



The Hatch-Waxman Act: Over a Quarter Century Later

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Summary

Congressional interest in health-related issues has refocused attention on legislative efforts to provide both new as well as lower-cost pharmaceuticals for the marketplace. P.L. 98-417, the Drug Price Competition and Patent Term Restoration Act of 1984 (commonly known as the Hatch-Waxman Act), made significant changes to the patent laws as they apply to pharmaceutical products in an attempt to balance the need for innovative new drugs and the availability of less expensive generic products. The act created several practices intended to facilitate the marketing of generic drugs while permitting brand name companies to recover a portion of their intellectual property rights lost during the pharmaceutical approval process. Twenty-five years later, the impact of the act on the pharmaceutical industry may have implications for current congressional efforts to facilitate the development of new, inventive products while reducing costs to consumers.

Prior to the implementation of the Hatch-Waxman Act, 35% of top-selling drugs had generic competitors after patent expiration; now almost all do. The Generic Pharmaceutical Association points out that of 12,751 drugs listed in the Orange Book, 10,072 have generic substitutes available to consumers. Concurrently, the time to market for these generic products has decreased substantially. According to the Congressional Budget Office, in 1984 the average time between the expiration of a patent on a brand name drug and the availability of a generic was three years. Today, upon FDA approval a generic may be introduced immediately after patents on the innovator drug expire as companies are permitted to undertake clinical testing during the time period associated patents are in force. In cases where the generic manufacturer is the patent holder, a substitute drug may be brought to market before the patent expires.

Industry support for pharmaceutical research and development has grown since the passage of the legislation although some recent figures indicate reduced R&D spending by several companies. In the absence of the research, development, and testing performed by the brand name pharmaceutical companies, generic drugs would not exist. The provisions of the Hatch-Waxman Act permit the generic industry to rely on information generated and financed by the brand name companies to obtain approval for their product by the FDA. However, the pharmaceutical industry today differs significantly from what it was in the early 1980s when the legislation was enacted. The cost of developing a drug has doubled, as has the number of clinical trials necessary to file a new drug application. The number of participants required for these trials has tripled. As the rate of return on investments in a new drug declined 12%, manufacturers often spend R&D dollars on developing improved versions of, or new delivery methods for an existing product.

Many experts agree that the Drug Price Competition and Patent Term Restoration Act has had a significant effect on the availability of generic substitutes for brand name drugs. Yet, congressional concerns remain whether or not the balance inherent in the act remains appropriate over 25 years later.

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Introduction

Health-related issues before Congress have refocused attention on legislative efforts to provide both new as well as lower-cost pharmaceuticals for the marketplace. P.L. 98-417, the Drug Price Competition and Patent Term Restoration Act of 1984 (commonly known as the Hatch-Waxman Act),¹ made several significant changes to the patent laws as they apply to pharmaceutical products in an attempt to balance the need for innovative new drugs and the availability of less expensive generic products. Twenty-five years later, effects of the act on the pharmaceutical industry may have implications for current congressional efforts to facilitate the development of new, inventive products while reducing costs to consumers.

The Hatch-Waxman Act established several practices intended to facilitate the marketing of generic drugs while permitting brand name companies to recover a portion of their intellectual property rights lost during the pharmaceutical approval process. The legislative changes include methods for extending the term of a patent to reflect regulatory delays encountered in obtaining marketing consent from the FDA; a statutory exemption from patent infringement for activities associated with regulatory marketing approval for a generic version of a patented drug; establishment of mechanisms to challenge the validity of a pharmaceutical patent; and a reward for disputing the validity, enforceability, or infringement of a patented and approved drug. The act also affords the FDA certain authority to offer periods of data and marketing exclusivity for a pharmaceutical independent of the rights conferred by patents.

The provisions in the Hatch-Waxman Act differ from traditional infringement procedures associated with other patented products and processes. The company making a generic product is permitted to rely upon data paid for and compiled by the original manufacturer to establish the drug's safety and efficacy necessary to obtain FDA marketing approval. This expedited approval process may allow a bioequivalent drug to reach the market as soon as the patent on the original pharmaceutical expires. Nowhere else in U.S. patent law does such a robust "experimental use" exemption exist.

Overview of the Original Act

Accelerated Generic Drug Approval Process

Patents are issued by the United States Patent and Trademark Office (USPTO), generally for a term of 20 years from the date of filing. A patent grants its owner the right to exclude others from making, using, selling, offering to sell, or importing into the United States the patented invention. To be afforded patent rights, an invention must be judged to consist of patentable subject matter, possess utility, and be novel and nonobvious. The application must fully disclose and distinctly claim the invention for which protection is sought.

The grant of a patent does not provide the owner with an affirmative right to market the patented invention. Pharmaceutical products are also subject to marketing approval by the FDA. Federal laws typically require that pharmaceutical manufacturers show that their products are safe and

¹ 21 U.S.C. §355 and following.

effective in order to bring these drugs to the marketplace.² USPTO issuance of a patent and FDA marketing consent are distinct events that depend upon different criteria.

The Hatch-Waxman Act modified the 1952 Patent Act³ by creating a statutory exemption from certain claims of patent infringement in the pharmaceutical sector. Generic manufacturers may commence work on a generic version of an approved brand name drug any time during the life of the patent, so long as that work furthers compliance with FDA regulations. Although the act provides a safe harbor from patent infringement, it also requires would-be manufacturers of generic drugs to engage in a specialized certification procedure. The core feature of this process is that a request for FDA marketing approval is treated as an “artificial” act of patent infringement. This action is intended to allow judicial resolution of the validity, enforceability, and infringement of patent rights afforded by the USPTO.

Under P.L. 98-417, each holder of an approved new drug application (NDA) is required to list patents it believes would be infringed if a generic drug were marketed before the expiration of these patents. The FDA maintains this list of patents in its publication, *Approved Drug Products with Therapeutic Equivalence Evaluations*, commonly known as the “Orange Book.” The Orange Book provides generic pharmaceutical manufacturers with an accessible list of approved drugs that are potentially eligible for an “Abbreviated New Drug Application” (ANDA) or a “paper NDA” (a 505(b)(2) application). An ANDA or paper NDA permits the generic manufacturer to rely upon the safety and efficacy data of the original manufacturer when applying to the FDA for approval of a generic drug.

A generic firm must certify to the FDA its intentions with regard to each patent associated with the generic drug it seeks to market. Four possibilities exist under the 1984 Act: (1) that patent information on the drug has not been filed; (2) that the patent has already expired; (3) the date on which the patent will expire; or (4) that the patent is invalid or will not be infringed by the manufacture, use or sale of the drug for which the ANDA is submitted. These certifications are respectively termed paragraph I, II, III, and IV certifications. An ANDA certified under paragraphs I or II is approved immediately after meeting all applicable regulatory and scientific requirements. An ANDA certified under paragraph III must, even after meeting pertinent regulatory and scientific requirements, wait for approval until the drug’s listed patent expires.

An ANDA applicant filing a paragraph IV certification must notify the proprietor of the patent. The patent holder may bring a patent infringement suit within 45 days of receiving such notification. If the patent owner timely brings a patent infringement charge against the ANDA applicant, then the FDA must suspend approval of the ANDA until (1) the date of the court’s decision that the listed drug’s patent is either invalid or not infringed; (2) the date the listed drug’s patent expires, if the court finds the listed drug’s patent infringed; or (3) subject to modification by the court, the date that is 30 months from the date the owner of the listed drug’s patent received notice of the filing of a Paragraph IV certification.

Once the brand name company indicates an intent to bring a patent infringement suit against the generic company as a result of the paragraph IV filing, the FDA is prohibited from approving the drug in question for 30 months or until such time that the patent is found to be invalid or not infringed. If, prior to the expiration of 30 months, the court holds that the patent is invalid or

² 21 U.S.C. §355(b).

³ P.L. 82-593; 35 U.S.C. §1 and following.

would not be infringed, then the FDA will approve the ANDA when that decision occurs. Conversely, if the court holds the patent is not invalid and would be infringed by the product proposed in the ANDA prior to the expiration of 30 months, then the FDA will not approve the ANDA until the patent expires.

Under the original Hatch-Waxman Act, the first generic applicant to file a paragraph IV certification was awarded a 180-day market exclusivity period by the FDA as a reward for challenging the patent associated with an approved pharmaceutical. This provision was intended to encourage generic applicants to challenge a listed patent for an approved drug product. The 180-day market exclusivity period ordinarily began on the earliest of two dates: (1) the day the drug is first commercially marketed; or (2) the day a court decision holds that the patent which is the subject of the certification is invalid or not infringed. The interpretation of a “court decision” included the decision of a U.S. district court. A successful defense of a patent infringement suit was not necessary to obtain this exclusivity period.

Patent Term Restoration

The 1984 legislation also provides for the extension of patent term. Ordinarily, patent term is set to 20 years from the date the patent application is filed.⁴ For pharmaceutical patents, the patent term may be extended for a portion of the time lost during clinical testing. More specifically, this term extension is equal to half of the time between the effective date of the investigational new drug application and the submission of the NDA, plus the entire time lost during FDA approval of the NDA.⁵

Certain caps on the length of the term restoration are established. The entire patent term restored may not exceed five years. Further, the remaining term of the restored patent following FDA approval of the NDA may not exceed 14 years.⁶ The legislation also provides that the patentee must exercise due diligence to seek patent term restoration from the USPTO, or the period of lack of diligence will be offset from the augmented patent term.⁷

Patent term extension does not occur automatically. The patent owner or its agent must file an application with the USPTO requesting term extension within 60 days of obtaining FDA marketing approval. In addition, only one patent may be subject to term extension with respect to each FDA-approved product. In the event the NDA holder owns multiple patents that pertain to a particular approved drug, it must select one of them for term extension.

Data Exclusivity

Provisions that create data exclusivity for certain FDA-approved drugs are included in the legislation. The term “data exclusivity” refers to a period of time during which the FDA affords

⁴ 35 U.S.C. §156. Prior to United States adherence to the World Trade Organization, patents were granted a term of 17 years from the date of issuance. On June 8, 1995, the effective patent term was changed to 20 years measured from the date the patent application was filed. Patents in existence as of June 8, 1995, or patents that issued from applications pending at the USPTO as of the date, have a term equal to the greater of 17 years from issuance or 20 years from grant.

⁵ 35 U.S.C. §156.

⁶ 35 U.S.C. §156(c).

⁷ 35 U.S.C. §156(d)(2)(B).

an approved drug protection from competing generic applications by limiting FDA's use of the innovator pharmaceutical's proprietary safety and efficacy information during the generic approval process for a specific period of time. A grant of data exclusivity does not depend on the existence of patent protection.

The length of data exclusivity is contingent on whether or not the drug is considered a new chemical entity (NCE). An NCE drug is defined as an approved drug which consists of active ingredients, including the ester or salt of an active ingredient, none of which has been approved in any other full NDA.⁸ If the approved drug is not an NCE, then the FDA may not approve an ANDA for a generic version of the approved drug until three years after the approval date of the pioneer NDA.⁹

In contrast, if the approved drug is an NCE, then a would-be generic manufacturer cannot submit an ANDA until five years after the date of the approval of the pioneer NDA.¹⁰ The effect of this provision is to restrict a potential generic manufacturer from bringing a product to market for five years plus the length of the FDA review of the ANDA.

Amendments: The Medicare Prescription Drug and Modernization Act of 2003

Title XI of P.L. 108-173, the Medicare Prescription Drug and Modernization Act of 2003, as signed into law by the President on December 8, 2003, made several changes to the original Hatch-Waxman Act that were designed to decrease the time needed to bring generic pharmaceuticals to the marketplace. The new provisions were designed to "close some of the loopholes" critics argued that the brand name companies used to delay the introduction of generic products. The legislation permits only one automatic 30-month stay on FDA approval of drugs for which patents are listed in the Orange Book at the time of a paragraph IV ANDA or 505(b)(2) filing. The applicant may not amend the paragraph IV certification to include a drug different from that approved by the FDA, but may amend the application if seeking marketing consent for a different strength of the same drug. Modifications to the default 30-month stay are allowed based on district court judgments.

The applicant for an abbreviated new drug approval containing a paragraph IV certification must provide the brand name company and any patent owners with notice of such action within 20 days of filing with the FDA. Upon receipt of this notice, the brand name manufacturer has 45 days within which to file an infringement suit and thereby be eligible for the automatic 30-month stay.

In a situation where a patent holder does not file an infringement action within 45 days of notification of a paragraph IV ANDA, the ANDA applicant may request that a district court issue a declaratory judgment regarding the validity of the patent. In order to request a declaratory judgment, the generic manufacturer must have made available to the brand name company and the patent owners the confidential information contained in the ANDA application.

⁸ 21 U.S.C. §355(j)(4)(D)(i).

⁹ 21 U.S.C. §355(j)(4)(D)(iii).

¹⁰ 21 U.S.C. §355(j)(D)(ii).

If sued, the generic firm may file a counter claim to require the patent holder make changes in the Orange Book listings. The generic firm may request that certain patents be delisted because they do not claim the drug to which they are attached. No monetary damages are to be awarded.

The Food and Drug Administration may approve the ANDA or 505(b)(2) filing containing a paragraph IV certification on the date of an appeals court decision, the date of a settlement order or consent decree, or when a district court decision is not appealed.

The 180-day market exclusivity is to begin with the first commercial marketing of the generic drug (rather than being triggered by a “court decision” as under the original legislation). This exclusivity can be forfeited in certain situations including failure to market under specific time constraints, withdrawal of the application, amendment of the certification, failure to obtain approval from the FDA, expiration of all patents, or the determination by the Federal Trade Commission or the Assistant Attorney General that an agreement between the brand name and generic firms violates antitrust laws. Subsequent applicants would not be permitted the 180-day exclusivity.

Multiple generic firms may qualify for the 180-day market exclusivity if several ANDA applicants file a substantially complete application on the same day.

Agreements tendered between brand name companies and generic firms concerning the production, sale, or marketing of a pharmaceutical or a 180-day market exclusivity must be filed with the Federal Trade Commission and the Department of Justice within 10 days of the agreement.

Implementation

Many experts agree that the Drug Price Competition and Patent Term Restoration Act has had a significant effect on the availability of generic substitutes for brand name drugs. Prior to the law, 35% of top-selling drugs had generic competitors after patent expiration; now almost all do.¹¹ The Generic Pharmaceutical Association (GPhA) points out that of 12,751 drugs listed in the Orange Book, 10,072 have generic substitutes available to consumers.¹² Concurrently, the time to market for these generic products has decreased substantially. According to the Congressional Budget Office (CBO), prior to passage of the act in 1984, the average time between the expiration of a brand name patent and the availability of a generic was three years. Today, upon FDA approval a generic may be introduced immediately after patents on the innovator drug expire, as companies are permitted to undertake clinical testing during the time period associated patents are in force. “By streamlining the approval process for a generic drug form, the Hatch-Waxman Act reduced the average delay between patent expiration and generic entry into the consumer market from *greater than three years to less than three months* for top-selling drugs.”¹³ In cases where the

¹¹ Michael A. O’Shea and Christopher M. Mikson, “The Hatch-Waxman Act: Still Critical, Still in Flux,” *The National Law Journal*, January 23, 2006.

¹² Generic Pharmaceutical Association, *Facts at a Glance*, available at <http://www.gphaonline.org/about-gpha/about-generics/facts>.

¹³ David A. Holdford and Bryan A. Liang, *The Growing Influence of Generic Drugs: What it Means to Pharmacists and Physicians*, Power-Pak C.E., December 2006, available at <http://www.centad.org/seminar/4.%20Generics/GrowingInfluencePowewrPak2006.pdf>.

generic manufacturer is the patent holder, a substitute drug may be brought to market before the patent expires.

According to one analysis, 18.6% of U.S. prescriptions were written for generic products in 1984, the year the Hatch-Waxman Act was passed, while today they account for 63% of all U.S. prescriptions.¹⁴ Similarly, CBO found that in 1980 13% of prescriptions for multi-source drugs were filled by generic prescriptions.¹⁵ By 2009, GPhA maintains that 74.2% of prescriptions were filled by generics (65.6% by unbranded generics, 8.6% by generics produced or licensed by the brand name company).¹⁶ The latest data from the IMS Institute for Healthcare Informatics demonstrate that in 2011, 80% of all retail prescriptions were filled by generics.¹⁷

While generics fill over two-thirds of written prescriptions, they represent a much smaller portion of the sales in the United States. According to GPhA, in 2009 unbranded generics generated 10.5% of U.S. pharmaceutical sales, branded generics generated 12.4% of sales, and brands generated 77.1% of total U.S. sales.¹⁸ Later data from IMS Institute for Healthcare Informatics indicates that generics made up 27% of U.S. sales in 2011.¹⁹ Projecting into the future, IMS argues that by 2016, 44% of 2011 spending on brand products in the U.S. market will shift to generic drugs.²⁰

If generic versions of the brand pharmaceutical are easy to produce, multiple competitors often come to market at prices that are up to 80% below the innovator drug.²¹ Studies have demonstrated that in the late 1980s a branded drug that went off patent would lose between 15% and 30% of sales volume within the first two years; in 2001 when Prozac faced generic competition, more than 70% of the market for the innovator pharmaceutical was lost within two months.²² However, prices for generic drugs themselves tend to fall over time.²³ In addition, the market share of generic drugs is not just dependent on prices; other factors such as perception of quality, as well as first to market, may make a difference.²⁴

Industry funding for pharmaceutical research and development has grown significantly since passage of the act in 1984. A Congressional Budget Office report notes that annual spending on R&D by drug companies has increased from approximately \$8 billion in 1984 to \$50 billion in

¹⁴ Richard G. Frank, "The Ongoing Regulation of Generic Drugs," *The New England Journal of Medicine*, November 15, 2007, 1993.

¹⁵ Congressional Budget Office, *How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry*, (Washington, DC, July 1998), available at <http://www.cbo.gov>.

¹⁶ Generic Pharmaceutical Association, *Generics, A Steady Course in a Sea of Change, 2010*, 17, available at <http://www.gphaonline.org/sites/default/files/Annual%20Report%202010.pdf>.

¹⁷ IMS Institute for Healthcare Informatics, *The Use of Medicines in the United States: Review of 2011*, April 2012, 26, available at <http://www.theimsinstitute.org>.

¹⁸ Ibid.

¹⁹ *The Use of Medicines in the United States: Review of 2011*, 26.

²⁰ IMS Institute for Healthcare Informatics, *The Global Use of Medicines: Outlook Through 2016*, July 2012, 24, available at <http://www.theimsinstitute.com>.

²¹ Herman Saftlas, "Industry Surveys, Healthcare: Pharmaceuticals," *Standard & Poor's*, June 4, 2009, 29, available at <http://www.standardandpoors.com>.

²² Richard G. Frank, "Regulation of Generic Drugs," *The New England Journal of Medicine*, August 30, 2007, 842.

²³ Henry G. Grabowski and John M. Vernon, "Brand Loyalty, Entry, and Price Competition in Pharmaceuticals After the 1984 Act," *Journal of Law and Economics*, October 1992, 347.

²⁴ Ibid.

2008 (2008 constant dollars). In addition, the average increase in private sector R&D over the time period from 1980 to 2008 was almost 9% per year.²⁵

However, other studies indicate that that R&D spending has recently declined. An analysis of the top 50 global pharmaceutical companies (as determined by their 2010 healthcare revenue) found that 18 of these firms, including AstraZeneca and GlaxoSmithKline, decreased their annual R&D spending from the previous year.²⁶ Similarly, research performed by CMR International noted that “R&D expenditure continued to drop in 2010 to an estimated three year low of \$68 billion, which is in stark contrast to the growth rate leading up to 2008.”²⁷ Research and development funding by members of the Pharmaceutical Research and Manufacturers Association (PhRMA) dropped an estimated 2.4% in 2011 from the record high spending the previous year.²⁸

In the absence of the research, development, and testing performed by the brand name pharmaceutical companies, generic drugs would not exist. The provisions of the Hatch-Waxman Act permit the generic industry to rely on information generated and financed by the brand name companies to obtain approval for their product by the FDA. However, the pharmaceutical industry today differs from what it was in the early 1980s. The cost of developing a drug has doubled²⁹ to where it now takes over \$1 billion to bring a new drug to market.³⁰ The cost of developing a generic is approximately \$1 million to \$2 million.³¹ The number of clinical trials necessary to file a new drug application has doubled since 1980 and the number of participants in these trials has tripled.³² Thus, the rate of return from investment in a new drug has dropped by 12% over this time period.³³

Concurrently, companies appear to be moving away from the development of drugs that address large patient populations, but for which they cannot charge high prices, toward more specialized medicines, primarily biologics, that may be used by fewer patients, but for which high prices can be secured. In 2007, 55 blockbuster drugs were considered specialized products, up from 12 in 2001.³⁴ In 2011, 25% of total U.S. spending for traditional medicines was for specialty products.³⁵

²⁵ Congressional Budget Office, “Pharmaceutical R&D and the Evolving Market for Prescription Drugs,” *Economic and Budget Issue Brief*, October 26, 2009, 3.

²⁶ *Top 50 Pharmaceutical Companies and Their Pipelines 2011*, PharmaLive.com Special Report, September 2011, 1 and 4, available at http://www.pharmalive.com/special_reports/sample.cfm?reportID=359.

²⁷ CMR International, “2011 Pharmaceutical R&D Factbook,” as noted in *Drug Dropout in Clinical Trials is at Unsustainable Levels, According to Thomson Reuters*, CMR International, June 27, 2011 Press Release, available at http://thomsonreuters.com/content/press_room/science/R+D-CMR-factbook-2011.

²⁸ PhRMA, *Pharmaceutical Industry 2012 Profile*, inside front cover, available at http://www.phrma.org/sites/default/files/159/phrma_industry_profile.pdf.

²⁹ *The Hatch-Waxman Act: Still Critical, Still in Flux*.

³⁰ Christopher Paul Adams and Van Vu Brantner, “Spending on New Drug Development,” *Health Economics*, (published online 26 February 2009) Epub ahead of print.

³¹ Henry Grabowski, “Patents, Innovation and Access to New Pharmaceuticals,” *Journal of International Economic Law*, 2002, 852, available at <http://jiel.oxfordjournals.org/cgi/reprint/5/4/849>, and Henry Grabowski, “Patents and New Product Development in the Pharmaceutical and Biotechnology Industries,” in *Science and Cents: Exploring the Economics of Biotechnology, Proceedings of a 2002 Conference sponsored by the Federal Reserve Bank of Dallas*, 90, available at <http://www.dallasfed.org/research/pubs/science/grabowski.pdf>

³² Gregory J. Glover, “The Influence of Market Exclusivity on Drug Availability and Medical Innovations,” *The AAPS Journal*, August 3, 2007, E313.

³³ *The Hatch-Waxman Act: Still Critical, Still in Flux*.

³⁴ PriceWaterhouseCoopers, *Pharma 2020: Marketing the Future*, February 2009, 13, available at <http://www.pwc.com/pharma>.

“Thus, the specialty category continues to be a major focus of new drug development and comprises a significant percentage of new approvals.”³⁶

Since passage of the Hatch-Waxman Act, the number of patents on each marketed pharmaceutical has increased such that “to shield themselves against competition, manufacturers now carry an average of 10 patents for each drug—as compared with an average of 2 a decade ago.”³⁷ Similarly, manufacturers are spending R&D dollars to develop new and improved forms of the original drug or new delivery methods (for example extended release tablets, liquid formulations) as related patents expire. The new version of the drug can be patented and users encouraged to switch to the new product.³⁸ According to PriceWaterhouseCoopers, “In 2007, only eight of the 27 new therapies launched worldwide were the first of their kind.... More than half were ‘me-too’ treatments with at least three predecessors.”³⁹ Another study found that

in 2004, more than 20% of the money 10 of the [world’s] largest pharmaceutical companies invested in R&D went to line extensions and other work, as distinct from new development projects. In smaller companies, the percentage was over 40%.⁴⁰

Between 1988 and 2006, over 500 pharmaceuticals received patent term extensions.⁴¹ In 2006, 26 of the 40 top selling drugs in the United States had patent terms restored. During the patent restoration period, about 20% of gross revenues may be generated.⁴² With the extension provided by the Hatch-Waxman Act, total time on the market prior to generic competition has been estimated at 11.5 years for drugs with annual sales of more than \$100 million.⁴³ Additional research indicates

(a) that newly approved NCEs have come on to the market with about eight to ten years of effective patent life or market exclusivity, and (b) that since 1997 the average exclusivity periods for newly approved NCEs have declined.⁴⁴

Despite the extension of patent protection afforded by the legislation, many drugs will soon lose patent protection.⁴⁵ PriceWaterhouseCoopers notes that in 2006, 90% of revenues generated by the large pharmaceutical companies came from drugs that were on the market for more than five

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³⁵ IMS Institute for Healthcare Informatics, *The Use of Medicines in the United States: Review of 2011*, April 2012, 27, available at <http://www.theimsinstitute.org>.

³⁶ Medco, *2011 Drug Trend Report*, 42, available at <http://www.drugtrendreport.com/2011-report>.

³⁷ *The Ongoing Regulation of Generic Drugs*, 1994.

³⁸ *Ibid.*

³⁹ *Pharma 2020: Marketing the Future*, 11.

⁴⁰ PriceWaterhouseCoopers, *Pharma 2020: The Vision*, June 2007, 8, available at <http://www.pwc.com/pharma>.

⁴¹ Charles Clift, “The value of patent term extensions to the pharmaceutical industry in the USA,” *Journal of Generic Medicines*, April 2008, 201.

⁴² *Ibid.*, 207-208.

⁴³ Pharmaceutical Research and Manufacturers Association, *Key Industry Facts About PhRMA*, available at http://www.phrma.org/key_industry_facts_about_phrma.

⁴⁴ James W. Hughes, Michael J. Moore, and Edward A. Snyder, “Napsterizing” *Pharmaceuticals: Access, Innovation, and Consumer Welfare*, National Bureau of Economic Research, October 2002, 7, available at <http://www.nber.org/papers/w9229>.

⁴⁵ For additional discussion see CRS Report R42399, *Drug Patent Expirations: Potential Effects on Pharmaceutical Innovation*, by (name redacted).

years and were therefore rapidly moving toward generic competition.⁴⁶ The estimates on the amount of sales lost by brand name companies when a drug loses patent protection vary. PriceWaterhouseCoopers argues that “the leading pharmaceutical companies will lose between 14% and 41% of their existing revenues as a result of patent expiries [sic],”⁴⁷ which exposes “an estimated \$157 billion worth of sales (measured in 2005 dollars) to generic competition.”⁴⁸ EvaluatePharma puts the amount of U.S. sales affected by patent expirations between 2011 and 2016 at \$133 billion; 2012 is expected to be the most severe with \$33.2 billion in sales affected.⁴⁹ The results of subsequent generic entry can be dramatic:

As more [generic] competitors enter the field, prices drop even further. For example, almost as soon as GlaxoSmithKline’s popular cardiovascular drug Coreg (\$1.7 billion in US sales for the 12 months trailing June 2007, according to IMS Health, Inc.) lost patent protection in September 2007, more than a dozen generic competitors entered the market, causing prices to fall immediately and dramatically. Within a month, generics accounted for 85% of the Coreg market, with prices substantially lower than those of the branded product prior to its patent expiration.⁵⁰

While there are various compilations of drugs that are expected to go off patent, it is apparent that many innovator pharmaceuticals will be affected. Lipitor, the world’s best-selling drug, lost patent protection at the close of 2011. Among the 2011 top selling drugs in the U.S. market that went off patent in 2012 are Plavix (\$5.7 billion), Singulair (\$4.4 billion), Seroquel (\$3.8 billion), Actos (\$2.8 billion), Lexapro (\$2.7 billion), and Diovan/Diovan HCT (\$1.7 billion and \$1.5 billion respectively).⁵¹ Other drugs that are expected to lose patent protection in the near future include Cymbalta (2011 U.S. sales of \$3.4 billion), Nexium (2011 U.S. sales of \$5.5 billion), Celebrex (\$1.6 billion), Nasonex (\$1.1 billion), Abilify (\$4.8 billion), Enbrel (2011 U.S. sales of \$1.3 billion), Crestor (\$3.9 billion) and Humira (\$1.3 billion).⁵²

The loss of patent protection on these drugs is occurring at a time when some experts claim that innovation and productivity has stalled in the pharmaceutical industry. According to Jean-Pierre Garnier, chief executive officer of GlaxoSmithKline, the value of “Big Pharma” is diminishing because of declining R&D productivity.⁵³ The pharmaceutical industry is particularly research intensive. In 2011, total worldwide spending on R&D was estimated at \$135 billion, with 18.8% of sales reinvested in R&D according to EvaluatePharma.⁵⁴ Members of PhRMA invested 21.1%

⁴⁶ *Pharma 2020: The Vision*, 6.

⁴⁷ *Ibid.*, 9.

⁴⁸ *Ibid.*, 6.

⁴⁹ EvaluatePharma, *Patent Storm Gathering Strength*, January 28, 2011, available at <http://www.evaluatepharma.com/Universal/View.aspx?type=Story&id=235841&isEPVantage=yes>.

⁵⁰ *Industry Surveys, Healthcare: Pharmaceuticals*, 29.

⁵¹ Data derived from Express Scripts/Medco, *Estimated Dates of Possible First time Generic/Rx-to-OTC Market Entry*, June 2012, available at https://host1.medcohealth.com/art/corporate/anticipatedfirsttime_generics.pdf; Express Scripts/Medco, *First-time Approved Generics: 2012**, August 13, 2012, available at https://host1.medcohealth.com/art/corporate/firsttime_generics.pdf; and Food and Drug Administration, *Original Abbreviated New Drug Application (ANDA) Approvals*, available at <http://www.fda.gov>.

⁵² *Estimated Dates of Possible First time Generic/Rx-to-OTC Market Entry*, June 2012.

⁵³ Jean-Pierre Garnier, “Rebuilding the R&D Engine in Big Pharma,” *Harvard Business Review*, May 1, 2008, 70.

⁵⁴ EvaluatePharma, *World Preview 2018, Embracing the Patent Cliff*, June 2012, 15, available at <https://www.evaluatepharma.com/secure/FileResourceDownload.aspx?id=98a75eab-95f6-41d8-903f-4732848fd78>.

of domestic sales in domestic R&D during 2011.⁵⁵ The Congressional Budget Office reports that “pharmaceutical firms invest as much as five times more in research and development, relative to their sales, than the average U.S. manufacturing firm.”⁵⁶ However, while pharmaceutical R&D expenditures have increased substantially over the past 15 years, drug approvals have remained relatively flat.⁵⁷ Research by Standard & Poors found that there is

a relative dearth of innovative new products launched in recent years relative to funds invested in R&D. According to the Pharmaceutical Research and Manufacturers Association ... US drug industry R&D spending expanded 30% from 2004 through 2008. Yet, the number of FDA-approved new molecular entities (NMEs) and novel biologics declined to 24 from 36 over the same period. This attrition occurred despite important advances in R&D technology platforms, such as rational drug design and genomics, that occurred earlier in the decade.⁵⁸

In addition to a decline in the number of new drug approvals, there is concern in the healthcare community that the number of products in the pipeline are insufficient to make up for losses to generics after patent expiration. According to one analysis, only 4 of the 10 major pharmaceutical companies have drugs in clinical trials that are “sufficiently valuable to offset these losses.”⁵⁹ The scarcity of new products in clinical trials may be a result of a situation that

as more targets are discovered, the body of knowledge required to understand them, let alone use them for new therapies, increases dramatically, which delays the time when new or better therapies become available. In short, there can be sharply diminishing returns in drug R&D.⁶⁰

Other experts maintain that counting NMEs is not an accurate measure of productivity. It is argued that the number of NME approvals has remained stable over the long term despite year to year changes. While R&D investments have increased, between 25% and 30% of R&D spending is directed at finding new indications for existing products. Thus, basing an assessment of decreased productivity on the number of new NMEs may not be accurate since a significant portion of the R&D spending has led to increased use of already approved drugs.⁶¹

An additional explanation for the slowdown in new drug approvals may be that the “easy” drugs have been developed. The targets of new pharmaceuticals are more complex and chronic diseases that require more complicated clinical trials.⁶² The time frame between research and the introduction of a product in the marketplace tends to be particularly long in the pharmaceutical arena. Experts maintain that it generally takes 12 to 15 years to bring a new drug from discovery

⁵⁵ *Pharmaceutical Industry 2012 Profile*, inside front cover.

⁵⁶ Congressional Budget Office, *Research and Development in the Pharmaceutical Industry*, October 2006, 9.

⁵⁷ Ernst & Young, *Beyond Borders, Global Biotechnology Reports 2008*, 18, available at <http://www.ey.com/beyondborders>.

⁵⁸ *Industry Surveys, Healthcare: Pharmaceuticals*, 16.

⁵⁹ PriceWaterhouseCoopers, *Pharma 2020: Virtual R&D*, June 2008, 2, available at <http://www.pwc.com>.

⁶⁰ Fabio Pammolli and Massimo Riccaboni, “Market Structure and Drug Innovation,” *Health Affairs*, January/February 2004, 49.

⁶¹ William S. Comanor, “The Economics of Research and Development in the Pharmaceutical Industry,” in Frank A. Sloan and Chee-Ruey Hsieh, eds, *Pharmaceutical Innovation*, (Cambridge University Press, 2007), 66-67.

⁶² *Beyond Borders, Global Biotechnology Report 2008*, 18.

to market.⁶³ The basic research leading to discovery may even begin many years prior to discovery. Therefore, it is argued, any productivity gap is short-term as new drugs move toward approval.⁶⁴ According to Boston University's Iain Cockburn,

These concerns about productivity are almost surely overblown: if past experience is any guide, the recent surge in R&D spending should generate a commensurate increase in new drug approvals of the next three to ten [years].... Today's new drugs are the result of R&D expenditures stretching back decades into the past, and undertaken by many different institutions.⁶⁵

Selected Issues

The implementation of the provisions of the Hatch-Waxman Act has raised several issues that have become the focus of congressional discussion. Among these concerns are an increase in the introduction of "authorized generics" marketed by brand name companies in response to the loss of revenue that accompanies the introduction of a generic product. Additionally, patent-related litigation has been replaced in certain situations by settlements between brand name and generic firms that include payments to the generic company in exchange for an agreement not to market the product. Concurrently, Congress is considering legislation to extend the act's accelerated marketing approach to biologic drugs. These issues are discussed briefly below; a detailed analysis of each can be found in the referenced CRS reports.

Authorized Generics⁶⁶

An "authorized generic" is a pharmaceutical that is marketed by or on behalf of a brand name drug company, but is sold under a generic name.⁶⁷ Authorized generics are thus similar to "private label" products, which are manufactured by one firm but sold under the brand of another. Either the innovator drug company can authorize another firm to make a generic version of their product or the company can manufacture its own generic. The arrangement to offer an authorized generic is often made at the point where patent protection is soon to be lost. The authorized version may be brought to the market prior to or on the same day as a generic drug approved by the FDA and manufactured by a company that has won a paragraph IV challenge. Such arrangements allow the innovator firm to recover some of the sales income on a drug that will become widely available in

⁶³ John A. Vernon, *Testimony at Hearings on Prescription Drug Price Inflation: Are Prices Rising Too Fast?*, House Committee on Energy and Commerce, December 8, 2009, 4 and Congressional Budget Office, "Pharmaceutical R&D and the Evolving Market for Prescription Drugs," *Economic and Budget Issue Brief*, October 26, 2009, 4.

⁶⁴ Boston Consulting Group, *Rising to the Productivity Challenge, A Strategic Framework for Biopharma*, July 2004, 4, available at <http://www.bcg.com/documents/file14392.pdf>.

⁶⁵ Iain Cockburn, *Blurred Boundaries: Tensions Between Open Scientific Resources and Commercial Exploitation of Knowledge in Biomedical Research*, April 30, 2005, 2, available at <http://people.bu.edu/cockburn/cockburn-blurred-boundaries.pdf>.

⁶⁶ For a detailed discussion see CRS Report RL33605, *Authorized Generic Pharmaceuticals: Effects on Innovation*, by (name redacted).

⁶⁷ Leila Abboud, "'Authorized Generics' Duel Grows," *Wall Street Journal*, March 25, 2004 and Leila Abboud, "Drug Makers Use New Tactic to Ding Generic-Drug Firms," *Wall Street Journal* January 27, 2004.

generic form. According to GPhA, in 2007, 9.3% of prescriptions filled by generic drugs were filled by branded generics, which accounted for 10.3% of generic sales.⁶⁸

There are potential benefits and costs to the consumer of these actions. On the one hand, authorized generics may dissuade other firms from filing paragraph IV challenges to brand name patents if the often significant financial investments cannot be recouped through the 180-day market exclusivity period. Thus, potentially invalid patents may delay the introduction of a generic version of certain pharmaceuticals. Conversely, even brand name authorized generics are less expensive than the innovator drug and often can be made available prior to patent expiration. In addition, through the introduction of an authorized generic, two lower cost products can be made available to the consumer. While research shows these actions may adversely affect the generic company, the brand name firm and the public benefit.⁶⁹

Authorized generics practice has proven controversial due to the Hatch-Waxman Act's architecture and incentive structures. Some commentators have voiced concerns that the introduction of authorized generics, particularly during the 180-day market exclusivity granted to the independent generic firm that brought a paragraph IV challenge, thwarts the policy goal of encouraging the introduction of generic pharmaceuticals.⁷⁰ In particular, critics argue that the use of authorized generics may discourage firms from filing paragraph IV patent challenges if their litigation expenses cannot be recouped through the 180-day market exclusivity period.⁷¹ As antitrust attorney David A. Balto explains:

The bounty from challenging a patent is very important. Pharmaceutical patent litigation is a multimillion-dollar proposition. But for the potential reward of six-month exclusivity that represents the vast majority of potential profits from generic entry, many firms might forgo challenging patents.⁷²

For example, the FDA ruled that the generic manufacturer Apotex was entitled to 180-day exclusivity for its version of the anti-depressant drug Paxil® in 2003. The brand name drug company, GlaxoSmithKline, introduced an authorized generic version of Paxil®. Although Apotex anticipated sales of up to \$575 million during the 180-day generic exclusivity period, its sales were reported to be between \$150 million and \$200 million.⁷³ In a 2004 filing with the FDA, attorneys for Apotex asserted "that the authorized generic crippled Apotex's 180-day exclusivity—it reduced Apotex's entitlement to about two-thirds—to the tune of approximately \$400 million."⁷⁴

In addition, brand name firms commonly introduce authorized generics on the eve of generic competition. Without an independent generic patent challenger in the first instance, brand name

⁶⁸ *Generic Pharmaceutical Association Annual Report*, 24.

⁶⁹ Morton I. Kamien and Israel Zang, "Virtual Patent Extension by Cannibalization," *Southern Economic Journal*, July 1999.

⁷⁰ Beth Understahl, "Authorized Generics: Careful Balance Undone," 16 *Fordham Intellectual Property, Media, and Entertainment Law Journal* (Autumn 2005), 355.

⁷¹ Tony Pugh, "Loophole May Dampen Generic-drug Boom," *San Jose Mercury News*, May 3, 2006, A1.

⁷² David A. Balto, "We'll Sell Generics Too: Innovator Drug Makers are Gaming the Regulatory System and Harming Competition," *Legal Times*, March 20, 2006.

⁷³ Jenna Greene, "The Drug Industry Has Figured Out a Way to Best Generic Competition, and Pharmaceutical Patent Litigation Could Free-Fall," *New Jersey Law Journal*, January 23, 2006, 217.

⁷⁴ See Pugh, *supra* note 54.

firms may themselves make diminished, or delayed, use of the authorized generic strategy. As a result, the pro-competitive benefits of authorized generics may be postponed, or not realized at all, should independent generic rivals become less willing to challenge patents held by brand name firms.⁷⁵

On the other hand, authorized generics potentially offer several benefits both to drug companies and to consumers. Authorized generics are commonly less expensive than the brand name drug. The introduction of an authorized generic therefore allows a lower-cost product to be made available to the consumer.⁷⁶ As the FDA opined in a statement issued in July 2004:

Marketing of authorized generics increases competition, promoting lower prices for pharmaceuticals, particularly during the 180-day exclusivity period in which the prices for generic drugs are often substantially higher than after other generic products are able to enter the market.⁷⁷

In addition, once a generic version of a drug becomes available following patent expiration, brand name firms may lose considerable market share. Indeed, many health management organizations and insurance companies reportedly promote the use of generic substitutes for brand-name medications once they become available.⁷⁸ Absent participation in the generic market, brand name firms may not be able to take advantage of investments they previously made with respect to their manufacturing facilities. Authorized generics therefore allow brand name firms to continue to employ their manufacturing facilities at or near peak capacity even following patent expiration.⁷⁹

Authorized generics may also support the research and development efforts of brand name firms by providing them with additional revenue. Authorized generics may supply the brand name firm with an additional income source, such as a royalty on sales made by its generic subsidiary or contracting partner.⁸⁰ These funds, or some portion of them, can potentially be employed in support of pharmaceutical innovation.

Authorized generics may also facilitate settlement of patent infringement suits between brand name and independent generic firms. A judicial holding of patent invalidity may have a severe impact upon a brand name firm in terms of its lost revenue. Many observers also believe that patent litigation is an uncertain venture.⁸¹ By settling patent litigation, and allowing an ANDA applicant to produce an authorized generic, brand name firms may potentially better manage risk.

⁷⁵ Narinder Banait, "Authorized Generics: Antitrust Issues and the Hatch-Waxman Act," *Mondaq*, November 4, 2005.

⁷⁶ *Virtual Patent Extension by Cannibalization*.

⁷⁷ U.S. Food and Drug Administration, *FDA Supports Broader Access to Lower Priced Drugs*, FDA Talk Paper, July 2, 2004. A study prepared by IMS Consulting for the Pharmaceutical Research and Manufacturers of America reached a similar conclusion, determining that the average price discount to brand name drugs during the 180-day exclusivity period is greater when an authorized generic has been marketed than when one has not. IMS Consulting, *Assessment of Authorized Generics in the U.S.*, Spring 2006, available at http://www.phrma.org/files/IMS%20Authorized%20Generics%20Report_6-22-06.pdf.

⁷⁸ Kathleen Kerr, "Prescription Hurdles: Need Brand-Name Drug? Generic May Come First," *Newsday*, March 16, 2006, B13.

⁷⁹ Jon Hess and Elio Evangelista, *Authorized Generics: Lifecycle Management's Compromise in the Patent Wars*, Cutting Edge Information, August 23, 2005, 4.

⁸⁰ *Ibid.*

⁸¹ James Bessen and Michael J. Meurer, "Lessons for Patent Policy from Empirical Research on Patent Litigation," *Lewis and Clark Law Review*, 2005.

Such a technique provides a more stable revenue stream, both in support of the brand name firm's research and development activities and for its investors. The generic company making an authorized generic can also benefit by not having to expend funds on litigation with an uncertain outcome or pursue an ANDA at the FDA, while expanding its product line, acquiring manufacturing experience, and gaining the first-mover advantage in the generic market.⁸²

The use of authorized generics as a litigation settlement mechanism also impacts consumers, but in a manner that is both less certain and likely varies on a case-by-case basis. On one hand, particular settlement agreements may provide for the sale of authorized generics years before the disputed patent is set to expire. As a result, consumers may gain early access to a lower-cost alternative to the brand name drug. On the other hand, had the generic firm refused to settle and ultimately prevailed in the litigation, then the market would have been open to full competition even earlier. The impact upon competition of a litigation settlement likely depends upon a number of complex factors, including the strength of the patent, the number of potential generic competitors, and the precise terms of the litigation settlement agreement.

Patent Settlements⁸³

Brand name and generic firms engaged in litigation within the Hatch-Waxman statutory framework have sometimes concluded their litigation through settlement, rather than await a formal decision from a court. A few of these settlements have called for the brand name company to pay the generic firm in exchange for the generic firm's agreement not to market the patented pharmaceutical. These arrangements have been termed "reverse payment" agreements because they are contrary to the usual situation in patent infringement settlements, where the plaintiff-patentee receives money from the accused patent infringer.⁸⁴

"Reverse payment" settlements potentially had significant market consequences prior to the enactment of P.L. 108-173. Under the old law, such an arrangement could sometimes prevent all other generic firms from entering the market. The reason is that the first generic challenger was entitled to a 180-day exclusivity against other generic firms that could not be revoked or forfeited. If the first generic challenger chose not to market at all, then no generic versions of a drug could be approved by the FDA until such time as the patent expired.⁸⁵

Amendments to the original Hatch-Waxman Act contained in P.L. 108-173 include two provisions that make "reverse payment" arrangement less likely to occur in the future. First, settlement agreements between brand name and generic firms must, in many cases, be filed with the Federal Trade Commission and the Department of Justice. This provision allows the FTC and DOJ to review the settlements for anticompetitive effects. Second, P.L. 108-173 establishes various events that cause the first generic challenger to forfeit its 180-day exclusivity. Other generic firms

⁸² Christopher Worrell, *Authorized Generics*, presentation given at The 5th Generic Drugs Summit, September 27-29, 2004, and David Reiffen and Michael R. Ward, *"Branded Generics" as a Strategy to Limit Cannibalization of Pharmaceutical Markets*, May 2005, 2-4 available at <http://www.uta.edu/faculty/mikeward/brandedgenerics.pdf>.

⁸³ See CRS Report RL33717, *Pharmaceutical Patent Litigation Settlements: Implications for Competition and Innovation*, by (name redacted).

⁸⁴ Herbert Hovenkamp *et al.*, "Anticompetitive Settlement of Intellectual Property Disputes," *Minnesota Law Review*, 2003, 1719.

⁸⁵ *Ibid* at 1764, n.196.

will therefore be less easily shut out of the market in the future in the event that the first generic challenger opts not to market a particular drug.

Notably, certain “reverse payment” settlements reached under the old law have been subject to scrutiny under the antitrust laws. Enacted with the goal of preserving a competitive, open market, the antitrust laws make illegal a variety of practices that restrain trade and reduce consumer choices. Both the FTC and private plaintiffs have succeeded in persuading the federal courts that particular “reverse payment” settlements constitute antitrust violations. Different federal courts have reached conflicting rulings, however, on whether “reverse payment” settlements should automatically be considered to violate the antitrust laws,⁸⁶ or whether they should be subjected to a detailed, case-by-case review to determine whether the settlement was sufficiently anti-competitive to constitute an antitrust violation.⁸⁷ These rulings may have considerable impact upon the extent to which the antitrust laws will be used to monitor past conduct by different actors within the pharmaceutical industry. The U.S. Supreme Court may choose to resolve these conflicting views by issuing a ruling that would be binding upon the lower courts.⁸⁸

Follow-On Biologics⁸⁹

The accelerated market approval process for chemical, small molecule pharmaceuticals created by the Hatch-Waxman Act does not apply to biologic drugs.⁹⁰ Today, 20% of the drugs on the market are biologics⁹¹ and many more new biologics reportedly are in the pipeline and/or in the approval process.⁹² Projections are that by 2010, 50% of approved pharmaceuticals will be the result of biotechnology.⁹³ This sector is highly innovative, invests extensively in research and development, and is instrumental in providing products that contribute to the health and well-being of the nation. Observers agree that the biologics market is rapidly expanding by any number of measures, including the quantity of approved products, the size of the market, and the importance of these drugs to the health of U.S. citizens.

Awareness of the increasing importance of biopharmaceuticals has been accompanied by an appreciation that patents covering many of these products will soon expire. Estimates vary on the number of biologics that will lose patent protection in the next several years and the amount of sales these products represent. One study notes that “between 2009 and 2019, 21 blockbuster

⁸⁶ *In re Cardizem CD Antitrust Litigation*, 332 F.3d 896 (6th Cir. 2003) (“reverse payment” settlement constitutes a *per se* illegal restraint of trade under Section 1 of the Sherman Act).

⁸⁷ *Valley Drug Co. v. Geneva Pharms.*, 344 F.3d 1294 (Fed. Cir. 2003) (“reverse payment” settlement **not** *per se* unlawful under Section 1 of the Sherman Act).

⁸⁸ Neal R. Stoll & Shepard Goldfein, “Patent Protection or *Per Se* Violation?,” *New York Law Journal*, November 18, 2003, 3.

⁸⁹ For a detailed discussion of this issue see CRS Report R41483, *Follow-On Biologics: The Law and Intellectual Property Issues*, by (name redacted) and (name redacted).

⁹⁰ The Public Health Service defines the term “biological product” to mean “a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.” 42 U.S.C. §262(i) (2006).

⁹¹ *Beyond Borders, Global Biotechnology Report 2008*, 30.

⁹² Kerry A. Dolan, “Biology Rising,” *Forbes.com*, May 12, 2006, available at http://www.forbes.com/2006/05/12/merck-pfizer-amgen-cz_kd_0512biologics_print.html.

⁹³ “Biogenerics: A Difficult Birth?” *IMS Global Insights*, available at <http://www.imshealth.com>.

biopharmaceuticals with a total market value of over 50 billion \$US will lose patent protection.”⁹⁴ Analysis by FierceBiotech estimates that biologics worth \$25 billion in sales will lose patent protection by 2016.⁹⁵ A report by PriceWaterhouseCoopers notes that between 2002 and 2013, the expiration of patents on blockbuster biopharmaceutical products will lead to an average loss of \$16.4 billion in sales.⁹⁶

While in the traditional pharmaceutical market, generic versions commonly become available to consumers as patents on brand name drugs expire due to the provisions of the Hatch-Waxman Act, Congress was concerned that loss of patent protection for biologics would not be accompanied by the introduction of competing, lower-cost products.⁹⁷ Biologics differ significantly from traditional pharmaceuticals in their complexity and method of manufacture. Typical pharmaceutical products consist of small molecules, on the order of dozens of atoms, that may be readily characterized and reproduced through well-understood chemical processes. In contrast, biologics are often made up of millions of atoms, feature a more complex structure than traditional pharmaceuticals, and are manufactured from living cells through biological processes.⁹⁸ As a result, the technical challenges that a competitor faces in developing a product that may be viewed as equivalent to a particular brand-name biologic product may be considerable, and in some cases perhaps even insurmountable.⁹⁹ For this reason, many experts do not describe competing biologic products as “generics,” as is the case for a small-molecule pharmaceuticals; the terms “follow-on biologic” or “biosimilar” are commonly used instead.¹⁰⁰

Some commentators asserted that these technical challenges also meant that the expedited approval pathways available under the Hatch-Waxman Act did not comfortably apply to biologics, most of which are approved under provisions of the Public Health Services Act (PHS Act). Because the complexity of biologics is an order of magnitude greater than that associated with pharmaceuticals, they say, an expedited marketing approval protocol would not ensure patient safety to the degree possible with respect to traditional drugs.¹⁰¹ Other experts observed that different kinds of biologics vary considerably in their size and structure, and that existing Hatch-Waxman mechanisms provided appropriate regulatory oversight for less complex biologics and therefore should be extended to those biologics approved under the PHS Act. These observers further argued that as scientific knowledge progresses, understanding of biologics will increase, thereby allowing expanded use of then existing procedures.¹⁰²

⁹⁴ Parexel Consulting, *Follow-on Biologics*, available at <http://www.parexelconsulting.com/services/follow-on-biologics.html>

⁹⁵ FierceBiotech, *The Top 10 Biosimilar Players: Positioning, performance and SWOT analyses*, April 20, 2009, available at <http://www.fiercebiotech.com/research/top-10-biosimilar-players-positioning-performance-and-swt-analyses>.

⁹⁶ PriceWaterhouseCoopers, *Biotech, Lifting Big Pharma's prospects with biologics*, 2009, 9, available at http://www.pwc.com/en_GX/gx/pharma-life-sciences/pdf/biotech-final.pdf

⁹⁷ David M. Dudzinski, “Reflections on Historical, Scientific, and Legal Issues Relevant to Designing Approval Pathways for Generic Versions of Recombinant Protein-Based Therapeutics and Monoclonal Antibodies,” *Food and Drug Law Journal*, 2005, 143.

⁹⁸ Melissa R. Leuenberger-Fisher, “The Road to Follow On Biologics: Are We There Yet?,” *Biotechnology Law Report*, August 2004, 389.

⁹⁹ Dawn Willow, “The Regulation of Biologic Medicine: Innovators’ Rights and Access to Healthcare,” *Chicago-Kent Journal of Intellectual Property*, 2006, 32.

¹⁰⁰ *Ibid.*

¹⁰¹ See Dudzinski, *supra* (noting such concerns).

¹⁰² Narinder S. Banait, *Follow-on Biological Products—Legal Issues*, 2005, available at <http://www.fenwick.com/> (continued...)

The 111th Congress turned to these concerns when it enacted the Biologics Price Competition and Innovation Act (BPCIA) of 2009, incorporated into Title VII of the Patient Protection and Affordable Care Act.¹⁰³ BPCIA established a licensure pathway for competing versions of previously marketed biologics. In particular, the legislation established a regulatory regime for two sorts of follow-on biologics, termed “biosimilar” and “interchangeable” biologics. The Food and Drug Administration (FDA) was afforded a prominent role in determining the particular standards for biosimilarity and interchangeability for individual products.

In addition, the legislation created FDA-administered periods of data protection and marketing exclusivity for certain brand-name drugs and follow-on products. Brand-name biologic products receive 4 years of marketing exclusivity and 12 years of data protection. The BPCIA also provides for a term of marketing exclusivity for the applicant that is the first to establish that its product is interchangeable with the brand-name product. Finally, the BPCIA created a patent dispute resolution procedure for use by brand-name and follow-on biologic manufacturers.

Concluding Observations

The Hatch-Waxman Act has been instrumental in providing patients with lower-cost generic copies of brand name drugs often the day that patents expire on the original product. At the same time, investment in pharmaceutical research and development has increased in real terms at an average of almost 9% a year. While the original legislation was amended in 2003 to address what were perceived as loopholes in the process, concerns still remain whether or not the balance achieved by the act remains appropriate over 25 years later. However, congressional legislation extending a similar accelerated marketing approach to biologic drugs may be indicative of a belief in the overall success of the Hatch-Waxman Act.

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¹⁰³ For a detailed discussion of this legislation see CRS Report R41483, *Follow-On Biologics: The Law and Intellectual Property Issues*, by (name redacted) and (name redacted).

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