Drug Patent Expirations: Potential Effects on Pharmaceutical Innovation

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Summary

Congress has exhibited a strong and ongoing interest in facilitating the development of new, innovative pharmaceuticals for the marketplace while reducing the cost of drugs to consumers. Policies pertaining to funding for research and development (R&D), intellectual property protection, and cooperative ventures have played an important role in the economic success of the pharmaceutical sector. Industry-specific legislation, including the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the "Hatch-Waxman Act," also work to encourage innovation in the pharmaceutical sector while facilitating the entry of lower cost generic competition.

A critical component of many of these federal efforts concerns patents. Patent ownership can provide an economic incentive for companies to take the results of research and make the often substantial investment necessary to bring new goods and services to the marketplace. In the pharmaceutical industry, patents are perceived as particularly important to innovation due, in part, to the ease of duplicating the invention.

Recently, patents on a significant number of "blockbuster" drugs have expired. Lipitor, the world's best selling medicine lost patent protection a the end of 2012 and immediately faced generic competition. Between 2012 and 2016, branded pharmaceuticals with an estimated $117.2 billion in U.S. sales are expected to go off patent. Once these drugs are no longer patent protected they are expected to lose up to 80% of the revenue generated for the innovator companies.

Brand firms depend on funds from sales of blockbuster pharmaceuticals for investments in additional research and development leading to new products that can improve the health and welfare of the public. The effect of blockbuster patent expirations on company revenues and R&D funding can be dramatic, particularly when there are insufficient products in the development pipeline to replace these drugs. Some experts point to indications that productivity is declining in this sector as revenues available for additional investment appear to be decreasing.

While many factors contribute to innovation in the brand pharmaceutical industry and its ability to bring new and inventive products to the marketplace, this sector is facing significant issues associated with the loss of revenue available for additional R&D due to patent expirations and generic competition. Generic versions of brand pharmaceuticals benefit the public due to their lower cost and greater availability. However, experts point out that without the research, development, and testing performed by the brand name pharmaceutical companies, generic drugs would not exist. Thus, there is ongoing congressional interest in striking the proper balance between lower cost drugs and maintaining an innovative domestic pharmaceutical sector.

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Introduction

Congress has exhibited a strong and ongoing interest in facilitating the development of new, innovative pharmaceuticals for the marketplace while reducing the cost of drugs to consumers. To date, the U.S. system of research, development, and commercialization has had a clear impact on the pharmaceutical and biotechnology industries. Policies pertaining to funding for research and development (R&D), intellectual property protection, and cooperative ventures have played an important role in the economic success of these sectors.[1] Industry-specific legislation, including the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the "Hatch-Waxman Act," also work to encourage innovation in the pharmaceutical sector while facilitating the entry of lower cost generic competition.[2]

A critical component of many of these federal efforts concerns patents.[3] Patent ownership can provide an economic incentive for companies to take the results of research and make the often substantial investment necessary to bring new goods and services to the marketplace. The grant of a patent provides the inventor with a mechanism to capture the returns to his invention through exclusive rights on its practice for a limited time. In the pharmaceutical industry, patents are perceived as particularly important to innovation due, in part, to the ease of duplicating the invention.

Recently, patents on a significant number of "blockbuster"[4] drugs have expired. At the end of 2011, Lipitor, with 2010 retail sales in the U.S. of $5.8 billion[5] and the world's best selling medication, lost patent protection. Between 2012 and 2016, branded pharmaceuticals with an estimated $117.2 billion in U.S. sales are expected to go off patent.[6] Once these drugs lose patent protection they are expected to lose up to 80% of the revenue generated for the innovator companies. "In the case of the top selling drugs, generics are capturing most of the market within weeks of their launch."[7]

Innovator companies depend on the funds generated from sales of blockbuster drugs to invest in additional R&D leading to new products that can improve the health and welfare of the public. At the same time, generic versions of these pharmaceuticals benefit the public due to their lower cost

[1] Iain Cockburn, Rebecca Henderson, Luigi Orsenigo, and Gary P. Pisano, "Pharmaceuticals and Biotechnology," *U.S. Industry in 2000* (National Academy Press, Washington, 1999), 365.

[2] See CRS Report R41114, *The Hatch-Waxman Act: A Quarter Century Later*, by Wendy H. Schacht and John R. Thomas.

[3] See CRS Report RL32076, *The Bayh-Dole Act: Selected Issues in Patent Policy and the Commercialization of Technology*, by Wendy H. Schacht, and CRS Report RL32324, *Federal R&D, Drug Discovery, and Pricing: Insights from the NIH-University-Industry Relationship*, by Wendy H. Schacht.

[4] A "blockbuster" drug is defined as a drug product having in excess of $1 billion (2000 deflated dollars) in U.S. annual sales. Ernst R. Berndt and Murray L. Aitken, *Brand Loyalty, Generic Entry and Price Competition in Pharmaceuticals in the Quarter Century After the 1984 Waxman-Hatch Legislation*, National Bureau of Economic Research, October 2010, available at http://www.nber.org/papers/w16431, 3.

[5] Medco Health Solutions, Inc., Estimated Dates of Possible First Time Generic/Rx-to-OTC Market Entry, July 2011, available at http://www.medcohealth.com/art/corporate/anticipatedfirsttime_generics.pdf.

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

[7] Henry Grabowski, "Competition Between Generic and Branded Drugs," in Frank A. Sloan and Chee-Ruey Hsieh, eds., *Pharmaceutical Innovation, Incentives, Competition, and Cost-Benefit Analysis in International Perspective* (Cambridge University Press, 2007), 160.

and greater availability; according to one estimate, over the 10 years between 2001 and 2010, generic drugs "saved the U.S. health care system more than $931 billion."[8] However, "while consumers and companies [that] provide health benefits could gain from the substantial slashes in costs, big pharma has to look at new ways and strategies to fill the [revenue] gap" created by the unprecedented number of patent expirations on blockbuster drugs. [9]

The Pharmaceutical Industry

The pharmaceutical industry is highly innovative and "stands as one of our nation's leading industries in high quality job creation ... and global competiveness."[10] American pharmaceutical firms have "consistently maintained a competitive edge in international markets" [11] and lead in new drug discoveries.[12] A review of the 75 best selling drugs in 2009 determined that more than half originated in the United States."[13] In 2010, 7 of the top 20 global drug companies were based in the United States.[14]

Estimates of employment in the pharmaceutical sector differ. A study by the Milken Institute found that "private-sector employment in the U.S. biomedical industry in 2009 was 1,219,200," including 283,700 biopharmaceutical jobs and "526,300 in related R&D, testing, and labs."[15] Research by the Battelle Technology Partnership Practice indicated that "the biopharmaceutical sector is responsible for more than four million jobs in the U.S. economy (674,000 direct jobs and an additional 3.4 million indirect and induced jobs) in 2009" which generated "$258 billion in wages and benefits."[16] Despite these different figures, it is clear that the wages paid to pharmaceutical sector employees are significantly higher than in other industries. According to the Milken Institute report, wages in the biomedical sector average 70% more than the national average wage.[17] Battelle found that the average total compensation per employee in the biopharmaceutical sector is more than twice that of the average wage in the U.S. private sector.[18]

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[8] IMS Healthcare Institute and IMS Health*, Savings, An Economic Analysis of Generic Drug Usage in the U.S., Executive Summary*, Generic Pharmaceutical Association, September 2011, 1, available at http://www.gphaonline.org/sites/default/files/GPhA%20IMS%20Study%20WEB%20Sep20%2011.pdf.

[9] Pharmaceutical Technology, *The Patent Cliff: Rise of the Generics*, October 5, 2011, available at http://www.pharmaceutical-technology.com/features/featurethe-patent-cliff-rise-of-the-generics/.

[10] Battelle Technology Partnership Practice, *The U.S. Biopharmaceuticals Sector: Economic Contribution to the Nation,* July 2011, 1, available at http://www.phrma.org/sites/default/files/159/2011_battelle_report_on_economic_impact.pdf.

[11] Department of Commerce, International Trade Administration, *U.S. Industry &Trade Outlook 2000* (McGraw-Hill, 2000), 11-16.

[12] Yali Friedman, "Location of Pharmaceutical Innovation: 2000-2009," *Nature Reviews/Drug Discovery*, November 2010, 835, available at http://www.nature.com/nrd/journal/v9/n11/full/nrd3298.html.

[13] Ross C. DeVol, Armen Bedroussian, and Benjamin Yeo, *The Global Biomedical Industry: Preserving U.S. Leadership*, Milken Institute, September 2011, 16, available at http://www.milkeninstitute.org/publications/publications.taf?function=detail&ID=38801285&cat=resrep.

[14] Ibid., 16.

[15] Ibid., 1.

[16] *The U.S. Biopharmaceuticals Sector: Economic Contribution to the Nation*, 5.

[17] *The Global Biomedical Industry: Preserving U.S. Leadership*, 1.

[18] *The U.S. Biopharmaceuticals Sector: Economic Contribution to the Nation*, 8.

Estimates on global pharmaceutical 2010 R&D funding range from $120 billion and $133 billion.[19] In the United States, research and development spending by the biopharmaceutical industry totaled between $67.4 billion and $68.0 billion.[20] This U.S. investment in health-related R&D exceeds all other countries and is one reason for the leadership of American pharmaceutical firms. In addition, U.S. companies have demonstrated a pattern of R&D support that has increased at a faster rate than R&D in Europe. In 1990, investments in the European biopharmaceutical industry were 50% above those in the United States; by 2006, investments in the U.S. biopharmaceutical industry were 40% more than in Europe.[21]

According to a study undertaken by Burrill & Co., 2010 R&D funding by members of the Pharmaceutical Researchers and Manufacturers Association (PhRMA) was 2.3% more than the previous year and a record high for the industry.[22] Other analysis revealed that the average annual growth rate in U.S. R&D expenditures between 2000 and 2007 is largest in the pharmaceutical sector when compared to all industries that produce products that can be imported or exported. This R&D support is almost twice as much per employee than the next closest industry included in the study.[23] Similarly, the National Science Foundation found that in 2008, the pharmaceutical and medicine industries invested over twice the amount of funding for R&D ($70 million) than the nearest R&D intensive sector (semiconductor and electronic components).[24]

In 2010, domestic R&D spending for members of PhRMA totaled an estimated $37.4 billion, with 20.3% of domestic sales reinvested in research and development.[25] This figure does not include the 5% reduction in spending by Roche, which ended its membership in PhRMA in 2009.[26] Four of the five PhRMA members with the largest R&D funding increased their spending in 2010. These five companies contributed approximately 56.6% of the $67.4 billion in total pharmaceutical industry R&D support.[27]

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[19] International Federation of Pharmaceutical Manufacturers & Associations, *The Pharmaceutical Industry and Global Health: Facts and Figures*, 2011, 15, available at http://www.ifpma.org/fileadmin/content/Publication/2011_The_Pharmaceutical_Industry_and_Global_Health_low_ver2.pdf, and Battelle, "2011 Global R&D Funding Forecast," *R&D Magazine*, December 2010, 12, available at http://www.battelle.org/aboutus/rd/2011.pdf.

[20] *2011 Global R&D Funding Forecast*, 9 and Pharmaceutical Research and Manufacturers of America, *Pharmaceutical Industry 2011 Profile,* inside cover, available at http://www.phrma.org/sites/default/files/159/phrma_profile_2011_final.pdf, and 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.

[21] *The Global Biomedical Industry: Preserving U.S. Leadership*, 20.

[22] Alex Philippidis, "Restructuring and Cuts Threaten to Lower Industry R&D Spending Next Year," *Genetic Engineering & Biotechnology News*, April 4, 2011 available at http://www.genengnews.com/analysis-and-insight/restructuring-and-cuts-threaten-to-lower-industry-r-d-spending-next-year/77899389/. See also, PhRMA, *R&D Investments by U.S. Biopharmaceutical Companies Reached Record Levels in 2010*, March 15, 2011, available at http://www.phrma.org/media/releases/rd-investment-us-biopharmaceutical-companies-reached-record-levels-2010.

[23] Nam D. Pham, The Impact of Innovation and the Role of Intellectual Property Rights on U.S. Productivity, Competitiveness, Jobs, Wages, and Exports, ndp consulting, April 2010, 16 and 13, available at http://www.theglobalipcenter.com/sites/default/files/reports/documents/NDP_IP_Jobs_Study_Hi_Res.pdf.

[24] National Science Foundation, "U.S. Businesses Report 2008 Worldwide R&D Expense of $330 Billion: Findings from New NSF Survey," *InfoBrief*, NSF 10-322, March 2010, 3, available at http://www.nsf.gov/statistics/infbrief/nsf10322/nsf10322.pdf.

[25] *Pharmaceutical Industry 2011 Profile,* inside front cover and 50.

[26] *Restructuring and Cuts Threaten to Lower Industry R&D Spending Next Year.*

[27] Ibid.

However, other studies indicate that that R&D spending is declining. 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.[28] 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."[29] According to one report, the world's largest pharmaceutical company, Pfizer, plans to reduce its R&D funding by 25% between 2010 and 2012 while other firms are expected to make less substantial cuts.[30] Analysis by Battelle indicated that:

> Some of the largest cuts still coming are from Merck ... , which is closing eight global R&D facilities as part of a larger operational consolidation effort. Pfizer ... is signaling cuts of up to $3 billion in its R&D budget over the next few years. AstraZeneca has announced plans to reduce R&D budgets by $1 billion in the next four years, and Abbott Laboratories ... has announced plans for big cuts in R&D among more than 3,500 job cuts globally. Roche also recently announced plans to cut 4,800 jobs globally.[31]

Role of Patents

Experts widely believe that patents encourage invention and innovation by simultaneously protecting the inventor and fostering competition. They provide the inventor with a right to exclude others, temporarily, from use of the invention without compensation. Patents give the owner an exclusive right for (typically) 20 years from date of filing to further develop an idea, commercialize a product or process, and potentially realize a return on the initial investment. Concurrently, the process of obtaining a patent places the concept in the public arena. As a disclosure system, the patent can, and often does, stimulate other firms or individuals to invent "around" existing patents to provide for parallel technical developments or meet similar market needs.[32] This may form the basis for technological progress as patents are used to create an environment of competitiveness with multiple sources of innovation. The value of widespread invention is reinforced by research performed by Professors Robert Merges and Richard Nelson which demonstrated that when only "a few organizations controlled the development of a technology, technical advance appeared sluggish."[33]

Innovation produces new knowledge but is often costly and resource intensive. One characteristic of this knowledge is that it is a "public good," a good that is not consumed when it is used. If discoveries were universally available without a means for the inventor to realize a return on investment, most commentators are convinced that there would result a "much lower and indeed

[28] *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.

[29] *Drug Dropout in Clinical Trials is at Unsustainable Levels, According to Thomson Reuters, CMR International.*

[30] Ben Hirschler, "Drug R&D Spending Fell in 2010, and Heading Lower," *Reuters*, June 26, 2011, available at http://www.reuters.com/article/2011/06/26/pharmaceuticals-rd-idUSL6E7HO1BL20110626.

[31] *2011 Global R&D Funding Forecast*, 12 – 13.

[32] For more information, see CRS Report RL32324, *Federal R&D, Drug Discovery, and Pricing: Insights from the NIH-University-Industry Relationship*, by Wendy H. Schacht.

[33] Robert P. Merges and Richard R. Nelson, "On the Complex Economics of Patent Scope," *Columbia Law Review*, May 1990, 908.

suboptimal level of innovation."[34] Thus, the patent process is designed to resolve the problem of appropriability; patents permit novel concepts or discoveries to become "property" when reduced to practice and therefore allow for control over their use.

Article I, Section 8, Clause 8 of the U.S. Constitution states: "The Congress Shall Have Power ... To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries...." Codified in Title 35 of the United States Code, one who "invents or discovers any new and useful process, machine, manufacture, or any composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title."[35] Patents are issued by the United States Patent and Trademark Office (USPTO). 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 Food and Drug Administration (FDA).[36] Federal laws typically require pharmaceutical manufacturers to demonstrate that their products are safe and effective in order to bring these drugs to the marketplace. USPTO issuance of a patent and FDA marketing consent are distinct events that depend upon different criteria.[37]

However, not everyone agrees that the patent system is a particularly effective means to stimulate innovation. Some observers believe that the patent system encourages industry concentration and presents a barrier to entry in some markets.[38] They suggest that the patent system often converts pioneering inventors into technological suppressors, who use their patents to block subsequent improvements and thereby impede technological progress.[39] Others believe that the patent system too frequently attracts speculators who prefer to acquire and enforce patents rather than engage in socially productive activity such as bringing new products and processes to the marketplace.[40]

Some experts argue that patents do not work as well in reality as in theory because they do not confer perfect appropriability. In other words, they allow the inventor to obtain a larger portion of the returns on his investment but do not permit him to capture all the benefits. Patents can be circumvented and infringement cannot always be proven. Thus, patents are not the only way, nor necessarily the most efficient means, for the inventor to protect the benefits generated by his efforts. A study by Yale University's Richard Levin and his colleagues concluded that lead time,

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[34] Kenneth W. Dam, "The Economic Underpinnings of Patent Law," *Journal of Legal Studies*, January 1994, 247.

[35] 35 U.S.C.§101.

[36] For more information see CRS Report R41114, *The Hatch-Waxman Act: A Quarter Century Later*, by Wendy H. Schacht and John R. Thomas, and CRS Report RL30756, *Patent Law and Its Application to the Pharmaceutical Industry: An Examination of the Drug Price Competition and Patent Term Restoration Act of 1984 ("The Hatch-Waxman Act")*, by Wendy H. Schacht and John R. Thomas.

[37] For more information see CRS Report RL33288, *Proprietary Rights in Pharmaceutical Innovation: Issues at the Intersection of Patents and Marketing Exclusivities*, by John R. Thomas.

[38] See John R. Thomas, "Collusion and Collective Action in the Patent System: A Proposal for Patent Bounties," *University of Illinois Law Review*, 2001, 305.

[39] *On the Complex Economics of Patent Scope*, 839.

[40] Elizabeth D. Ferrill, "Patent Investment Trusts: Let's Build a Pit to Catch the Patent Trolls," *6 North Carolina Journal of Law and Technology*, 2005, 367.

learning curve advantages (e.g., familiarity with the science and technology under consideration), and sales/service activities were typically more important in exploiting appropriability than were patents. That was true for both products and processes. However, patents were found to be better at protecting products than processes. The novel ideas associated with a product often can be determined through reverse engineering—taking the item apart to assess how it was made. That information then could be used by competitors if not covered by a patent. Because it is more difficult to identify the procedures related to a process, other means of appropriation often are seen as preferable to patents, with the attendant disclosure requirements.[41]

An analysis of the literature in this area performed for the World Intellectual Property Organization[42] highlights several conclusions concerning the use of patents that mirror much of the above discussion. The research surveyed indicates that "lead time and secrecy seem to be the most relevant appropriability devices for most sectors" and that while patents may not be the most effective means to protect inventions, they are still utilized by firms in all industries. There is a consensus that "disclosure and ease of inventing-around are the most important reasons for not patenting." At the same time, "patents are more relevant as an appropriability mechanism for product than for process innovations and for some sectors such as chemicals (especially pharmaceuticals), some machinery industries and biotechnology."

While studies show that the value of patents differs across industries and between firms of different maturation levels within a sector,[43] the pharmaceutical industry perceives patents as critical to protecting innovation. Several studies over the years have demonstrated the important role patents play in the pharmaceutical sector. Of the 18 major manufacturing industries analyzed by Richard Levin and his colleagues, only drug companies rated product patents the most effective means of ensuring that firms can capture the profits associated with their innovations.[44] Later research by Professor Wesley Cohen and his colleagues demonstrated that patents were considered the most effective method to protect inventions in the drug industry, particularly when biotechnology is included.[45] A recent paper by several professors at the Berkeley School of Law, University of California, found that there were "substantial differences between the health-related sectors (biotechnology and medical devices), in which patents are more commonly used and considered important, and the software and Internet fields, in which patents are reported to be less useful."[46] These studies reinforce earlier work by the late Professor Edwin Mansfield that indicated 65% of pharmaceutical inventions would not have been brought to market without patent protection in contrast to the 8% of innovations made in other industries.[47]

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[41] Richard C. Levin, Alvin K. Klevorick, Richard R. Nelson, and Sidney G. Winter. "Appropriating the Returns for Industrial Research and Development," *Brookings Papers on Economic Activity*, 1987, in *The Economics of Technical Change*, eds. Edwin Mansfield and Elizabeth Mansfield (Vermont, Edward Elgar Publishing Co., 1993), 254.

[42] Andres Lopez, "Innovation and Appropriability, Empirical Evidence and Research Agenda," in *The Economics of Intellectual Property*, World Intellectual Property Organization, January 2009, 21, available at http://www.wipo/int/export/sites/www/ip-development/en/economics/pdf/wo_1012_e.pdf.

[43] Stuart J.H. Graham, Robert P. Merges, Pam Samuelson, and Ted Sichelman, "High Technology Entrepreneurs and the Patent System: Results of the 2008 Berkeley Patent Survey," *Berkeley Technology Law Journal*, April 16, 2010, 1255, available at http://www.btlj.org/data/articles/24_feature.pdf.

[44] *Appropriating the Returns for Industrial Research and Development*, 255 and 257.

[45] Wesley M. Cohen, Richard R. Nelson, and John P. Walsh, *Protecting Their Intellectual Assets: Appropriability Conditions and Why U.S. Manufacturing Firms Patent (or Not)*, NBER Working Paper 7552, Cambridge, National Bureau of Economic Research, February 2000, available at http://www.nber.org/papers/w7552.

[46] *High Technology Entrepreneurs and the Patent System: Results of the 2008 Berkeley Patent Survey*, 1255.

[47] Edwin Mansfield, "Patents and Innovation: An Empirical Study," *Management Science*, February 1986, 173-181.

Patents may be particularly important in the pharmaceutical sector because of the relative ease of replicating the finished product. Imitation costs vary among industries. For example, while it is expensive, complicated, and time consuming to duplicate an airplane, it is relatively simple to chemically analyze a pill and reproduce it.[48] The degree to which industry perceives patents as effective has been characterized as "positively correlated with the increase in duplication costs and time associated with patents."[49] Early research in this area by Mansfield indicated that, in certain industries, patents significantly raise the costs incurred by nonpatent holders wishing to use the idea or invent around the patent—an estimated 40% in the pharmaceutical sector, 30% for major new chemical products, and 25% for typical chemical goods—and are thus viewed as significant. However, in other industries, patents have much smaller impact on the costs associated with imitation (e.g., in the 7%-15% range for electronics), and may be considered less successful in protecting resource investments.[50]

The Hatch-Waxman Act

P.L. 98-417, the Drug Price Competition and Patent Term Restoration Act of 1984 (commonly known as the Hatch-Waxman Act), as amended, 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 increased availability of less expensive generic products.[51] 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. Among the legislative provisions are 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 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. As described by Patricia Danzon of the Wharton School, University of Pennsylvania, and Michael Furukawa, W.P. Carey School of Business, Arizona State University, "generics can largely free-ride on the R&D and informational investments made by originator firms, thereby realizing much lower cost structures."[52] 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.

[48] Federic M. Scherer, "The Economics of Human Gene Patents," 77 *Academic Medicine*, December 2002, 1350.

[49] *Appropriating the Returns for Industrial Research and Development*, 269.

[50] Edwin Mansfield, Mark Schwartz, and Samuel Wagner, "Imitation Costs and Patents: An Empirical Study," *The Economic Journal*, December 1981, in *The Economics of Technical Change*, 270.

[51] For a detailed discussion of this legislation see *The Hatch-Waxman Act: A Quarter Century Later*.

[52] Patricia M. Danzon and Michael F. Furukawa, *Cross-National Evidence on Generic Pharmaceuticals: Pharmacy vs. Physician-Driven Markets*, National Bureau of Economic Research, July 2011, 3, available at http://nber.org/papers/w17226.

Many commentators agree that the Hatch-Waxman 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.[53] The Generic Pharmaceutical Association (GPhA) points out that of 12,751 drugs listed in the Orange Book,[54] 10,072 have generic versions available to consumers.[55] 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 expires 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."[56] In cases where the generic manufacturer is the patent holder, a substitute drug may be brought to market before the patent expires.

The use of generic drugs has expanded dramatically since passage of the act. CBO found that in 1980, 13% of prescriptions for multi-source drugs were filled by generic prescriptions.[57] Another analysis indicated that in 1984, the year the Hatch-Waxman Act became law, 18.6% of U.S. prescriptions were written for generic products.[58] 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).[59] The latest information from IMS Health demonstrates that in 2010, 78% of all retail prescriptions were filled by generics.[60]

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 in dollars, branded generics generated 12.4% of sales, and brands generated 77.1 of total U.S. sales.[61] Projecting into the future, IMS Institute for Healthcare

[53] Michael A. O'Shea and Christopher M. Mikson, "The Hatch-Waxman Act: Still Critical, Still in Flux," *The National Law Journal*, January 23, 2006.

[54] 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.

[55] Generic Pharmaceutical Association, *Facts at a Glance*, available at http://www.gphaonline.org/about-gpha/about-generics/facts.

[56] 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.

[57] 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.

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

[59] 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.

[60] IMS Institute for Healthcare Informatics, *The Use of Medicines in the United States: Review of 2010*, April 2011, 22 available at http://www.theimsinstitute.org.

[61] Ibid.

Informatics argues that by 2015, 21%-22% of spending in the U.S. market will be for generic drugs.[62]

Patent Expirations

Patents on a number of major selling drugs recently have expired and additional blockbuster pharmaceuticals are expected to go off patent in the near future. According to recent estimates, more than 80 blockbuster drugs are set to expire between 2011 and 2015.[63] IMS Institute for Healthcare Informatics predicts that patent expirations during this time are anticipated to reduce worldwide spending on brand drugs by $120 billion.[64] "Globally, market share for branded medicines, which fell from 70 percent in 2005 to 64 percent in 2010, is expected to decline further through 2015, to 53 percent."[65] The United States will experience the greatest increase in purchases of generic drugs as new ones come available in the marketplace due to patent expiration.[66] Research by Medco found that "[m]ore than $50 billion in U.S. brand drugs, accounting for about 20% of current plan drug spending, will open to generic competition from late 2011 through 2013...."[67] 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.[68]

The number one selling drug in the United States, Lipitor, with 2010 sales of $7.2 billion, lost patent protection at the end of 2011.[69] Zyprexa, with 2010 U.S. sales of $3.0 billion,[70] and Keppra XR, with 2010 U.S. sales of $130 million,[71] also went off patent in 2011. That same year, an authorized generic version of Caduet (2010 U.S. sales of $296 million) became available as well as a generic version of Combivir (2010 U.S. sales of $252 million).[72]

Among the top selling drugs (2010) in the U.S. market that are expected to go off patent in 2012 are Plavix (number three at $6.1 billion), Seroquel (number six at $4.4 billion), Singulair (number seven at $4.1 billion), Actos (number nine at $3.5 billion), and Lexapro (number 19 at $2.8 billion). Cymbalta (number 13 at $3.2 billion) is anticipated to lose patent protection in 2013 and Copaxone (number 24 at $2.2 billion) in 2014. Patents on Nexium, the number two best selling

[62] IMS Institute for Healthcare Informatics, *The Global Use of Medicines: Outlook Through 2015*, May 2011, 11, available at http://www.theimsinstitute.com.

[63] Ken Krizner, "Major Brand-Name Drugs Face Patent Expiration," *Drug Topics*, March 15, 2011, available at http://drugtopics.modernmedicine.com/drugtopics/Modern+Medicine+Now/Major-brand-name-drugs-face-patent-expiration/ArticleStandard/Article/detail/711836.

[64] *The Global Use of Medicines: Outlook Through 2015*, 3.

[65] Gary Balyas, "IMS Institute Forecasts Global Spending on Medicines to Reach Nearly $1.1 Trillion by 2015," *IMS Health,* May 18, 2011, available at http://www.imshealth.com/portal/site/ims/menuitem.d248e29c86589c9c30e81c033208c22a/?vgnextoid=01146b46f9aff210VgnVCM100000ed152ca2RCRD.

[66] *The Global Use of Medicines: Outlook Through 2015,* 11.

[67] Medco, *2011 Drug Trend Report, Executive Summary*, 5, available at http://www.drugtrendreport.com/Medco-2011-Drug-Trend-Report-Executive-Summary.pdf.

[68] *Patent Storm Gathering Strength.*

[69] *The Use of Medicines in the United States: Review of 2010,* 32.

[70] Ibid.

[71] *Estimated Dates of Possible First time Generic/Rx-to-OTC Market Entry.*

[72] *Estimated Dates of Possible First time Generic/Rx-to-OTC Market Entry.*

drug in the U.S., with 2010 sales of $6.3 billion, are expected to expire in 2014, while Abilify (number five at $4.6 billion) and Crestor (number eight at $3.8 billion) are expected to be open for generic competition in 2015.[73]

Innovation Issues

Blockbuster Drugs and the Innovation Pipeline

The effect of patent expirations on the sale of brand name pharmaceuticals can be dramatic. 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.[74] In 2010, spending on branded products declined 0.7% at the same time spending for unbranded generics increased 21.7% and 4.5% for branded generics.[75] Studies have demonstrated that in the late 1980s, an innovator 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 was lost within two months.[76] Today, one report finds that average sales of a brand drug drop 72% within six months of generic competition;[77] other research finds that "more than 80 percent of a brand's prescription volume is replaced by generics within six months of patent loss."[78]

In addition to the rapid loss of market share, recent analysis has demonstrated that the monthly erosion of the innovator drug's share of the market over the 12 months following entry of the first generic has significantly accelerated over the past 10 years.[79] An earlier study by Duke University's Henry Grabowski and Margaret Kyle of the London Business School indicated that between 1995 and 2005, generic competition intensified.[80] During this time period, not only have blockbuster drugs faced increasing generic competition, but "even very modest selling drugs" have generic equivalents.[81]

The effects of blockbuster drug patent expirations on companies can be amplified when they have no other products in development to replace lost sales. Research and development "pipelines and new drug introductions have been insufficient to replace the loss of sales revenues to generic

[73] Data derived from *Estimated Dates of Possible First time Generic/Rx-to-OTC Market Entry*, and *The Use of Medicines in the United States: Review of 2010*, 32.

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

[75] *The Use of Medicines in the United States: Review of 2010*, 6.

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

[77] *Major Brand-Name Drugs Face Patent Expiration.*

[78] Gary Gatyas, "IMS Institute Reports U.S. Spending on Medicines Grew 2.3 Percent in 2010, to $307.4 Billion," *IMS Health,* April 19, 2011, available at http://www.imshealth.com/portal/site/imshealth/menuitem.a46c6d4df3db4b3d88f611019418c22a/?vgnextoid=1648679328d6f210VgnVCM100000ed152ca2RCRD&vgnextchannel=41a67900b55a5110VgnVCM10000071812ca2RCRD&vgnextfmt=default.

[79] Henry G. Grabowski, Margaret Kyle, Richard Mortimer, Genia Long, and Noam Kirson, "Evolving Brand-Name and Generic Drug Competition May Warrant a Revision of the Hatch-Waxman Act," *Health Affairs*, November 2011, 2160.

[80] Henry G. Grabowski and Margaret Kyle, "Generic Competition and Market Exclusivity Periods in Pharmaceuticals," *Managerial and Decision Economics*, 2007, 500-501.

[81] Ibid.

competition over the past decade, and this is likely to continue."[82] According to an analysis by PriceWaterhouseCoopers, only four of the ten major pharmaceutical companies have drugs in clinical trials that are "sufficiently valuable to offset these losses."[83] As described by Grabowski,

> there are also fewer products that appear capable of achieving blockbuster levels of sales revenues.... As a consequence, many of the large pharma firms are facing an R&D pipeline replacement problem, with the sales of new product introductions unable to replace pending losses from generic competition as their leading products face patent expiration and patent challenges."[84]

It has been noted that at the time Lipitor lost patent protection in 2011, the drug comprised 20% of Pfizer's total revenue, yet the company does not appear to have sufficient new products in the pipeline that could replace the funds lost to generic versions of the drug.[85] Compounding this, analysis by EvaluatePharma found that within three years, 68% of the total Pfizer portfolio will be at risk due to patent expirations on pharmaceuticals which include Protonix, Viagra, and Geodon in 2012.[86] Other companies expected to lose more than half of their brand drug portfolios to patent expirations include Eli Lilly (66%), Bristol-Myers Squibb (58%), and Johnson & Johnson (52%).[87] A similar situation is anticipated to affect Sanofi-Aventis. With Lovenox and Plavix expected to go off patents in 2012, Sanofi-Aventis may "lose $9 billion in revenue owing to competition from generic versions of these products" over the next 10 years.[88] Efforts to replace the income stream generated by these two drugs have not been as successful as expected according to one analysis.[89]

Concurrent with the significant number of blockbuster drugs that have or are expected to lose patent protection, the sales generated by these products has declined: "the share of total U.S. pharmaceutical sales accounted for by blockbusters increased from 12 to 42% between 1997-2006, fell to 38% in 2007, and has remained relatively stable since then."[90] Similarly, a study by the global management consulting firm Oliver Wyman found a decreasing number of blockbuster drugs. This analysis indicated that while the average number of new blockbuster pharmaceuticals marketed each year between 1996-2004 was 12, that number declined to an average of 6 per year between 2005-2010. This "drop in blockbusters, in turn, is partly the result of an industry shift from large primary care categories to specialty markets."[91]

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[82] *Evolving Brand-Name and Generic Drug Competition May Warrant a Revision of the Hatch-Waxman Act*, 2163.

[83] PriceWaterhouseCoopers, *Pharma 2020: Virtual R&D*, June 2008, 2, available at http://www.pwc.com.

[84] Henry Grabowski, "The Evolution of the Pharmaceutical Industry Over the Past 50 Years: A Personal Reflection," *International Journal of the Economics of Business*, July 2011, 173.

[85] Charlotte Harrison, "The Patent Cliff Steepens," *Nature Reviews/Drug Discovery*, January 2011, 12.

[86] EvaluatePharma, *Pfizer Patent Cliff Dwarfs Peers as Loss of Lipitor Looms*, February 1, 2011, available at http://www.evaluatepharma.com/Universal/View.aspx?type=Story&id=236194&isEPVantage=yes.

[87] Ibid.

[88] *The Patent Cliff Steepens*, 12.

[89] Ibid.

[90] *Brand Loyalty, Generic Entry and Price Competition in Pharmaceuticals in the Quarter Century After the 1984 Waxman-Hatch Legislation*, 3.

[91] Jeff Hewitt, J. David Campbell, and Jerry Cacciotti, "Beyond the Shadow of a Drought, The Need for a New Mindset in Pharma R&D," *Oliver Wyman Health & Life Sciences*, 2011, 3, available at http://www.oliverwyman.com/media/OW_EN_HLS_Publ_2011_Beyond_the_Shadow_of_a_Drought%282%29.pdf.

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.[92] More than half of the new drugs approved by the FDA in 2010 were specialty drugs. "Thus, the specialty category continues to be a major focus of new drug development and comprises a significant percentage of new approvals."[93]

The loss of blockbuster drug sales revenue may result in a significant reduction in funds to invest in R&D and, thus, fewer new pharmaceuticals. Even beyond the value of these new products "from a therapeutic standpoint," innovator companies "are critically dependent on the revenues from these top decile compounds to earn a positive return on their overall portfolios."[94] Terry Hisey, Deloitte US Life Sciences Leader vice chairman, commented that the loss of revenue is expected to negatively affect the level of R&D investment: "We're going to see scores of products that have the potential to improve the quality of life, and in effect save lives that will not make it to market because of the lack of available investment funds."[95] Without branded drugs, there are no generics. Fewer blockbuster drugs may detrimentally affect generic companies and the public in the long run as there may be fewer innovator drugs to replicate.[96]

"With blockbuster sales slowing and expected to remain sluggish for the foreseeable future, pharma already feels the economic pinch of weak innovation," according to the report published by Bain & Company.[97] This is compounded by an environment in which the cost of developing a drug has doubled since the early 1980s when the Hatch-Waxman Act was legislated;[98] it now takes over $1 billion to bring a new drug to market. [99] This is in contrast to the approximately $1 to $2 million necessary to bring a new generic to market.[100] The number of clinical trials necessary to file a new drug application also has doubled while the number of participants in

[92] PriceWaterhouseCoopers, *Pharma 2020: Marketing the Future,* February 2009, 13, available at http://www.pwc.com/pharma.

[93] Medco, *2011 Drug Trend Report*, 42, available at http://www.drugtrendreport.com/2011-report.

[94] *Generic Competition and Market Exclusivity Periods in Pharmaceuticals,* 496.

[95] Quoted in *The Patent Cliff: Rise of the Generics.*

[96] Melly Alazraki, "The 10 Biggest-Selling Drugs That are About to Lose Their Patent," *Daily Finance,* February 27, 2011, available at http://www.dailyfinance.com/2011/02/27/top-selling-drugs-are-about-to-lose-patent-protection-ready/.

[97] Patrick O'Hagan and Charles Farkas, "Bringing Pharma R&D Back to Health," *Bain & Company*, 2009, 1, available at http://www.bain.com/Images/BB_Managing_RandD_HC.pdf.

[98] Michael A. O'Shea and Christopher M. Mikson, "The Hatch-Waxman Act: Still Critical, Still in Flux," *The National Law Journal*, January 23, 2006.

[99] Christopher Paul Adams and Van Vu Brantner, "Spending on New Drug Development," *Health Economics* (published online Feb. 26, 2009) Epub ahead of print.

[100] 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.

these trials has tripled.[101] Thus, the rate of return from investment in a new drug is seen as dropping by 12% over this time period.[102]

Drug Approvals

Most analysts agree that "new drug approvals peaked in the mid- to late 1990s and have declined to a much lower level of annual introductions ... even though R&D expenditures continue to escalate upward at a fairly rapid rate of real growth."[103] Assessing the FDA data on new molecular entities (NMEs), a report from Medco found that "New drug approvals over the past few years have slowed considerably from the pace of approval in the late 1990s."[104] Since 1997, the annual number of new pharmaceuticals marketed decreased 44% despite increasing amounts of R&D spending according to CMR International.[105] While the number of new products that received FDA approval increased in 2011, many experts feel that this is an anomaly rather than the beginning of a trend.[106]

A recent study of the 450 new drugs approved by the FDA between 1996 and 2010 performed by the consulting firm Oliver Wyman indicates a significant demarcation between the years 1996-2004, a period when new drug approvals were "robust" and return on investment strong, and the years 2005-2010, when approvals declined, sales weakened, and return on investment was low.[107] The number of drug approvals fell 40% from the first time period to the second. This analysis also determined that each approved pharmaceutical generated fewer sales in the 2005-2010 time frame while R&D spending doubled.[108]

Productivity Issues

Many experts claim that the loss of patent protection on these drugs is occurring at a time when innovation and productivity have stalled in the pharmaceutical industry. Murray Aiken, Executive Director of the IMS Institute for Healthcare Informatics, noted that while R&D investments are increasing, raising productivity associated with this spending "continues to be a struggle."[109]

> In recent years, the R&D productivity challenge has become particularly difficult to overcome in the pharmaceutical sector. The cost of developing a new drug has increased, as have total R&D expenditures, while the rate of introduction of new molecular entities

[101] Gregory J. Glover, "The Influence of Market Exclusivity on Drug Availability and Medical Innovations," *The AAPS Journal*, August 3, 2007, E313.

[102] *The Hatch-Waxman Act: Still Critical, Still in Flux.*

[103] *The Evolution of the Pharmaceutical Industry*, 172.

[104] *Drug Trend Report*, 42.

[105] Ben Hirschler, "Last Chance for Sickly Pharma to Deliver on R&D," *Reuters*, February 10, 2011, available at http://www.reuters.com/article/2011/02/10/pharmaceuticals-rd-idUSLDE71912R20110210.

[106] *Beyond the Shadow of a Drought, The Need for a New Mindset in Pharma R&D,* 2.

[107] Ibid.

[108] Ibid., 2-3.

[109] As quoted in Pat Wechsler and Alex Nussbaum, "Drug Spending Growth Drops as Brands are Replaced by Generics," *Bloomberg.com*, May 18, 2011, available at http://www.bloomberg.com/news/2011-05-18/drug-spending-growth-drops-as-brands-are-replaced-by-generics.html.

> (NMEs) has at best remained constant and attrition rates have risen sharply, especially in late-phase clinical trials.[110]

According to Jean-Pierre Garnier, Chief Executive Officer of GlaxoSmithKline, the value of "Big Pharma" is diminishing because of declining R&D productivity.[111] As evidence of this, one study found that in 2010, domestic spending on drugs that were on the market for less than 24 months comprised 2.8% of brand spending, down from 5.0% in 2006. In addition, "The number of products in this group totaled 69 in 2010, down from 96 in 2006, reflecting the decline in products emerging from research and development laboratories and receiving regulatory approval."[112]

The pharmaceutical industry is particularly research intensive. In 2009, total pharmaceutical industry investment in R&D was estimated to be $65.3 billion;[113] domestic research and development spending for members of PhRMA in 2009 was an estimated $45.8 billion, with 19% of domestic sales reinvested in R&D.[114] The Congressional Budget Office reported 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."[115] However, while pharmaceutical R&D expenditures have increased substantially over the past 15 years, drug approvals have remained relatively flat.[116] Analysis 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.[117]

Addressing R&D productivity, an August 2011 report by KPMG LLP stated that "industry success rates in bringing a drug from research to market was just 4% between 2005 and 2009. This is clearly an unsustainably low rate."[118] Research by analysts from McKinsey & Company found that "the internal rate of return (IRR) on small-molecule R&D is now ~7.5%, which is less than the industry's cost of capital."[119] Additional analysis by Bain & Company indicated that

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[110] Fabio Pammolli, Laura Magazzini, and Massimo Riccaboni, "The Productivity Crisis in Pharmaceutical R&D," *Nature Reviews Drug Discovery*, June 2011, 428.

[111] Jean-Pierre Garnier, "Rebuilding the R&D Engine in Big Pharma," *Harvard Business Review*, May 1, 2008, 70.

[112] *The Use of Medicines in the United States: Review of 2010*, 18.

[113] *Pharmaceutical Industry Profile 2010*, inside front cover.

[114] Ibid., inside front cover and 45.

[115] Congressional Budget Office, *Research and Development in the Pharmaceutical Industry*, October 2006, 9, available at http://cbo.gov/sites/default/files/cbofiles/ftpdocs/76xx/doc7615/10-02-drugr-d.pdf.

[116] Ernst & Young, *Beyond Borders, Global Biotechnology Reports 2008,* 18, available at http://www.ey.com/beyondborders.

[117] *Industry Surveys, Healthcare: Pharmaceuticals*, 16.

[118]KPMG, *Future Pharma, Five Strategies to Accelerate the Transformation of the Pharmaceutical Industry by 2020*, August 2011, 12, available at http://www.kpmg.com/CH/en/Library/Articles-Publications/Documents/Sectors/pub-20111017-future-pharma-en.pdf.

[119] Eric David, Tony Tramontin, and Rodney Zemmel, "Pharmaceutical R&D: The Road to Positive Returns," *Nature Reviews/ Drug Discovery*, August 2009, 609.

"The return on invested capital (ROIC) for new-drug development has dropped from 9 percent in 1995-2000 to an anemic 4 percent today."[120] In another Bain & Company study, the authors argued that "the pace of innovation remains anemic.... Despite R&D spending at a high 18 percent of revenues, Big Pharma's R&D productivity declined by 20 percent between 2001 and 2007."[121]

Similarly, the authors of the Oliver Wyman report determined that "R&D productivity declined by more than 70 percent between 1996-2004 and 2005-2010."[122] Looking at the 20 largest pharmaceutical companies, the study found that 17 of these firms experienced reduced productivity.[123] Research on the top 12 pharmaceutical firms, measured by R&D spending, conducted by the Deloitte Centre for Health Solutions also indicated that there were decreasing returns to investments between 2010 and 2011.[124] Thus, according to David Redfern, head of strategy at GlaxoSmithKline, "I am absolutely convinced that this will be the last generation of R&D spending unless a decent return is generated."[125]

Many of the studies on pharmaceutical productivity count the number of NMEs approved by the FDA. However, other experts maintain that calculating new drug approvals 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%-30% of R&D spending is directed at finding new indications for existing products. 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.[126]

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.[127] 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 to market.[128] The basic research leading to the new product may even begin many years prior to the actual discovery, thus, any productivity gap is short-term as new drugs move toward approval.[129] According to Boston University's Iain Cockburn:

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[120] *Bringing Pharma R&D Back to Health*, 1.

[121] Nils Behnke and Norbert Hueltenschmidt, "Changing Pharma's Innovation DNA," *Bain & Company*, 2010, 1, available at http://www.bain.com/Images/BAIN_BRIEF_Changing_pharmas_innovation_DNA.pdf.

[122] *Beyond the Shadow of a Drought, The Need for a New Mindset in Pharma R&D,* 3.

[123] Ibid.

[124] Deloitte Centre for Health Solutions, *Measuring the Return from Innovation, Is R&D Earning its Investment?,* 2011, 1, available at http://www.deloitte.com/assets/Dcom-Switzerland/Local%20Assets/Documents/EN/LSHC/ch_en_measuring_the_return_from_innovation_2011.pdf.

[125] "*Last Chance" for Sickly Pharma to Deliver on R&D.*

[126] 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.

[127] *Beyond Borders, Global Biotechnology Report 2008*, 18.

[128] 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.

[129] 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.

> 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.[130]

Other commentators point out that any perceived decline in productivity is partially a result of pharmaceutical companies' investments in high risk areas. It is argued

> that the number of NMEs is an imperfect measure of R&D outcomes, as it does not reflect changes in the quality of the output. In addition, the productivity crisis might be a temporary phenomenon, as radical technological changes, such as the genomic revolution, could initially increase the time lag between investment and outcome, thereby reducing R&D productivity in the short term.[131]

Concluding Observations

Companies have developed certain strategies for addressing the issues associated with the loss of patent protection on those pharmaceuticals that contribute significantly to the companies' bottom line. Among these are branded generics,[132] reformulations of the original brand product, price increases, or "deals" with insurance companies to lower the cost of the drug. Manufacturers are spending R&D dollars to develop new and improved forms of the original pharmaceutical 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.[133] 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."[134] 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%.[135]

However, according to Danzon and Furukawa, the majority of these defensive strategies do not work in the United States, with the exception of delayed release formulations that act to deter generic penetration in the domestic market.[136] Similar findings were reported on by Bain & Company: "Mergers and acquisitions and the creation of mega-companies have not compensated for the slowdown in innovation." Nor will "geographic expansion and diversification into new areas like consumer health."[137] Thus, as stated by analyst Michael Hay,

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[130] 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.

[131] *The Productivity Crisis in Pharmaceutical R&D*, 428.

[132] See CRS Report RL33605, *Authorized Generic Pharmaceuticals: Effects on Innovation*, by John R. Thomas.

[133] Ibid.

[134] *Pharma 2020: Marketing the Future*, 11.

[135] PriceWaterhouseCoopers, *Pharma 2020: The Vision*, June 2007, 8, available at http://www.pwc.com/pharma.

[136] *Cross-National Evidence on Generic Pharmaceuticals: Pharmacy vs Physician-Driven Markets*, 6.

[137] *Changing Pharma's Innovation DNA*, 1.

> if companies are unable to bring new drugs to market they will either need to cut spending to maintain profit or acquire new drugs that are generating sales, through mergers and acquisitions. But given the scale of revenue being lost, it is difficult and expensive to gain enough revenue through the latter route.[138]

Deloitte's Terry Hisey argues that the loss of patent protection on branded drugs is both a "threat and an opportunity." For brand-name firms, despite the steep decrease in price and the resulting loss of revenue,

> innovator companies have a well-established brand and product and there is an opportunity to leverage that, to expand into other markets and to continue to do a certain level of promotion. Even though it's off-patent it's got a clear clinical history and a well-known track record with people.[139]

For the consumer, prices for generic drugs themselves tend to fall over time.[140] As noted by Danzon and Furukawa, "Expiry of patent barriers to entry also makes generic markets potentially more competitive than originator markets."[141] Analysis indicates that within the past five years, the rapid and extensive generic entry has caused prices for these drugs to decline rapidly:

> The generic price index [indexed at 100 at month zero] falls to a level of about 78 at month six [after launch of the first generic], with an average number of generic entrants at seven. At months 12 and 24, the average generic price index falls to about 50 and 23, respectively, and then stabilizes at about -6 after month 25, even as the average number of generic manufacturers gradually increased to about 10, 11, and 12, respectively.[142]

In the absence of the research, development, and testing performed by the brand name pharmaceutical companies, generic drugs would not exist. However, as argued by Hans Poulsen, head of life sciences consulting at Thomson Reuters, "For the first time, drug companies are reducing costs in their R&D organizations and I believe we will see that trend continue."[143] There appears to be a declining number of new products in the clinical pipeline as well as "sharply diminishing returns in drug R&D."[144]

Many factors contribute to innovation in the pharmaceutical industry and its ability to bring new and inventive products to the marketplace, including the cost of capital, FDA approval requirements, and insurance coverage. At the same time, this sector is facing significant issues associated with the loss of revenue available for additional R&D as blockbuster drugs lose patent protection and are subject to generic competition. It appears that "Big Pharma (the large-capitalization pharmaceutical sector) remains in transition."[145] As such, Congress may act to

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[138] *The Patent Cliff Steepens*, 13.

[139] Quoted in *The Patent Cliff: Rise of the Generics.*

[140] 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.

[141] *Cross-National Evidence on Generic Pharmaceuticals: Pharmacy vs Physician-Driven Markets*, 3.

[142] *Brand Loyalty, Generic Entry and Price Competition in Pharmaceuticals in the Quarter Century After the 1984 Waxman-Hatch Legislation*, 9.

[143] *Drug R&D Spending Fell in 2010, and Heading Lower*.

[144] Fabio Pammolli and Massimo Riccaboni, "Market Structure and Drug Innovation," *Health Affairs*, January/February 2004, 49.

[145] *Industry Surveys, Healthcare: Pharmaceuticals*, 13.

explore ways to incentivize firms to increase innovation in the pharmaceutical industry through changes to data and/or marketing exclusivities for new and improved drugs, reevaluating patent term extension, patent reform, and/or other regulatory mechanisms associated with intellectual property ownership. Yet, while the "data show a subtle relative decrease in pharmaceutical innovation in the United States, ... the United States remains the single-largest location of pharmaceutical invention."[146] At issue are what congressional actions, if any, may be necessary to maintain this innovative environment.

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[146] *Location of Pharmaceutical Innovation: 2000-2009*, 836.