/exclusivity period for the 42 chemical pharmaceutical products approved between 2003 and 2008 with sales greater than $250 million. The effective patent/exclusivity period is the time between the approval of the innovator and the first generic approval, which is the period of time during which the brand product was not subject to generic competition. For this segment of drugs, the average effective patent/exclusivity period was 10.25 years. The range of market protection is from 3.75 years to 16.7 years.

Reliance on the protection afforded to chemical drugs as a basis for determining exclusivity is misplaced because the industry is trying to take a number that is an average and make it a minimum. *See* page 18. Moreover, the ten-year average is driven in large part by patent protection, not exclusivity. As discussed above, exclusivity protection is stronger because it cannot be challenged. The implications of this distinction also are further discussed below.

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approval, which is the effective intellectual property protection and could include patent protection and/or any other type of exclusivity.

[24] As he notes, these projections are extremely sensitive to the discount rate assumptions. Presumably a discount rate of less than 11.5% would yield a break-point substantially less than 12.9 years.

THE APPROPRIATE EXCLUSIVITY FOR BIOLOGICS

The key to a successful biosimilars pathway is to identify the minimal amount of intellectual property protection that will provide a sufficient incentive to invest in research leading to the discovery of new drugs that make a significant medical advance. In fact, there is a strong case that too much exclusivity will actually diminish the incentives to conduct research since as long as a manufacturer can maintain a monopoly, it has an incentive to invest in maintaining that monopoly rather than in inventing new products. [25] Once the minimal period is identified, then it is important not to grant exclusivity beyond that minimal period because each additional year of exclusivity will exact an enormous cost on patients and other purchasers of biological drugs.

Table 1 illustrates how much it would cost if the generic versions of chemical drugs with sales over $250 million per year were delayed for just one year. The table includes three different scenarios: (1) a 70% conversion to generics and a 30% generic drug discount; (2) a 70% conversion and a 50% discount; and (3) an 80% conversion and a 60% discount. The generic conversion and price discount assumptions used in the three different scenarios are all fairly conservative. For example, in 2004, the average generic substitution rate for State Medicaid programs was 89%.[26] In 2006, the generic substitution rate in the Medicare Part D program was 88%.[27] Similarly, in 2007, the National Association of Chain Drug Stores found that generics were, on average, 71% cheaper.[28] Using even these conservative assumptions, as set forth in Table 1, if the period of intellectual property protection had been extended for a single year on each chemical drug with sales greater than $250 million, then the total lost savings from generics would be 9.1, 15.2 or 20.8

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[25] Laurence J. Kotlikoff, "Stimulating Innovation in the Biologics Industry: A Balanced Approach to Market Exclusivity", (Sept. 2008); *See also* Scott Gottlieb, M.D., "Biologics Legislation Will Speed Progress", Forbes.com (posted April 17, 2007) (a generic pathway for biologics will accelerate competition).

[26] HHS Office of the Inspector General: Generic Drug Utilization in State Medicaid Programs (2006) (www.oig.hhs.gov/oei/reports/oei-05-05-00360.pdf).

[27] HHS Office of the Inspector General: Generic Utilization in the Medicare Part D Program (2007) (www.oig.hhs.gov/oei/reports/oei-05-07-00130.pdf.).

[28] *See* www.nacds.org/wmspage.cfm?parm1=507.

billion dollars, depending on which scenario is used.[29]

Too much exclusivity for the brand also may undermine the incentive for developing generics. At some point in the life of a drug, its sales diminish as other similar products are developed and marketed. According to the recent analysis by Dr. Grabowski, this period starts at approximately year 10 in the lifecycle of a biologic.[30] As sales diminish after the 10 year point, the value of generics in terms of health care savings also diminishes. Given the anticipated costs of developing biosimilars, which are likely to be significantly greater than the costs of developing generic chemical drugs, at some point sales will have diminished to the point where there will be an insufficient incentive to develop generic products. For this reason as well, it is critical that any exclusivity granted to biologic products not be in excess of the period of time necessary to create a sufficient incentive to innovation.

THE AVAILABLE EVIDENCE INDICATES THAT THERE IS NO BASIS FOR GRANTING MORE EXCLUSIVITY TO BIOLOGICS THAN TO CHEMICAL DRUGS

Given the success of Hatch-Waxman, I would propose that the question to be answered is whether there is a justification for adopting a different package of patent protection and exclusivity than provided by the Hatch-Waxman Act. Hatch-Waxman patent extensions and exclusivity for chemical drugs has been in effect since 1984. For almost 25 years, Hatch-Waxman has worked well in balancing the need to create incentives for research and get less expensive generic drugs to patients more quickly. As further discussed below, my conclusion is that there is no justification for departing from Hatch-Waxman by granting more exclusivity to biologics.

As discussed above, in addition to the patent extensions, Hatch-Waxman provides for five years of exclusivity (which can be extended up to 7.5 years, if there is a

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[29] It is arguable that the generic conversion rate for biologics could be lower than it is for chemical drugs. On the other hand, biologics generally cost more than chemical drugs. As a result, savings lost by additional years of exclusivity would likely be of the same magnitude or greater.

[30] 7 Nature Reviews at 485 (figure 5).

patent challenge). The exclusivity gives chemical drug companies a guaranteed period of time when their investment and data would be protected regardless of what happens to their patent challenges. When Hatch-Waxman passed, chemical drug patents had not been tested as they would be after it passed and the brand companies successfully argued for a five-year exclusivity period during which they would be protected from generic competition. In fact, since Hatch-Waxman, the pharmaceutical industry's basic product patents have fared well. For example, products subject to Hatch-Waxman with sales greater than $250 million receive an average of 10.25 years of intellectual property protection.[31] In addition, chemical drug company profits remained high after passage of Hatch-Waxman. According to the Congressional Budget Office, the increase in generic sales since 1984 has probably not reduced expected returns below the average capitalized costs of research and development.[32] It is generally accepted that Hatch-Waxman provides sufficient intellectual property protection.

Thus, in evaluating biologics legislation, we should start with the presumption that the Hatch-Waxman structure will work, and the burden should be on those advocating a longer period of exclusivity to demonstrate that there are differences between chemical drugs and biologics and thus, public policy justifications supporting more exclusivity. As demonstrated below, to date, the advocates of a long exclusivity period have not identified any such differences.

Dr. Grabowski and others identify three possible factors that could justify increasing the period of exclusivity currently available for Hatch-Waxman products. They are: (1) the cost of developing biologics is greater; (2) the time required to develop biologics is greater; and (3) biologic patents are weaker. I address each of those issues below.

Costs of Developing a Biologic. Over the years there have been numerous estimates of the cost of developing a prescription drug. In 1990, a study conducted by the industry-funded Tufts Center for the Study of Drug Development estimated

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[31] *See* Table 1.

[32] The Congressional Budget Office, "How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry," (July 1998). The authors of this study used a 9% discount rate.

that it costs $231million to develop a prescription drug.[33] In 1993, the Office of Technology Assessment estimated that the cost is between $259 million and $359 million, depending on the assumptions made regarding the cost of capital.[34] Since that time, there have been numerous papers published on this question, but recent papers estimate the cost of development to be $1 billion.[35]

According to Dr. Grabowski, investment in biologics is $1.24-1.33 billion based on the assumption that the cost of capital is between 11.5% and 12.5%. Even assuming this number is correct, and there is reason to believe it is too high,[36] the estimates for chemical drugs and biologics are in fact comparable and do not support granting biologics more exclusivity. When Dr. Grabowski testified before Congress last year he too noted that the cost of developing biologics is comparable to the cost of developing chemical drugs.[37] Dr. Grabowski also makes a related argument -- that the R&D process for biologics is riskier. Dr. Grabowski seems to be saying that biologics have overall greater clinical success rate than chemical drugs but they have more failures in Phase III, which is the most expensive phase. If the ultimate success rate for biologics is greater, however, the argument that more failures during Phase III warrant greater market protection does not support additional exclusivity.

Development time. Another argument the biologics industry has made is that development time for biologics is longer because biologics are more complex. Since products are often patented before they are developed, a longer development time can diminish the effective patent life of a product. It is also relevant, however, that to a significant extent development time is within the control of the companies

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[33] Joseph DiMasi, *et al*., "Cost of Innovation in the Pharmaceutical Industry," 10 Journal of Health Economics 107 (1991).

[34] Office of Technology Assessment, "Pharmaceutical R&D: Costs, Risks and Rewards" (1993).

[35] *See* Joseph DiMasi and Henry Grabowski, "The cost of biopharmaceutical R&D: Is biotech different." 28 Managerial &Decision Economics 469, 470 (2007). In this article DiMasi and Grabowski cite industry insider estimates of $1 billion and reference an earlier study they conducted in which (using a discount rate of 11%) they estimated the R&D cost of new drugs at $800 million (in year 2000 dollars).

[36] *See, e.g.,* Alex M. Brill, "Proper Duration of Data Exclusivity for Generic Biologics: A Critique" (November 2008). Brill argues that the correct discount rate is 10%. *Id*. at 8. It is also worth noting that, as Grabowski himself acknowledges, the selection of the discount rate significantly affects the biologic development cost estimate.

[37] *See* March 26, 2007 Testimony of Henry G. Grabowski before the House Oversight and Government Reform Committee at page 10.

developing the product, since they can determine the pace of research and clinical trials. In any event, according to Dr. Grabowski, the development time for biologics is about the same as for chemical drugs: 97.7 months for biologics versus 90.3 months for chemical drugs.[38] This difference of less than 10% certainly does not justify a significant additional period of exclusivity.

Strength of patents. Finally, the biologics industry has argued that biologics patents are weaker and easier to design around and that additional exclusivity is needed to account for this. Specifically they are arguing that because generic biologics will not be identical to the innovator-products, the innovator's patent may be easy to design around. This argument is dubious. If this were true, then under current law, competitors would have an incentive to do the full testing (which is likely to cost significantly less than the initial full testing) and then successfully litigate the weak patents. This would be particularly true for some of the more profitable biologics. Although there have been a handful of instances where competitors have challenged patents, we have only been able to identify a single instance where a competitor has defeated an innovator patent and entered the market. [39]

Evidence of the strength of biologic patents is demonstrated by the case of Erythropoietin. Erythropoietin or EPO, sold under the trade name Epogen® by Amgen, is the largest selling biotech drug ever. Amgen spent about $150 million to develop EPO, which was first approved in 1989, and since 2001, its sales have been greater than $2 billion per year.[40] Amgen has prevailed in numerous infringement actions concerning its patents on EPO, which according to Amgen, will not expire until 2015, 26 years after EPO was first marketed.[41]

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[38] Grabowski article, Figure 1 at page 481, citing DiMasi, J.A. and Grabowski, H.G., "The cost of biopharmaceutical R&D: is biotech different?," Manag. Decis. Econ. 28, 469-479 (2007).

[39] In this single instance, Teva and Sandoz (two generic firms) successfully litigated patents on human growth hormone (HgH) with the brand, Nova Nordisk, in order to market a generic version of HgH.

[40] Amgen 10Q for Year Ended Dec. 31, 2006, available at http://investors.amgen.com/phoenix.zhtml?c=61656&p=irol-sec.

[41] Amgen 10Q for Year Ended Dec. 31, 2007, available at http://investors.amgen.com/phoenix.zhtml?c=61656&p=irol-sec.

Epogen® is not the only example of a biologic subject to enforceable patents. It is joined by a number of additional best sellers that include Enbrel®, Rituxan®, Avastin®, Herceptin®, Avonex®, Synagis®, and Neupogen®, which all continue to enjoy patent protection.[42]

The biologics industry also argues that because many of their patents are "process" patents, they can be more easily defeated. What this argument ignores is that these process patents are not the only patents; they are additional patents that provide additional protection. Thus, even if they are more easily defeated than product patents, the brand still has more patent protection.

In sum, none of the factors identified by the brand biologics industry supports more exclusivity. If anything, there are arguments to be made that brand biologics should get less exclusivity than chemical drugs. For example, the high cost of these products means that they are likely to be much more profitable. This would mean that less exclusivity/intellectual property protection is needed to spur innovation because the brand can recoup its R&D costs more quickly. In addition, because generic biologics will be more difficult to make than generic chemical drugs, brand biologics are likely to face less generic competition than brand chemical drug makers. This also argues for less exclusivity. Finally, it will probably take FDA longer to approve a generic biologic than it does to approve a generic chemical drug. This effectively provides an extended period of exclusivity.

GRANTING MORE EXCLUSIVITY THAN THAT AFFORDED TO CHEMICAL DRUGS UNDER HATCH-WAXMAN WOULD HAVE ENORMOUS COST IMPLICATIONS

As stated above, since Hatch-Waxman was enacted in 1984, the pharmaceutical industry has been consistently profitable.[43] As further stated above, there is no basis for giving brand biologics more exclusivity than chemical drugs received under

[42] Citigroup Investment Research, Company Reports, "A Global Generic Biologics Guidebook" (November 6, 2006).
[43] *See, e.g.,* The Congressional Budget Office, "How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry," July 1998.

Hatch-Waxman. The biologics industry has not demonstrated that biologics cost more to develop, take longer to develop or have weaker patents, To the extent the biologics industry is arguing that they need 14 years of market exclusivity so that they will be on equal footing with the chemical drug industry, which BIO argues gets an average of 13.5 years of protection from generic competition under Hatch-Waxman, this argument too must fail. First, the average cited by BIO is misleading. As set forth above, this average includes all drug products, even those that are not big sellers, for which there is little competition and presumably little incentive to challenge patents. When the analysis is limited to products with profits over $250 million, the segment of drugs for which there is likely to be the greatest interest in competition and for which there are the greatest potential savings, a different picture emerges. The time between the approval of the innovator and the first generic approval for this segment of drugs was 10.25 years. The range of market protection is from 3.75 years to 16.7 years.

Second, the 10.25 year average protection is not from Hatch-Waxman exclusivity, which is five years, but is largely due to patents. And it is important to recognize that a 10-year exclusivity period is much more valuable than a 10 year patent. Exclusivity cannot be challenged. Also with 10 years of exclusivity, a company gets the best of both worlds – 10 years unless the patent time is stronger, in which case it gets the longer period.

Third, it is important to note that the 10-year average effective patent/exclusivity period provided to chemical pharmaceuticals would not be a basis for providing a 10-year exclusivity period for biologics. A ten-year exclusivity period then would be a minimum rather than an average. In order to demonstrate the impact of a 10-year exclusivity period, in Table 2 I have presented the chemical drugs where the first generic was approved between 2003 and 2008 and have shown the lost savings from delayed generic entry if chemical drugs had been subject to a 10- year exclusivity period rather than the combination of exclusivity and patent life given by Hatch-Waxman. If during the 2003-2008 period described above, there had been a minimum exclusivity of 10 years, then 22 of the 42 drugs listed would have received between one month and 6½ years of additional intellectual property

protection, and the lost savings to purchasers of drugs would have been 18.4 billion dollars.

If during the 2003-2008 period described above, there had been a minimum exclusivity of 14 years, as the biologics industry is asking, then 32 of the 42 drugs listed would have received between one month and 10½ years of additional intellectual property protection, and the lost savings to purchasers of drugs would have been 55.1 billion dollars. While the biologics market will undoubtedly act differently than the chemical drugs market, these calculations demonstrate that there is an enormous amount at stake if any exclusivity is awarded to brand biologic products beyond that which is available for chemical drugs under Hatch-Waxman.

CONCLUSION

As Congress is considering legislation to create a pathway for biosimilars, it must decide, as it did for chemical drugs, how much market protection will ensure innovation of biologics but not unnecessarily keep generics off of the market. In 1984, when Congress struck the balance for chemical drugs, it was breaking new ground so it had to rely on assumptions and predictions. Fortunately, Congress does not have to do that for biosimilars.

Hatch-Waxman, which has been in effect for almost 25 years, provides a tested framework. The balance struck by Hatch-Waxman has been working well for the chemical drug industry for more than two decades. The only reason to deviate from this framework would be if there were differences between chemical drugs and biologics that would make the Hatch-Waxman framework inappropriate for biologics. As set forth in this paper, those differences do not exist or at least they have not been identified by the biologics industry, which is advocating for 14 years of exclusivity. The biologics industry has presented no evidence to demonstrate that biologic patents are weaker than chemical drug patents such that additional exclusivity is needed. Similarly, there is no evidence that research and development costs are greater for biologics or that their development time is longer.

The biologics industry has put forth a request for two to three times the exclusivity provided under Hatch-Waxman. Rather than showing why more exclusivity is warranted, they are relying only on simulated economic analyses and predictions. While such analyses would be helpful and necessary if Congress had no other place to start, that is not the case here. Congress has the Hatch-Waxman approach on which to rely. Congress should reject the industry's attempt to ignore the balanced approach that has made Hatch-Waxman so successful. It is the patients, third party payors and State and Federal Governments who will pay if industry's approach is adopted.

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On Behalf of Barr Pharmaceuticals, Inc.

TABLE 1

Estimated Lost Savings Resulting from One-Year delay in Generic Approval
(First-Time Generic Approvals January 2003-April 2008 with Annual Brand Sales > $250m at the Time of Generic Approval)

Branded Product	Innovator	Brand Approved	Generic Product	First Generic Approval	Time Between Brand Approval and First Generic Approval	Annual Brand Sales at Time of First Generic Approval ($MM)	Lost Savings if Generic Delayed One Year Scenario 1a ($MM)	Lost Savings if Generic Delayed One Year Scenario 2b ($MM)	Lost Savings if Generic Delayed One Year Scenario 3c ($MM)
Aricept 5mg, 10mg Tablets	Eisai (donepezil)	25-Nov-96	donepezil	28-Apr-08	11y 5m	$983	$206	$344	$472
Mirapex 0.125mg, 0.25mg, 0.5mg, 1mg, 1.5mg T	Boehringer (pramipexole	1-Jul-97	pramipexole	19-Feb-08	10y 6m	$250	$53	$88	$120
Fosamax 5mg, 10mg, 35mg, 40mg, 70mg Table	Merck (alendronate)	29-Sep-95	alendronate	6-Feb-08	12y 4m	$1,400	$294	$490	$672
Trileptal 150mg, 300mg, 600mg Tablets	Novartis (oxcarbazepine)	14-Jan-00	oxcarbazepin	9-Oct-07	6y 10m	$532	$112	$186	$255
Actonel 5mg, 30mg, 35mg Tablets	P&G (risedronate)	27-Mar-98	risedronate	5-Oct-07	9y 6m	$791	$166	$277	$380
Coreg 3.125mg, 6.25mg, 12.5mg, 25mg Tablets	GSK (carvedilol)	14-Sep-95	carvedilol	5-Sep-07	12y 0m	$1,000	$210	$350	$480
Protonix 20mg, 40mg Tablets	Wyeth (pantoprazole)	2-Feb-02	pantoprazole	2-Aug-07	5y 6m	$2,100	$441	$735	$1,008
Paxil CR 12.5mg, 25mg	GSK (paroxetine)	16-Feb-99	paroxetine	29-Jun-07	8y 4m	$281	$59	$98	$135
Ambien 5mg, 10mg Tablet	Sanofi-Aventis (zolpidem	16-Dec-92	zolpidem	23-Apr-07	14y 4m	$920	$193	$322	$442
Aciphex 20mg	Eisai (rabeprazole)	19-Aug-99	rabeprazole	21-Feb-07	7y 6m	$1,100	$231	$385	$528
Valtrex 500mg, 1g Tablets	GSK (valacyclovir)	23-Jun-95	valacyclovir	31-Jan-07	11y 7m	$1,400	$294	$490	$672
Zofran ODT 4mg, 8mg Tablets	GSK (ondansetron)	27-Jan-99	ondansetron	26-Dec-06	7y 11m	$267	$56	$93	$128
Ditropan XL 5mg, 10mg Tablets	Alza (oxybutynin)	16-Dec-98	oxybutynin	9-Nov-06	7y 11m	$294	$62	$103	$141
Topamax 25mg, 100mg, 200mg Tablets	Ortho-McNeil (topiramate	24-Dec-96	topiramate	11-Sep-06	9y 9m	$1,500	$315	$525	$720
Lamictal 25mg 100mg 150mg 200mg Tablets	GSK (lamotrigine)	27-Dec-94	lamotrigine	30-Aug-06	11y 8m	$1,300	$273	$455	$624
Effexor 25mg, 37.5mg, 50mg, 75mg, 100mg Tab	Wyeth (venlafaxine)	28-Dec-93	venlafaxine	3-Aug-06	12y 7m	$2,200	$462	$770	$1,056
Topol-XL 25 mg Tablets	AstraZeneca (metoprolol	10-Jan-92	metoprolol	31-Jul-06	14y 6m	$888	$186	$311	$426
Mobic 7.5mg 15mg Tablets	Boehringer (meloxicam)	13-Apr-00	meloxicam	19-Jul-06	6y 3m	$914	$192	$320	$439
Zoloft 50mg, 100mg Tablets	Pfizer (sertraline)	30-Dec-91	sertraline	30-Jun-06	14y 6m	$2,600	$546	$910	$1,248
Zocor 5mg 10mg, 20mg, 40mg Tablets	Merck (simvastatin)	23-Dec-91	simvastatin	23-Jun-06	14y 6m	$3,200	$672	$1,120	$1,536
Lexapro 5mg, 10mg, 20mg Tablets	Forest (escitalopram)	14-Aug-02	escitalopram	22-May-06	3y 9m	$2,300	$483	$805	$1,104
Pravachol Tablets 10mg, 20mg, 40mg Tablets	BMS (pravastatin)	31-Oct-91	pravastatin	24-Apr-06	14y 6m	$1,300	$273	$455	$624
Zithromax Tablets 250mg, 500mg, 600mg	Pfizer (azithromycin)	18-Jul-96	azithromycin	14-Nov-05	9y 4m	$386	$81	$135	$185
Altace Capsules 1.25mg, 2.5mg, 5mg, 10mg	King (ramipril)	28-Jan-91	ramipril	24-Oct-05	14y 10m	$701	$147	$245	$336
Amaryl Tablets 1mg, 2mg, 4mg	Sanofi-Aventis (glimepirid	30-Nov-95	glimepiride	6-Oct-05	9y 11m	$263	$55	$92	$126
Norvasc Tablets 2.5mg, 5mg, 10mg	Pfizer (amlodipine)	13-Jul-92	amlodipine	3-Oct-05	13y 3m	$2,100	$441	$735	$1,008
Allegra Tablets 30mg, 60mg, 180mg	Sanofi-Aventis (fexofena	25-Feb-00	fexofenadine	31-Aug-05	5y 6m	$957	$201	$335	$459
Niaspan XR Tablets 500mg, 750mg, 1000mg	Abbott (niacin)	28-Jul-97	niacin	26-Apr-05	7y 9m	$381	$80	$133	$183
Allegra D Tablets 60mg/120mg	Sanofi-Aventis (fexofena	24-Dec-97	fexofenadine	14-Apr-05	7y 4m	$398	$84	$139	$191
Duragesic Patch 25, 50, 75, 100mcg/hr	Alza (fentanyl)	7-Aug-90	fentanyl	28-Jan-05	14y 5m	$569	$119	$199	$273
Wellbrtrin SR Tablets 200mg	GSK (bupropion)	4-Oct-96	bupropion	3-Dec-04	8y 2m	$529	$111	$185	$254
Celexa Tablets 10mg, 20mg, 40mg	Forest (citalopram)	17-Jul-98	citalopram	28-Oct-04	6y 3m	$857	$180	$300	$411
LevaquinTablets 250mg, 500mg	Ortho-McNeil (levofloxac	20-Dec-96	levofloxacin	15-Oct-04	7y 10m	$1,400	$294	$490	$672
Diflucan Tablets 50mg, 100mg, 150mg, 200mg	Pfizer (fluconazole)	29-Jan-90	fluconazole	29-Jul-04	14y 6m	$313	$66	$110	$150
Cipro Tablets 250mg, 500mg, 750mg	Bayer (ciprofloxacin)	22-Oct-87	ciprofloxacin	9-Jun-04	16y 8m	$250	$53	$88	$120
Oxycontin Tablets 10mg, 20mg, 40mg, 80mg	Purdue (oxycodone)	12-Dec-95	oxycodone	23-Mar-04	8y 3m	$1,700	$357	$595	$816
Glocotrol XL Tablets 10mg	Pfizer (glipizide)	26-Apr-94	glipizide	7-Nov-03	9y 7m	$290	$61	$102	$139
Glucophage ER Tablets 500mg	BMS (pravastatin)	3-Mar-95	metformin	28-Oct-02	7y 7m	$429	$90	$150	$206
Neurontin Capsules 100mg, 300mg, 400mg	Pfizer (gabapentin)	30-Dec-93	gabapentin	12-Sep-03	9y 9m	$2,100	$441	$735	$1,008
Paxil Tablets 10mg, 20mg, 30mg, 40mg	GSK (paroxetine)	29-Dec-92	paroxetine	30-Jul-03	10y 7m	$1,400	$294	$490	$672
Accutane Capsules 30mg	HLR (isotretinoin)	7-May-92	isotretinoin	20-Jun-03	11y 1m	$302	$63	$106	$145
Accupril Tablets 5mg, 10mg, 20mg, 40mg	Pfizer (quinapril)	19-Nov-91	quinapril	30-May-03	11y 6m	$535	$112	$187	$257
	Average time between brand approval and first generic approval:				**10y 3m**	**Tot Lost Savings**	**$9.1 billion**	**$15.2 billion**	**$20.8 billion**

a Assuming aggregate first year generic conversion of 70% with average generic price discount of 30% off the brand price.

b Assuming aggregate first year generic conversion of 70% with average generic price discount of 50% off the brand price.

c Assuming aggregate first year generic conversion of 80% with average generic price discount of 60% off the brand price.

ÎSources:
First-time generic approvals and approval date at http://www.fda.gov/cder/ogd/approvals/default.htm
Brand approval date and brand company at http://www.fda.gov/cder/ob/docs/querytn.htm
Annual brand sales in year of first generic approval athttp://drugtopics.modernmedicine.com/Top+200+Drugs

TABLE 2

Projected Lost Savings Resulting from 10-Year and 14-Year Exclusivity Period

(First-Time Generic Approvals January 2003-April 2008 with Annual Brand Sales > $250m at the Time of Generic Approval)

Branded Product	Innovator	Brand Approved	First Generic Approval *	Time Between Brand Approval and First Generic Approval	Annual Brand Sales at Time of First Generic Approval ($MM)	Estimated Lost Savings Had 10-year Exclusivity Been in Place ** ($MM)	Estimated Lost Savings Had 14-year Exclusivity Been in Place ** ($MM)
Aricept 5mg, 10mg Tablets	Eisai (donepezil)	25-Nov-96	28-Apr-08	11y 5m	$983	na	$889
Mirapex 0.125mg, 0.25mg, 0.5mg, 1mg, 1.5mg Tablets	Boehringer (pramipexole)	1-Jul-97	19-Feb-08	10y 6m	$250	na	$306
Fosamax 5mg, 10mg, 35mg, 40mg, 70mg Tablets	Merck (alendronate)	29-Sep-95	6-Feb-08	12y 4m	$1,400	na	$817
Trileptal 150mg, 300mg, 600mg Tablets	Novartis (oxcarbazepine)	14-Jan-00	9-Oct-07	6y 10m	$532	$590	$1,335
Actonel 5mg, 30mg, 35mg Tablets	P&G (risedronate)	27-Mar-98	5-Oct-07	9y 6m	$791	$138	$1,245
Coreg 3.125mg, 6.25mg, 12.5mg, 25mg Tablets	GSK (carvedilol)	14-Sep-95	5-Sep-07	12y 0m	$1,000	na	$700
Protonix 20mg, 40mg Tablets	Wyeth (pantoprazole)	2-Feb-02	2-Aug-07	5y 6m	$2,100	$3,307	$6,248
Paxil CR 12.5mg, 25mg Tablets	GSK (paroxetine)	16-Feb-99	29-Jun-07	8y 4m	$281	$164	$557
Ambien 5mg, 10mg Tablet	Sanofi-Aventis (zolpidem)	16-Dec-92	23-Apr-07	14y 4m	$920	na	na
Aciphex 20mg Tablets	Eisai (rabeprazole)	19-Aug-99	21-Feb-07	7y 6m	$1,100	$963	$2,503
Valtrex 500mg, 1g Tablets	GSK (valacyclovir)	23-Jun-95	31-Jan-07	11y 7m	$1,400	na	$1,184
Zofran ODT 4mg, 8mg Tablets	GSK (ondansetron)	27-Jan-99	26-Dec-06	7y 11m	$267	$195	$568
Ditropan XL 5mg, 10mg Tablets	Alza (oxybutynin)	16-Dec-98	9-Nov-06	7y 11m	$294	$214	$628
Topamax 25mg, 100mg, 200mg Tablets	Ortho-McNeil (topiramate)	24-Dec-96	11-Sep-06	9y 9m	$1,500	$131	$2,231
Lamictal 25mg 100mg 150mg 200mg Tablets	GSK (lamotrigine)	27-Dec-94	30-Aug-06	11y 8m	$1,300	na	$1,062
Effexor 25mg, 37.5mg, 50mg, 75mg, 100mg Tablets	Wyeth (venlafaxine)	28-Dec-93	3-Aug-06	12y 7m	$2,200	na	$1,091
Topol-XL 25 mg Tablets	AstraZeneca (metoprolol)	10-Jan-92	31-Jul-06	14y 6m	$888	na	na
Mobic 7.5mg 15mg Tablets	Boehringer (meloxicam)	13-Apr-00	19-Jul-06	6y 3m	$914	$1,199	$2,479
Zoloft 50mg, 100mg Tablets	Pfizer (sertraline)	30-Dec-91	30-Jun-06	14y 6m	$2,600	na	na
Zocor 5mg 10mg, 20mg, 40mg Tablets	Merck (simvastatin)	23-Dec-91	23-Jun-06	14y 6m	$3,200	na	na
Lexapro 5mg, 10mg, 20mg Tablets	Forest (escitalopram)	14-Aug-02	22-May-06	3y 9m	$2,300	$5,031	$8,251
Pravachol Tablets 10mg, 20mg, 40mg Tablets	BMS (pravastatin)	31-Oct-91	24-Apr-06	14y 6m	$1,300	na	na
Zithromax Tablets 250mg, 500mg, 600mg	Pfizer (azithromycin)	18-Jul-96	14-Nov-05	9y 4m	$386	$90	$662
Altace Capsules 1.25mg, 2.5mg, 5mg, 10mg	King (ramipril)	28-Jan-91	24-Oct-05	14y 10m	$701	na	na
Amaryl Tablets 1mg, 2mg, 4mg	Sanofi-Aventis (glimepiride)	30-Nov-95	6-Oct-05	9y 11m	$263	$8	$376
Norvasc Tablets 2.5mg, 5mg, 10mg	Pfizer (amlodipine)	13-Jul-92	3-Oct-05	13y 3m	$2,100	na	$551
Allegra Tablets 30mg, 60mg, 180mg	Sanofi-Aventis (fexofenadine)	25-Feb-00	31-Aug-05	5y 6m	$957	$1,507	$2,847
Niaspan XR Tablets 500mg, 750mg, 1000mg	Abbott (niacin)	28-Jul-97	26-Apr-05	7y 9m	$381	$300	$833
Allegra D Tablets 60mg/120mg	Sanofi-Aventis (fexofenadine)	24-Dec-97	14-Apr-05	7y 4m	$398	$371	$929
Duragesic Patch 25, 50, 75, 100mcg/hr	Alza (fentanyl)	7-Aug-90	28-Jan-05	14y 5m	$569	na	na
Wellbrtrin SR Tablets 200mg	GSK (bupropion)	4-Oct-96	3-Dec-04	8y 2m	$529	$339	$1,080
Celexa Tablets 10mg, 20mg, 40mg	Forest (citalopram)	17-Jul-98	28-Oct-04	6y 3m	$857	$1,125	$2,325
LevaquinTablets 250mg, 500mg	Ortho-McNeil (levofloxacin)	20-Dec-96	15-Oct-04	7y 10m	$1,400	$1,062	$3,022
Diflucan Tablets 50mg, 100mg, 150mg, 200mg	Pfizer (fluconazole)	29-Jan-90	29-Jul-04	14y 6m	$313	na	na
Cipro Tablets 250mg, 500mg, 750mg	Bayer (ciprofloxacin)	22-Oct-87	9-Jun-04	16y 8m	$250	na	na
Oxycontin Tablets 10mg, 20mg, 40mg, 80mg	Purdue (oxycodone)	12-Dec-95	23-Mar-04	8y 3m	$1,700	$1,041	$3,421
Glocotrol XL Tablets 10mg	Pfizer (glipizide)	26-Apr-94	7-Nov-03	9y 7m	$290	$42	$448
Glucophage ER Tablets 500mg	BMS (pravastatin)	3-Mar-95	28-Oct-02	7y 7m	$429	$363	$964
Neurontin Capsules 100mg, 300mg, 400mg	Pfizer (gabapentin)	30-Dec-93	12-Sep-03	9y 9m	$2,100	$184	$3,124
Paxil Tablets 10mg, 20mg, 30mg, 40mg	GSK (paroxetine)	29-Dec-92	30-Jul-03	10y 7m	$1,400	na	$1,674
Accutane Capsules 30mg	HLR (isotretinoin)	7-May-92	20-Jun-03	11y 1m	$302	na	$308
Accupril Tablets 5mg, 10mg, 20mg, 40mg	Pfizer (quinapril)	19-Nov-91	30-May-03	11y 6m	$535	na	$468
Average time between brand approval and first generic approval:				**10y 3m**		$18.4 billion	$55.1 billion

***** First generic approval date is the date of first ANDA approval issued by FDA as reported at http://www.fda.gov/cder/ob/docs/querytn.htm

****** Assuming generic utilization rate of 70% with average generic price discount of 50% off the brand price, based on annual brand sales at time of first generic entry.

Sources:

First-time generic approvals and approval date at http://www.fda.gov/cder/ogd/approvals/default.htm
Brand approval date and brand company at http://www.fda.gov/cder/ob/docs/querytn.htm
Annual brand sales in year of first generic approval athttp://drugtopics.modernmedicine.com/Top+200+Drugs