The Assault on Pharmaceutical Intellectual Property

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Pharmaceutical research and development is a lengthy, risky, and expensive enterprise. The industry depends uniquely on patent and trade secret protections to support its investments in innovative activities. However, recent legislative and regulatory developments threaten the value of pharmaceutical intellectual property in two distinct respects. First, patent and related protections are being restricted, and effective enforcement of these rights is being made increasingly difficult. Second, price controls and similar initiatives are interfering with market-based returns during the limited period in which patent rights are in force. This Essay describes the importance of intellectual property rights to the pharmaceutical industry, reviews recent efforts to restrict these rights, and urges that pharmaceutical intellectual property rights should be protected in order to foster continued innovation in the interests of patients and society at large.

INTRODUCTION

Intellectual property rights drive innovation in the pharmaceutical and biotechnology industries. The value of these rights is under attack on two fronts. First, regulations and statutes increasingly restrict patent and trade secret protections and make it more difficult to enforce those that remain. Second, federal and state governments increasingly rely on price controls and other restrictions that interfere with market mechanisms during the period of exclusivity. Taken together, these developments threaten the large investments in research and development that support continued innovation.

This Essay reviews the importance of intellectual property rights for the pharmaceutical industry’s research and development activities and provides examples of restrictions on these rights and on the pharmaceutical market.

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1 For convenience, this Essay will use the term “pharmaceutical industry” to include the biotechnology industry. In point of fact, the distinction between the two is largely artificial. Most biotechnology medicines are developed or distributed by what are traditionally thought of as pharmaceutical companies.

2 While not the focus of this Essay, it should be noted that the premise of many industry critics—that drug prices and spending are “out of control”—is not supported by the facts. Prescription drug spending has remained stable for many years at approximately 10 percent of total healthcare spending, and most of the growth in such spending is the result of increasing use of medicines, particularly newer medicines, rather than price increases. See, for example, Pharmaceutical Research and Manufacturers of America (PhRMA), Focus on Health Policy: How Much
I. THE IMPORTANCE OF PHARMACEUTICAL INTELLECTUAL PROPERTY RIGHTS

The pharmaceutical research and development process is long, risky, and expensive. It typically takes from ten to fifteen years from drug discovery to approval by the Food and Drug Administration (FDA). Of every five thousand medicines tested, only one ultimately receives FDA approval. The average cost of developing a new drug has been estimated at $802 million. Only three out of every ten marketed drugs generate revenues that match or exceed average research and development costs.

The prospect of earning substantial revenues for successful drugs is a necessary incentive to encourage these investments. In addition to the expected competition from drugs with different active ingredients in the same therapeutic class, there are two factors that make compen-

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4 Id. FDA approval of a new drug requires proof of safety and effectiveness as demonstrated through preclinical (laboratory and animal) and clinical (human) studies, and the submission of a new drug or biologics license application. See 21 USC § 355 (2000); 42 USC § 262 (2000); 21 CFR §§ 314, 601 (2003).


8 See Frank R. Lichtenberg and Tomas J. Philipson, The Dual Effects of Intellectual Property Regulations: Within- and Between-Patent Competition in the US Pharmaceuticals Industry (Oct 2002), online at http://papers.nber.org/papers/w9303.pdf (visited Jan 21, 2004). Further complicating the situation, one or more products in the class may be off-patent while others are not. In fact, the time period between the introduction of the first drug in a new therapeutic class and the second has been shrinking steadily over the last thirty-five years. See PhRMA, Industry Profile at 61 (cited in note 5).
tition from copies of the original (so-called "generics" because they typically are unbranded) especially challenging.

First, the end product of the investment in most cases consists overwhelmingly in the information that is generated about the drug's safety and effectiveness, rather than in the physical properties of the compound. At least for most small-molecule products, it may be a relatively straightforward exercise to reverse engineer a drug product that conforms to the physical chemical specifications of the original and is absorbed into the bloodstream in a comparable manner. To the extent that generic manufacturers need not invest in duplicating the innovator's safety and effectiveness information, their costs are reduced substantially.

Second, a number of legal and economic considerations, largely unique to the pharmaceutical industry, substantially favor use of generic copies over use of the original brand product. Under state pharmacy laws, pharmacists are permitted, and in some states required, to dispense a generic copy when presented with a physician's prescription for the brand product, unless the physician has expressly prohibited substitution. Even where substitution is only permissive, pharmacists typically earn a significantly greater margin on a generic product, despite its lower price to the consumer or insurer. Moreover, the FDA generally prohibits brand companies from making any claims of superiority or even differences between their products and those of generic competitors. Finally, managed care organizations and

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9 The difficulties tend to be greater for biotechnology products that consist of proteins and other large molecules. Certain small-molecule products also can present unusual challenges because of their physical properties or formulation characteristics, for example. The FDA defines drugs as "bioequivalent" if they do not exhibit a significant difference in the rate and extent of absorption. See 21 USC § 355(j)(8); 21 CFR § 320.1(e) (2003).

10 In addition, of course, generic manufacturers do not bear the cost of investing in dry holes but need only duplicate drugs that are proven successes. They also need not bear the expense of disseminating product information to physicians.

11 See, for example, Inwood Labs, Inc v Ives Labs, Inc, 456 US 844, 847 n 4 (1982) (noting that since the 1970s most states have adopted laws allowing generic substitutions and that New York's law requires a pharmacist to substitute a generic if the doctor indicates such substitution is "permissible" and if a generic drug is on the state's approved list); Bruce N. Kuhlik, The FDA's Regulation of Pharmaceutical Communications in the Context of Managed Care: A Suggested Approach, 50 Food & Drug L J 23, 29 (1995).

12 See, for example, Peter Alagona, Jr., Generic Drug Substitution, American College of Cardiology, Florida Chapter Newsletter (June 2001), online at http://www.accfl.org/news-june2001.htm (visited Jan 21, 2004).

other insurers employ a variety of utilization controls and powerful financial incentives to favor use of generics."

Taken together, these factors make the market for the brand product highly elastic and lead rapidly to substantial loss of market share once generic copies enter the market. Indeed, in the case of the widely used antidepressant Prozac (fluoxetine hydrochloride), a large pharmaceutical benefits manager serving sixty-five million members reported that it had switched 80 percent of its mail-order customers filling a prescription for the drug to a single generic within the first week that it became available.15

In the absence of intellectual property protections, generic market entry could occur within a few years of brand entry, depending primarily on the time needed to develop the generic copy and secure FDA approval.16 Such a short period would be inadequate to attract anything approaching the current level of investment in pharmaceutical research and development. That investment rests on two principal forms of intellectual property protection: patents and, to a lesser extent, trade secrets.17 The pharmaceutical industry is more dependent on these protections, particularly patent protections, than any other industry.18

Patents typically are applied for relatively early in the research and development process, soon after there are initial indications from laboratory studies that a compound may have beneficial biological activity. Although the term of a patent is twenty years from filing, the ef-
effective patent life for pharmaceuticals—the time remaining following FDA approval—is approximately eleven to twelve years in practice. Effective patent life for other industries averages approximately 18.5 years.

In the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the “Hatch-Waxman Act,” Congress for the first time linked drug approvals to patents. A generic copy can be approved based on the safety and effectiveness of the innovator product, but only if the generic applicant agrees either to wait for relevant patents to expire or provides a notice to the patent holder that allows for thirty months in which to litigate the patent issues before the FDA may approve the generic product. Importantly, the law also provides a 180-day exclusivity period for the first generic to challenge a patent as an incentive for such challenges.

The other relevant intellectual property right consists of protection for the safety and effectiveness data developed by the innovator company. Prior to the enactment of the Hatch-Waxman Act, the FDA regarded these data as trade secrets that could neither be publicly re-

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19 PhRMA, Industry Profile at 62 (cited in note 5). This takes into account the partial restoration of the patent term for time lost during the FDA approval process pursuant to 35 USC § 156 (2000). Counterbalancing that additional time is the exemption to infringement under 35 USC § 271(e)(1), which permits generic companies to manufacture and test their products before patent expiration for the purpose of seeking FDA approval. Both section 156 and section 271(e)(1) were added to the Patent Code by the Drug Price Competition and Patent Term Restoration Act of 1984, Pub L No 98-417, 98 Stat 1585. Section 271(e)(1) overruled Roche Products, Inc v Bolar Pharmaceutical Co, 733 F2d 858, 863 (Fed Cir 1984), and is commonly referred to as the “Bolar exception.”

20 PhRMA, Industry Profile at 62 (cited in note 5).

21 See note 19.

22 “Previously, FDA approved all forms of [new drug applications] without any consideration of patent status.” Peter Barton Hutt and Richard A. Merrill, Food and Drug Law 572 (Foundation 2d ed 1991). The Hatch-Waxman Act does not apply to products regulated by the FDA as biologics pursuant to section 351 of the Public Health Service Act, 42 USC § 262. Biologics include many, but not all, large-molecule medicines. See note 59.

23 See 21 USC § 355(j)(2)(A)(vii)(III)–(IV) and (j)(5)(B)(ii)–(iii). The Hatch-Waxman Act established a new act of infringement under 35 USC § 271(e)(2)(A) based on submission of the generic application in order to allow the litigation to proceed before approval and marketing of the accused product. In effect, the thirty-month stay functions as an automatic preliminary injunction during that litigation. It was instituted in significant part as a balance to the Bolar exception (see note 19), which prevents patent holders from suing for otherwise infringing activities occurring prior to submission of the generic drug application. See Closing the Gaps in Hatch-Waxman: Assuring Greater Access to Affordable Pharmaceuticals, Hearing before the Senate Committee on Health, Education, Labor, and Pensions, 107th Cong, 2d Sess 11–15 (2002) (statement of Senator Orrin Hatch).

24 21 USC § 355(j)(5)(D)(iv). Some generic companies rely on early patent challenges as a primary business strategy. See, for example, Rob Wherry, Lawyers in Lab Coats, Forbes 60 (Sept 4, 2000) (discussing Barr Laboratories' successful campaign to strike down Eli Lilly's patent protection for Prozac); Barr Laboratories, Corporate Profile, online at http://www.barrlabs.com/pages/corpmiss.html (visited Jan 21, 2004) (describing Barr's corporate policy of challenging patents that it believes are invalid, unenforceable, or not infringed by their products).
leased nor relied upon by the FDA or any other company for the approval of a copy of the innovator product. As stated by the agency in the preamble to its Freedom of Information Act (FOIA) regulations in 1974:

[T]here can be no question, under present law, about the tremendous economic value of the full reports of the safety and effectiveness data contained in [new drug applications]. . . . Release of such information would allow a competitor to obtain approval from the Food and Drug Administration for marketing the identical product, at a mere fraction of the cost.

Under the pre-1984 regime, safety and effectiveness data were considered proprietary and non-disclosable in perpetuity. In the Hatch-Waxman Act, Congress limited the term of exclusivity for safety and effectiveness data to five years for data submitted in support of the approval of a new chemical entity and three years for other data. After that, a generic company may rely on the innovator's data to gain approval of its own product through an "abbreviated new drug application."

The five-year and three-year data exclusivity periods have proven to be of relatively limited importance as compared to patents. In most cases, the five-year period will expire before the basic composition-of-matter patent. It remains important, however, in those cases involving unpatentable drugs or drugs with shorter patent lives. It also is im-

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25 See, for example, Hutt and Merrill, Food and Drug Law at 572 (cited in note 22).
26 FDA, Public Information, 39 Fed Reg 44602, 44633–34 (1974). A court later determined that these data are not entitled to treatment as common-law trade secrets because they do not relate to the manufacturing process, but it nonetheless recognized that they can be protected from disclosure under FOIA as confidential commercial information. See Public Citizen Health Research Group v FDA, 704 F2d 1280 (DC Cir 1983); 5 USC § 552(b)(4) (2000); 21 CFR § 20.61 (2003).
27 See 21 USC § 355(j)(5)(D)(ii)–(iv); 21 CFR § 314.108 (2003). A ten-year period of exclusivity was provided for new chemical entities approved between January 1, 1982, and the date of enactment of the law, September 24, 1984, and a two-year period of exclusivity for other approvals between those dates. See 21 USC § 355(j)(5)(D)(i), (v). No challenge was ever brought to the law on the basis of an argument that it unconstitutionally defeated reasonable investment-backed expectations of confidential treatment of safety and effectiveness data, compare Ruckelshaus v Monsanto Co, 467 US 986 (1984) (finding a taking when a federal agency discloses information that the applicant had a reasonable expectation would remain confidential), nor did industry challenge the constitutionality of the Bolar exception.
28 See 21 USC § 355(j).
29 In Europe, by contrast, a ten-year period of data exclusivity generally is provided for new chemical entities. See Richard F. Kingham and Grant H. Castle, Data and Marketing Exclusivity for Pharmaceuticals in the European Community, 55 Food & Drug J 209, 210–11 (2000). Such a period would exceed the remaining patent term for a greater number of products than the five- and three-year periods provided for by United States law. Moreover, exclusivity in many cases offers greater certainty of protection because it operates as an absolute bar against approval (unless the competitor generates its own data package) and does not entail litigation regarding patent validity and scope.
important because it prevents a generic company from filing an abbreviated new drug application until five years after FDA approval of the innovator drug, or four years in conjunction with a patent challenge.\textsuperscript{30} The three-year period can be significant for certain new dosage forms, but it does not offer meaningful protection for data developed to support new indications (drug uses), because generics may leave those indications out of their labeling and still be approved and eligible for substitution by the pharmacy.

Investments in pharmaceutical research and development thus rest on the framework of patent rights, data exclusivity, and generic drug approval procedures established by the Hatch-Waxman Act. While the effect of the Act on innovation since 1984 can be debated, the focus of this Essay is instead on recent developments that threaten to diminish the value of pharmaceutical patent rights, taking the existing Hatch-Waxman framework as a baseline.\textsuperscript{31}

II. EMERGING RESTRICTIONS ON PHARMACEUTICAL INTELLECTUAL PROPERTY PROTECTIONS

A number of recent legislative and regulatory initiatives seek to restrict pharmaceutical intellectual property rights and to make it more difficult for owners of these rights to enforce them. These developments increase uncertainties surrounding the length of time during which pharmaceutical companies will have exclusive marketing rights for their inventions. This Part focuses on three significant areas in which these developments are occurring: changes in the Hatch-Waxman Act and its implementing regulations relating to patents; expansion of the circumstances in which the FDA will rely on proprietary safety and effectiveness data; and consideration of abbreviated approval routes for generic biological products.

\textsuperscript{30} See 21 USC § 355(j)(5)(D)(ii). A competitor willing to develop its own full package of safety and effectiveness data need not wait for the exclusivity period to expire before challenging a patent.

\textsuperscript{31} See 21 CFR § 314.94(a)(8)(iv); Bristol-Myers Squibb Co v Shalala, 91 F3d 1493 (DC Cir 1996). Accordingly, the incentives for continued innovation surrounding already-patented compounds are limited. They have been further limited by new restrictions on the thirty-month stay as applied to litigation on new patents. See text accompanying notes 40–46.

\textsuperscript{32} Professor Grabowski recently observed that the Waxman-Hatch Act has provided a relatively balanced approach to the trade-offs between pharmaceutical R&D and generic competition. Improvements on the margin could be considered by policymakers, such as a longer minimum [data] exclusivity period . . . . Given the critical role that patents and effective patent life play in terms of R&D incentives for this industry, . . . [the suggestion that changes be made in the law in favor of generics] would not appear to be a desirable course of action on social welfare grounds.

A. Hatch-Waxman Patent Developments

On July 31, 2002, the U.S. Senate passed S 812, the "Greater Access to Affordable Pharmaceuticals Act," by a bipartisan vote of 78–21. The bill would have made several significant changes in the Hatch-Waxman Act, including the following:

- the thirty-month stay would have been limited to patents issued and listed with the FDA within thirty days of approval of the innovator drug;
- patent holders would have been barred from bringing an infringement action against a generic applicant on a listed patent if they failed to do so within forty-five days of receiving notice from the generic company asserting that the patent was invalid or not infringed;
- the requirements for listing a patent with the FDA would have been made more numerous and burdensome; at the same time, patent holders would have been barred from bringing infringement actions based on patents that should have been—but were not—listed with the FDA; and
- a private cause of action would have been established to allow generic companies to seek delisting of patents independent of infringement litigation.

Supporters of the bill stated that it was necessary to address alleged abuses of the thirty-month stay and patent listing provisions. The Bush Administration opposed the bill, stating that it would "unnecessarily encourage litigation . . . and would complicate the process of filing and protecting patents on new drugs," thereby "reduc[ing] ac-

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33 Greater Access to Affordable Pharmaceuticals Act, S 812, 107th Cong, 2d Sess, in 148 Cong Rec S 6884 (July 17, 2002).
34 See 148 Cong Rec S 7651 (July 31, 2002).
35 S 812 §§ 103–04 (cited in note 33). The bill also would have made substantial changes to the 180-day exclusivity provision. See id § 105.
36 See, for example, Remarks of Senator Kohl, 107th Cong, 2d Sess, in 148 Cong Rec S 7649 (July 31, 2002). For a rebuttal, see Examining Issues related to Competition in the Pharmaceutical Marketplace: A Review of the FTC Report, 'Generic Drug Entry Prior to Patent Expiration,' Hearing before the House Subcommittee on Health of the House Committee on Energy and Commerce, 107th Cong, 2d Sess (2002) (testimony of Dr. Gregory Glover). Just as the Senate was passing S 812, the Federal Trade Commission (FTC) issued a report finding that the thirty-month stay generally had not delayed generic drug entry but that there had been eight instances of multiple thirty-month stays. See FTC, Generic Drug Entry Prior to Patent Expiration: An FTC Study 39, 48 (July 2002), online at http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf (visited Jan 21, 2004). In its report, the FTC recommended much more limited changes in the law than those in S 812. Id at ii–xi. The FTC has taken action in cases involving multiple thirty-month stays and allegedly anticompetitive agreements between brand and generic companies involving the 180-day exclusivity provision. See, for example, The FTC Study on Barriers to Entry in the Pharmaceutical Marketplace, Hearing before the Senate Committee on the Judiciary, 108th Cong, 1st Sess (2003) (testimony of Timothy Muris, FTC Chairman). In fact, both practices appeared to have ended by the time the agency issued its report.
cess to new breakthrough drugs.” Similarly, the Patent and Trademark Office stated that the bill “would likely do the opposite of what its title suggests—by limiting access to cutting-edge drugs, decreasing innovation, and ultimately harming the quality of treatments available to patients.” The House of Representatives did not act on a companion measure to S 812.

On October 21, 2002, President Bush took the unusual step of personally announcing from the Rose Garden that the FDA was proposing to change its Hatch-Waxman regulations to limit patent holders to a single thirty-month stay against each generic applicant and to tighten the restrictions on patent listings. The final regulations were published on June 18, 2003. The innovator industry had noted in comments to the proposed regulations that they contained substantial loopholes that could allow generic applicants to avoid even one thirty-month stay. The FDA declined to change the regulations to close these loopholes, concluding that “any advantage that a party can find in manipulating the regulatory program will be pursued,” and “we do not believe we can completely prevent attempts at ‘creative compliance’ by the parties.”

38 Letter from James E. Rogan, Under Secretary of Commerce and Director, Patent and Trademark Office, to Senator Orrin Hatch (July 30, 2002) (on file with author).
39 See Library of Congress, Bill Summary and Status for the 107th Congress: HR 1862, online at http://thomas.loc.gov/cgi-bin/bdquery/z?d107:HR01862:@@@L&summ2=m&bss/d107query.html (visited Jan 21, 2004) (showing that the bill had been referred to House subcommittee with a discharge petition filed).
40 See Office of the Press Secretary, President Takes Action to Lower Prescription Drug Prices by Improving Access to Generic Drugs (Oct 21, 2002), online at http://www.whitehouse.gov/news/releases/2002/10/20021021-4.html (visited Jan 21, 2004). The proposed regulations were published in the Federal Register on October 24, 2002. See FDA, Applications for FDA Approval to Market a New Drug: Patent Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug Is Invalid or Will Not Be Infringed, 67 Fed Reg 65448 (2002). The basis for the thirty-month stay proposal—which represented a complete shift from the interpretation that the FDA had followed for eighteen years—was that a generic drug application would not be amended to “include” a certification of patent invalidity or noninfringement if it already included such a certification to a different patent.
43 68 Fed Reg at 36688 (cited in note 41). The agency apparently either discounted the possibility or importance of gaming by generic companies, or considered it an acceptable price for preventing innovator companies from obtaining multiple thirty-month stays.
Congress recently enacted amendments to the Hatch-Waxman Act as part of Medicare prescription drug benefit legislation. These amendments restrict the availability of a thirty-month stay to patents listed with the FDA before the generic application was filed and allow generic companies to seek patent delisting as a counterclaim in an infringement suit. The amendments also make substantial changes in the 180-day exclusivity provision, which may well increase the attractiveness of this incentive and thereby encourage patent challenges by generic applicants. Patent challenges by generic companies have been on the rise in recent years. While relatively few patents were challenged for the first decade or so under Hatch-Waxman, these challenges are now becoming commonplace, particularly for the best-selling innovator drugs, whose success funds the research and development process. Recent findings of willful infringement against generic companies have shown that some patent challenges are "simply ... calculated longshot gamble[s]" premised only on taking advantage of the uncertainties inherent in litigation, especially litigation involving such complex subjects as patent validity and infringement.

45 This was the recommendation made by the FTC. It generally limits patent holders to a single thirty-month stay, unless a generic applicant decides to change its certification later for a patent listed before it filed its application.
46 The new law also provides that a generic company may file a declaratory judgment action under certain circumstances if it is not sued within forty-five days of its certification. See id § 1101. The law does not include a provision in the Senate bill that would have established jurisdiction over these cases, and the legislative history is clear that the law is not intended to change the Article III standards for jurisdiction, particularly the requirement that the plaintiff in a declaratory judgment action involving a patent demonstrate a "reasonable apprehension" that it will be sued for infringement. See Conference Report to Accompany HR 1, HR Rep No 108-391, 108th Cong, 1st Sess 836 (2003).
47 For example, the amendments will allow generics to retain their exclusivity and avoid triggering the beginning of the 180-day period even after they prevail in litigation in the district court. See MPDIMA § 1102, 117 Stat at 2457.
48 See FTC, Generic Entry Prior to Patent Expiration at ii (cited in note 36):
An increasing number of generic applicants have sought entry prior to patent expiration. During the 1980s, only 2 percent of generic applications sought entry this way, but from 1998 to 2000, approximately 20 percent of the generic applications sought entry prior to patent expiration.... [These include] some of the largest drug products as measured by annual sales.
49 Eli Lilly & Co v Zenith Goldline Pharmaceuticals, Inc, 264 F Supp 2d 753, 759 (SD Ind 2003). The court continued: "Before a party like Zenith forces a drug patent holder to defend its patent, at considerable expense, it is reasonable to expect the party filing the notice under the Hatch-Waxman Act to have something more solid than hope on its side." Id.
50 See Yamanouchi Pharmaceutical Co v Danbury Pharmacal, Inc, 231 F3d 1339, 1347 (Fed Cir 2000) (stating that the generic committed "misconduct in filing a wholly unjustified [abbreviated new drug application] certification" of patent invalidity); Glaxo Group Ltd v Apotex, Inc, 268 F Supp 2d 1013, 1033 (ND Ill 2003) (noting that the generic company chief executive officer
B. Hatch-Waxman Data Protection Developments

The FDA is in the process of expanding the circumstances under which it will rely on an innovator's proprietary safety and effectiveness data to approve another manufacturer's product. The Hatch-Waxman Act contemplates such reliance only through the abbreviated application process for copies of innovator products. The Act also permits follow-on companies to rely on published safety and effectiveness studies performed by innovators (or others), even when they do not have a "right of access" to the data underlying those studies. This process, referred to as a "section 505(b)(2)" application, was intended to codify the FDA's pre-1984 "paper NDA" (new drug application) policy, which likewise permitted such reliance. In 1999, however, the FDA published a draft guidance document stating that the agency would accept section 505(b)(2) applications that rely not only on published data, but also on the unpublished safety and effectiveness data in the innovator company's approved new drug applications. This would substantially expand the circumstances under which these applications could be used. One significant example would be to allow a follow-on company to obtain approval of a different salt of an approved innovator drug, something that is not permitted under the abbreviated application route because the active ingredients are not identical. Depending on the scope of the innovator's patent protection, this approach could allow closely related com-

had filed a notice of noninfringement without obtaining the opinion of counsel); Astra Aktiebolag v Andrx Pharmaceuticals, Inc, 222 F Supp 2d 423, 513 (SD NY 2002) (stating that the generic "did not have a good faith basis for asserting that its product did not infringe"), affd, 2003 US App LEXIS 24899 (Fed Cir).

51 See 21 USC § 355(j).

52 See Federal Food, Drug, and Cosmetics Act § 505(b)(2), 52 Stat 1052 (1938), codified at 21 USC § 355(b)(2). The "paper NDA" policy is set forth at 46 Fed Reg 27396 (1981). For discussions of the intended scope of section 505(b)(2) applications, see, for example, Biotechnology Industry Organization, Citizen Petition: Follow-on Therapeutic Proteins, FDA Docket No 03P-0176, 14-20 (Apr 23, 2003), online at www.bio.org/adv/BIO_CP--FINAL_DRAFT_4_22_03.pdf (visited Jan 21, 2004) (arguing that section 505(b)(2) only codifies the FDA's then-existing policy and was not intended to apply to follow-on versions of biological products); Pfizer, Inc. Reply of Pfizer, Inc. to Comments of Dr. Reddy's Laboratories, Inc. on Pfizer's October 11, 2002 Citizen Petition, FDA Docket No 02P-0447 (Apr 28, 2003), online at http://www.fda.gov/ohrms/dockets/dailys/03/ Apr03/043003/f02p-0447-r00001-vol1.pdf (visited Jan 21, 2004) (arguing that Congress did not intend to change the standard of what data are afforded trade secret protection). For a contrary view of the scope of section 505(b)(2), see, for example, Dr. Reddy's Laboratories, Inc. Response to Citizen Petition filed by Pfizer, Inc., on October 11, 2002, FDA Docket No 02P-0447 (June 4, 2003), online at http://www.fda.gov/ohrms/dockets/dailys/03/June03/060903/02p-0447-sup0001-01-vol1.pdf (visited Jan 21, 2004) (claiming that section 505(b)(2) allows reliance on data from approved applications to the extent allowed by § 505(j)).


54 See 21 USC § 355(j)(2)(A)(ii)(1) (requiring the active ingredient of the new drug to be the same as that of the listed drug in abbreviated applications); 21 CFR § 314.92(a)(1).
peting products to enter the market years before what had been anticipated. The issue will be particularly acute if the Federal Circuit affirms a lower court decision holding that patent rights during the restoration period under 35 USC § 156(b) are limited to the precise form of the active ingredient present in the innovator product and do not extend to different salts or other variants, even if those are claimed by the patent.

The FDA also is considering whether it can force a pharmaceutical company to switch a drug from prescription to over-the-counter status. Historically, the decision whether to initiate a switch request has rested solely with the manufacturer. However, health insurers—seeking to reduce their prescription drug coverage costs—have asked the FDA to switch certain nonsedating antihistamines, which would take those drugs out of the insurance benefit and require consumers to bear the full cost. Putting aside the question whether the FDA has the statutory authority to force a switch under the prescription limitation and new drug provisions of the law, it is difficult to see how the FDA could effectuate a switch without relying to a significant degree on the proprietary safety data contained in the innovator's new drug application. Because of the different economics of the prescription and nonprescription drug markets, the prospect of a forced switch during the period of patent exclusivity would inject substantial new uncertainty into an innovator's investment decisions and life-cycle revenue projections.

C. Approval Requirements for Generic Biological Products

Most biologics—including proteins and other large molecules—are licensed by the FDA under a different statutory and regulatory

55 As with generics approved through the abbreviated process, the ability of section 505(b)(2) applicants to rely on the innovator's safety and effectiveness data will dramatically lower their development costs.

56 See Pfizer Inc v Dr. Reddy's Laboratories, Ltd. 2002 WL 31833744 (D NJ 2002), appeal pending (Fed Cir Nos 03-1227 and 03-1258). On October 14, 2003, FDA issued a response to various citizen petitions in which it decided that section 505(b)(2) does provide authority for the agency to rely on unpublished innovator safety and effectiveness data to approve applications for different salts and other products that could not be approved through the abbreviated-application process. See FDA Letter to Counsel in Docket Nos 2001P-0323, 2002P-0447, and 2003-0408, online at http://www.fda.gov/cder/ogd/505b2-CPResponse.pdf (visited Jan 21, 2004). On November 13, 2003, Pfizer filed a lawsuit against FDA challenging the agency's approval of the section 505(b)(2) application filed by Dr. Reddy's Laboratories for amlodipine maleate tablets, a different salt of the active ingredient in Pfizer's hypertension medication Norvasc (amlodipine besylate). See Pfizer Inc v FDA. No 1:03CV02346 (D DC 2003).


58 See 21 USC §§ 353(b), 355(e). All sides of the arguments are explored in the comments to Docket No 98P-0610 (cited in note 57).
scheme from the one applicable to "new drugs." The Hatch-Waxman Act does not apply to these biologics, and there is no other mechanism available for abbreviated biologics license applications. Accordingly, the approval of generic biological products must be supported by a full data package, without reliance on the innovator's safety and effectiveness data.

There is good reason for this, because the complexities of biological product manufacturing and testing would make any determination of comparability between different manufacturers' products daunting, if not impossible.

Nonetheless, there have been numerous calls for the FDA to begin approving so-called generic biologics by reinterpreting its authority under the Public Health Service Act, by reclassifying products as new drugs subject to the Hatch-Waxman Act, and by using the section 505(b)(2) process for those large-molecule products regulated as new drugs, such as insulin and human growth hormone. Some in Congress also have suggested that statutory changes should be considered.

The possibility that the FDA or Congress would allow generic biologics manufacturers to obtain approvals based on abbreviated data packages casts a significant shadow over the scope of intellectual property protections for innovator biological products.

59 Compare 42 USC § 262 and 21 CFR § 600 et seq (biologics), with 21 USC § 355 and 21 CFR § 314 (new drugs). However, the basis for certain classification decisions has proven elusive: for example, some hormones and enzyme replacement products have been regulated as drugs and others as biologics. See generally FDA, Intercenter Agreement between the Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research (Oct 25, 1991), online at http://www.fda.gov/oc/ombudsman/drug-bio.htm (visited Jan 21, 2004). The FDA recently transferred review and approval responsibilities for certain classes of biologics to the drug center, although this is not intended to affect the applicable legal requirements. See FDA, Drug and Biological Product Consolidation, 68 Fed Reg 38067, 38068 (2003); FDA, Press Release, FDA to Consolidate Review Responsibilities for New Pharmaceutical Products (Sept 6, 2002), online at http://www.fda.gov/bbs/topics/NEWS/2002/NEW00834.html (visited Jan 21, 2004) (“Current FDA policy on generic biologics will not be affected by this decision.”).

60 See, for example, Recent Developments Which May Impact Consumer Access to, and Demand for, Pharmaceuticals, Hearing before the Subcommittee on Health of the House Committee on Energy and Commerce, 107th Cong, 1st Sess (2001) (prepared statement of Dr. Janet Woodcock, Director, Center for Drug Evaluation and Research, Food and Drug Administration).


III. EMERGING RESTRICTIONS ON THE PHARMACEUTICAL MARKET

In addition to strong, predictable, and enforceable proprietary rights, the other major variable in determining the value of pharmaceutical intellectual property is the nature of the end-product market. Restrictions on competition in the market through price controls and other mechanisms will decrease expected returns during a product's patent life and thereby reduce incentives for investment in innovation. Although there are a number of other types of restrictions on the pharmaceutical market, this Essay will focus on summarizing recent price-control initiatives in two areas: those relating to Medicaid and those relating to importation.

A. Medicaid Developments

Under a federal law in effect since 1990, Medicaid—the cooperative federal-state medical assistance program for the poor—receives significant price concessions from pharmaceutical manufacturers. Specifically, manufacturers pay a rebate for each drug unit based on the larger of 15.1 percent of the drug's average manufacturer price or the difference between that price and the "best price" at which the drug is sold to private purchasers.\(^64\)

States have used the Medicaid rebate as the entering wedge for several new price-control initiatives. In one variant, states are seeking to expand the rebate beyond the Medicaid population to cover all, or a substantial portion, of their residents. This is accomplished by the threat that Medicaid patients' access to a manufacturer's drugs will be restricted unless the manufacturer agrees to price concessions for the non-Medicaid population.\(^65\) In a case that challenged a Maine law with

\(^{64}\) For example, there have been calls for restrictions on direct-to-consumer advertising of prescription drugs, and the fraud and abuse laws have been interpreted to prohibit a variety of activities—including many arrangements between buyers and sellers linking price concessions or other favorable terms with measures of product utilization—that would be regarded as lawful in other markets. See, for example, Say No to Drug Ads Act, HR 149, 108th Cong, 1st Sess (Jan 7, 2003), available at http://www.gpoaccess.gov/bills (visited Jan 21, 2004) (prohibiting tax deduction for direct-to-consumer advertising expenses); 42 USC § 1320a-7b(b) (prohibiting any inducement to use a product covered by a government healthcare program); Office of Inspector General, Department of Health and Human Services, OIG Compliance Program Guidance for Pharmaceutical Manufacturers, 68 Fed Reg 23731 (2003) (fraud and abuse compliance program guidance for pharmaceutical manufacturers).

\(^{65}\) See 42 USC § 1396r-8. The rebate also includes an inflation component under which an additional rebate is due if the average manufacturer price increases faster than the consumer price index. Manufacturers of generic drugs pay a flat 11 percent rebate.

\(^{66}\) Restrictions are imposed through a "prior authorization" process under which a physician cannot prescribe a drug of a nonparticipating manufacturer without first receiving permission from the state Medicaid agency on a patient-by-patient basis. Some prior authorization programs have proven cumbersome and difficult for physicians and patients to navigate, resulting in denials of access to needed medications. See Kaiser Commission on Medicaid and the Unin-
such provisions principally on the ground that it violated the Medicaid statute by restricting medical care to beneficiaries for a non-Medicaid purpose, the Supreme Court ruled in favor of the state at the preliminary injunction stage.67

Other states have sought to reduce prices within the Medicaid program below the statutory Medicaid “best price” rebate by requiring “supplemental” rebates and by creating restrictive lists of covered drugs limited to those of manufacturers that agree to pay the additional rebates.68 The Eleventh Circuit upheld such a program, and the Supreme Court denied certiorari following its decision in the Maine case.69 States also are seeking to join together and negotiate as a group for supplemental rebates.70

Taken together, these developments threaten the competitive dynamics of the pharmaceutical market. Although it embodies price-control features, the rebate structure established in 1990 within the Medicaid program borrows substantially from the private market through the “best price” requirement. Demands for supplemental rebates, especially those backed up through monopsony power and access restrictions, fundamentally change the program into one characterized by pervasive governmental price controls. Two aspects of this shift are particularly questionable: first, it is being driven by the states, with relatively little oversight by the federal government; second, it comes at a time when Congress has just rejected a governmental price-control model for the delivery of a Medicare prescription drug benefit.71

67 See Pharmaceutical Research and Manufacturers of America v Walsh, 123 S Ct 1855 (2003). There was no opinion for the Court on the critical issue. Writing for a plurality, Justice Stevens concluded that there was an insufficient showing of harm to Medicaid patients at this stage of the proceeding. See id at 1870. Justice Breyer wrote separately to emphasize that the appropriate balancing of benefits and harms should be done by the Secretary of Health and Human Services in the first instance. See id at 1872–73 (Breyer concurring). Justices Scalia and Thomas wrote separate opinions concurring in the judgment on other grounds. Justice O’Connor, joined by Chief Justice Rehnquist and Justice Kennedy, dissented. See also Pharmaceutical Research and Manufacturers of America v Thompson, 259 F Supp 2d 39 (D DC 2003) (upholding the Michigan program).

68 Drugs not on the list may be covered through a prior authorization process. See note 66.

69 Pharmaceutical Research and Manufacturers of America v Meadows, 304 F3d 1197 (11th Cir 2002), cert denied, 123 S Ct 2213 (2003).

70 See, for example, South Carolina Governor’s Office, Press Release, Gov. Sanford to Seek Additional Medicaid Drug Savings: South Carolina to “Pool” Buying Power with Other States (Feb 26, 2003), online at http://www.state.sc.us/governor/News%20Releases/News/pool%20buying%20power.htm (visited Jan 21, 2004).

71 See MPDIMA, 117 Stat 2006. The Supreme Court in Walsh rejected a dormant Com-
B. Importation Developments

Virtually the entire developed world outside the United States imposes price controls on pharmaceuticals as part of larger tax-based social welfare systems. Drugs are therefore available in these countries at prices lower than in the United States, prompting numerous efforts to obtain them through the internet, mail order, and travel abroad. The FDA has made clear that this practice is illegal and unsafe. In 2000, Congress passed a law liberalizing drug importation, but it does not go into effect unless there is a demonstration by the Secretary of Health and Human Services that implementation would not pose safety risks and would save money. Both Secretary Shalala and Secretary Thompson stated that they could not make such a certification.

Nonetheless, Congress has continued to consider legislation that would make importation easier. Many of these bills also contain language intended to require manufacturers to sell drugs in the United States at prices no higher than those prevailing overseas under various governmental price-control regimes and to prohibit manufacturers from restricting the ability of foreign distributors to resell into this country. The upshot would be the importation not just of drugs, but of foreign drug price controls. The bills thus would effectively prohibit market-based pricing and thereby undermine the returns necessary for innovation.

72 See generally PhRMA, Industry Profile at 18–19 (cited in note 5).
75 21 USC § 384().
76 See Letter from Secretary Donna Shalala to President William Clinton (Dec 26, 2000) (on file with author); Letter from Secretary Tommy Thompson to Senator James Jeffords (July 9, 2001), online at http://www.fda.gov/oc/po/thompson/medsact.html#letter (visited Jan 21, 2004).
77 Such provisions were included in the Medicare prescription drug bills as well as in stand-alone legislation. See, for example, HR 2427, 108th Cong, 1st Sess (June 11, 2003), in 149 Cong Rec H 7595 (July 24, 2003). This bill passed the House on July 25, 2003. The final Medicare law includes importation provisions but also retains the requirement of certification by the Secretary of Health and Human Services before it goes into effect. See MPDIMA § 1121, 117 Stat at 2464.
78 See, for example, Richard Epstein, Parallel Importation as a Perversion of Free Trade (Institute for Policy Innovation July 9, 2003), online at http://www.ipi.org/mt/publications.nsf/PublicationLookupFullText/85A2F72F9001FAA486256D5E008016ED (visited Jan 21, 2004). Under the new Medicare law, the Administration will conduct a study of trade laws relating to...
CONCLUSION

Critics of the pharmaceutical industry support limitations on intellectual property rights and on operation of the market as mechanisms to control drug prices. Industry supporters urge that intellectual property and market incentives are necessary to fund the discovery and development of innovative medicines. There are sound reasons to believe that pharmaceutical innovation produces net benefits to society, and that even the current high levels of pharmaceutical research and development investment are far too low. The issues are too important to allow advocates for lower prices at the expense of innovation to continue to dominate the public debate. Access to medicines and other healthcare goods and services should be assured through programs that are consistent with the framework of intellectual property and market-based incentives necessary for continued innovation.

pharmaceuticals and will develop a strategy to address foreign price controls. See MPDIMA § 1123, 117 Stat at 2469; MPDIMA Conference Report at 834–35 (cited in note 46).


The patent system gives inventors a period of exclusivity in which to try to get their return. Market-based pricing allows successful innovators to actually achieve the level of return their investors require. . . . But those incentives are now threatened on a number of fronts. . . . My key point is that, under a regime of weaker IP protection or harsher market controls, our R&D would no longer be able to deliver true innovation.

See, for example, David M. Cutler and Mark McClellan, Is Technological Change in Medicine Worth It?, 20 Health Aff 11 (2001) (stating that medical spending as a whole is worth the increased cost of care); Frank R. Lichtenberg, Are Benefits of Newer Drugs Worth Their Cost?, 20 Health Aff 241 (2001) (finding that new drugs tend to lower all types of nondrug medical spending, resulting in reduced cost of care).

See Kevin A. Hassett and Robert Shapiro, The Importance of the Pharmaceutical Industry in the U.S. Economy (Oct 23, 2002) (paper prepared for PhRMA: on file with author). The reason, as explained in the paper, is that the social return on pharmaceutical innovation exceeds the private return.