

Hatch-Waxman, Generics, and Patents: Balancing Prescription Drug Innovation, Competition, and Affordability

In its ongoing efforts to enact a Medicare prescription drug benefit, the U.S. Congress continues to be confounded by the many challenges inherent in this deceptively complex goal. The price tag for such a benefit—regardless of its political stripe—has been one of the biggest barriers to enactment thus far. In order to make a dent in the various cost estimates, analysts and Hill staff continue to search for cost-reducing options. Generics, not surprisingly, have been a beacon in this quest for greater affordability. But generics also come with a price. That price, some have argued, could take the form of weakened patent protection for “innovator” (branded) products. Research-based pharmaceutical companies, as well as many economists, stress the importance of patent protection in insuring the viability of future innovation. In the end, consumers want continued access to prescription drugs—at affordable prices. One of the first legislative attempts to balance innovation, competition, and prescription drug affordability—the Drug Price Competition and Patent Term Restoration Act of 1984, often referred to as Hatch-Waxman or the Hatch-Waxman Act for its framers—made headlines when it was enacted. Almost 20 years later, it is again making headlines as some in Congress seek to reform sections of the original law.

In those two decades, extraordinary changes have occurred, many of which could not have been anticipated in the early 1980s. Quantum leaps in scientific research and the development of a complex, dynamic marketplace have resulted in thorny policy and legal challenges. Some of these changes, it is alleged, have led to loopholes in the Hatch-Waxman legislation.¹ But, where some see fraud and manipulation of the patent system, others see opportunities to recover risky research investments. Resolving these legal and policy puzzles requires not only an understanding of patents, Hatch-Waxman, and generics but also an appreciation of the delicate balance that exists between innovation, competition, and access to affordable drug products.

PATENTS

Intellectual property protection is provided for in the U.S. Constitution. Congress enacted the basic Patent Act of 1793 under the authority of

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Article I (Section 8, 8) that calls for the patent system “to promote the progress of science and useful arts, by securing for limited times to authors and inventors exclusive right to their respective writings and discoveries.” Patents can cover “any new and useful process, machine, manufacture or composition of matter, or any new and useful improvement thereof.”²

Each invention or product can and often does have more than one patent. There are actually three types of patents that are relevant to pharmaceutical products: (a) product patents, (b) use patents, and (c) process patents. A product patent, which is typically the easiest for a branded drug company to defend, is conferred on the final marketable product, that is, the new molecular entity, or NME. The actual molecular entity that makes a drug unique, and therefore patentable, can itself be made up of separate components—each of which may also be patentable. All of these patents are not necessarily obtained at the same time, however. The drug discovery and development processes are time-intensive, unpredictable, and nonlinear. As new discoveries are made, perhaps over the course of many years, separate product patents can be applied for and granted. Each patent has its own individual time clock.

In addition to the multiple product patents that a company can hold on an individual drug, companies can also apply for use patents (for particular indications), as well as for process patents. A process patent would be granted if a drug product necessitated that the drug be manufactured in a unique way.

Patents can be thought of as a type of insurance policy for inventors, including research-based pharmaceutical companies. Because of the risk, expense, and time associated with drug development, only a small number of prescription drug products actually make it to market. According to the Pharmaceutical Research and Manufacturers of America (PhRMA), only 250 out of 5,000 screened compounds ever enter into preclinical testing. And only one out of five drugs entering clinical trials is approved by the Food and Drug Administration (FDA) for marketing. When a drug does succeed, therefore, the company strives to protect its investment, maximize its profits, provide returns on shareholders' investments, and reinvest profits into research, development, marketing, and other business-related expenses.

There has been much criticism of the patent system as it applies to pharmaceuticals. Some of the criticism has centered on whether the U.S. Patent and Trademark Office (PTO) is granting patents for products that should not be patentable. Others are concerned with the monopoly patents create, effectively keeping out competitors. But the research-based pharmaceutical companies point out that there is strong competition between products within therapeutic classes.³

Prescription drugs are categorized by therapeutic class (for example, one therapeutic class of medicine reduces cholesterol, while another improves

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allergy symptoms). Patents do not preclude other manufacturers from producing and marketing different drugs to treat the same disease in a given therapeutic class. There are, for instance, a variety of branded medicines that could be prescribed for high blood pressure or depression or pain reduction. Drugs from different therapeutic classes can be used to treat the same disease or indication (Table 1).

TABLE 1
Similar Indications, Different Therapeutic Classes

| Indications | Therapeutic Classes |
|---|--|
| Pain and inflammation associated with osteo- and rheumatoid arthritis | COX-2 Inhibitors — Vioxx* — Celebrex* |
| Pain and inflammation associated with osteo- and rheumatoid arthritis; short-term pain relief | Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) — Feldene* — Naproxen* (generic/over-the-counter) — Ibuprofen* (generic/over-the-counter) |

*One of the FDA-approved products in this therapeutic class.

A physician treating a patient presenting with arthritic pain, for example, has several prescription and nonprescription treatment options. Among the COX-2 inhibitors, the newest therapeutic class of drugs, are at least two branded, patented products to treat the pain and inflammation associated with arthritis. The physician can choose between these two products or between a similar therapeutic class of drugs, the nonsteroidal anti-inflammatory drugs (NSAIDs). The NSAIDs include patented innovator products and generics as well as over-the-counter medicines.

COX-2 inhibitors were hailed as breakthrough products because of their seeming ability to decrease the troubling side effects associated with more traditional NSAIDs. These side effects include gastric bleeding and ulcers, conditions that can be very serious. On the other hand, there have been increased reports of serious cardiac events associated with at least one of the COX-2 products. In addition, COX-2 products are considerably more expensive than the prescription NSAIDs. That cost comparison is even more vivid when COX-2s are compared to over-the-counter products. In the best of all worlds, all of these factors would be taken into account every time a physician writes a prescription.

When both patented and generic products are available to treat the same condition, the burden is on the physician—"the learned intermediary"—

to prescribe the most appropriate therapeutic option for the individual patient. The physician, who presumably is familiar with published clinical trial results and package inserts (which contain information from pivotal clinical trials that support the labeled indications, adverse effects, dosing regimens, warnings, and precautions) ultimately decides what is best for the patient. Sometimes that decision is influenced by the patient's insurance policy, which may specify formulary requirements. A patient's lack of health insurance (or drug coverage) may also influence a physician's prescribing decision. The physician's decision may be further complicated by patient interest generated not only by the intense direct-to-consumer advertising by drug companies that has occurred over the past few years but also by recent efforts of some pharmacies to influence patients. Ultimately, however, it is the physician,⁴ perhaps in consultation with the patient, who determines the most appropriate treatment therapy.

Effective Patent Life

Patents provide exclusive rights to market a product for a specified period of time. Before enactment of the Uruguay Rounds Agreement Act (P.L. 103-465) on June 8, 1995, patents had 17 years of patent life from the date the patent was issued. The act increased the patent life to 20 years from the date of the first filing of the patent application. The effective patent life, however, is often less than 20 years because patents, especially for prescription drugs, are typically obtained prior to marketing. Patents on drug products are typically conferred very early in the development process. Therefore, many years of additional research and clinical trials must be conducted to obtain FDA approval to market the drug. The time it takes for the FDA approval process also "counts against" the drug's patent time clock. The full patent term in the United States is 20 years. Effective patent life—the period of market exclusivity when the product is actually on the market (without generic competition)—is generally calculated by subtracting the number of years it took to receive final FDA marketing approval from the date the patent was filed (not the date the patent was granted).

According to research conducted for PhRMA, "The average period of effective patent life for new medicines introduced in the early to mid-1990s with patent term restoration has been 11 to 12 years. Innovators in other industries, who don't receive regulatory approval before going to market, typically receive more than 18.5 years of effective patent life."

Others have taken issue with the notion of "effective patent life," referring to that period of time as a commercial monopoly. Alfred B. Engelberg, an attorney who has worked with the generic drug industry, wrote:

Clearly, the search for the definition of 'effective patent life' or the belief that meaningful statistics may be developed to establish that it is shrinking as a result of government regulation, is an exercise in futility. Each product has its own unique development, commercialization, and patent history, which makes any generalization in this area highly suspect. An

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average effective patent life figure that is derived solely by subtracting the NDA [new drug application] approval date from the patent expiration date without considering that history has no validity.⁵

Patent Term Restoration

As pointed out above by the research-based pharmaceutical companies, even with patent term restoration, periods of market exclusivity for drug products are typically shorter than for other products. On the other hand, even in their truncated number of effective patent life years, many of the drug products earn enormous returns, some topping \$1 billion in sales annually. The branded, patent-protected drug products are virtually always priced higher, often significantly higher than their generic counterparts. The innovator drug companies argue that the cost of research and development contribute to the higher prices of the innovator product. (Table 2)

TABLE 2
Cost of Drug Innovation Versus Imitation

| Pioneer Product | Generic Product |
|---|---|
| Long gestation periods — 10 to 14 years | Short gestation periods — 1 to 2 years |
| Low success rates — only 1 in 5 NCE (<i>new chemical entity</i>) candidates entering clinical testing become marketed drugs | High success rates |
| High R&D costs — \$350 to \$600 million and higher per NCE | Low R&D costs — \$1 to \$2 million to demonstrate bioequivalence* |

Based on a presentation by Henry Grabowski, Patents and Generic Competition, American Enterprise Institute, March 28, 2001.

**Some have pointed out that generics face additional R&D expenses when there are unexpired patents requiring the design of the generic around the branded company's patents.*

Critics contend that it is advertising, marketing, greed and the insatiable demands of shareholders that drive the price of these drugs out of reach of significant numbers of (often the most vulnerable) patients. These arguments are not new; they have been circulating on and around Capitol Hill for many years, paving the way for increased interest in generics.

GENERICS

Generics save consumers—and third-party payers—money (see Table 3). A July 1998 Congressional Budget Office report estimated annual savings

TABLE 3
Comparisons of Prices for Prescription Drugs (P), Generics (G), and
Over-the-Counter (OTC) Drugs in Several Categories

| Drugs (Availability) ¹ | Dose per Tablet | Doses per Bottle | Price per Bottle | Comments |
|-----------------------------------|-----------------|------------------|------------------|--|
| Depression | | | | |
| Fluoxetine Hydrochloride (G) | 20 mg | 30 | \$46.99 | The antidepressants have similar effectiveness and side effects, but results vary somewhat by patient. |
| Zoloft (P) | 50 mg | 30 | \$67.42 | |
| Paxil (P) | 20 mg | 30 | \$76.80 | |
| Prozac (P) | 20 mg | 30 | \$85.98 | |
| Arthritis/Joint Pain | | | | |
| Ibuprofen (G) | 600 mg | 30 | \$7.99 | Ibuprofen and Motrin can cause serious stomach problems in rare cases; Vioxx is notably gentler. |
| Motrin (OTC) | 200 mg | 100 | \$8.49 | |
| Celebrex (P) | 200 mg | 30 | \$71.73 | |
| Vioxx (P) | 25 mg | 30 | \$73.29 | |
| Heartburn | | | | |
| Pepcid AC (OTC) | 10 mg | 30 | \$9.99 | Zantac and the generic, ranitidine work differently from Prilosec and Prevacid, but are generally used to treat the same ailments. |
| Ranitidine hydrochloride (G) | 150 mg | 60 | \$10.80 | |
| Zantac (P) | 150 mg | 60 | \$101.57 | |
| Prevacid (P) | 30 mg | 30 | \$113.70 | |
| Nexium (P) | 20 mg | 30 | \$115.51 | |
| Prilosec (P) | 20 mg | 30 | \$115.80 | |
| High Cholesterol | | | | |
| Lovastatin (G) | 20 mg | 30 | \$36.00 | Lovastatin, the generic version of Mevacor, may not lower cholesterol as much or as quickly as Zocor and Lipitor. |
| Lipitor (P) | 10 mg | 30 | \$59.86 | |
| Zocor (P) | 10 mg | 30 | \$66.94 | |
| Mevacor (P) | 20 mg | 30 | \$68.99 | |
| Allergies | | | | |
| Benadryl (OTC) | 25 mg* | 24 | \$4.49 | Benadryl may cause drowsiness but also may be more effective than some prescription nonsedating antihistamines. |
| Clarinet (P) | 5 mg | 20 | \$66.41 | |
| Allegra (P) | 60 mg | 60 | \$70.98 | |
| Claritin (P) | 10 mg | 30 | \$78.60 | |

*25 mg of diphenhydramine hydrochloride.

Source: Wall Street Journal Research; pricing from Drugstore.com (See Scott Hensley, "How New Generics Can Cut Your Drug Expenses," Wall Street Journal, June 6, 2002).

to consumers of \$8 billion to \$10 billion dollars from generic substitution in the mid-1990s.⁶ In December 2000, General Motors Corporation, which spends over \$1 billion on pharmaceuticals annually, calculated that “for each one percent increase in the use of generic drugs, GM can save \$3 million a year.”⁷

Before Hatch-Waxman, generics represented only 13 percent of all prescription medication. Since the 1980s, however, the use of generics has greatly increased; 45 percent of all prescriptions in 2001 were filled with generic drugs, although that figure represents only about 8 percent of all dollars spent on drugs.⁸ Along with the enactment of Hatch-Waxman, the passage of state-level drug-product substitution laws allowing pharmacists to dispense a generic, even when a brand-name drug had been prescribed, and the active promotion of generic substitution by government health programs and private health plans have spurred the increase in generic sales. Congressional interest in drug prices and drug patents were at the center of the original discussions surrounding the Drug Price Competition and Patent Term Restoration Act of 1984, just as they are today.

HATCH-WAXMAN

Gerald J. Mossinghoff, a former commissioner of patents and trademarks at the PTO, provided some historical context on the passage of Hatch-Waxman in a 1999 article in the *Food and Drug Law Journal*:

The plan for patent term restoration had its beginnings in President Carter’s Administration. In 1978 President Carter launched a major domestic policy review on industrial innovation and that team recommended patent term restoration for pharmaceuticals and any other product that required regulatory review—to compensate for, or restore to the term of the patents, the time lost in regulatory review. President Reagan’s Cabinet Council on Commerce and Trade also supported the proposal....Then-Secretary of Commerce Malcolm Baldrige set up an intellectual property committee under the Cabinet Council on Commerce and Trade....The committee recommended, and the Cabinet Council supported, patent term restoration. That recommendation turned into the bill, S. 255 (98th Cong., 2d Sess. 1984) that passed in the Senate and was referred to the House of Representatives.

In the House, the bill’s supporters put it on the suspension calendar, which requires a majority of two-thirds to suspend all the rules and enact the bill....S. 255 failed....The vote, however, served as a wake-up call for generic drug manufacturers. Congressman Henry A. Waxman (D-CA), one of the most effective in the House of Representatives and then-Chairman of the Health Subcommittee, took on the issue. Suddenly, what had been a patent term restoration bill became a patent term restoration and drug price competition bill, and a whole new title was added that complicated the bill even further.⁹

When enacted, Hatch-Waxman (P.L. 98-417) contained provisions covering drug price competition and the abbreviated new drug application

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(ANDA) process for generics (Title I) and patent term restoration (primarily Title II).

Abbreviated New Drug Application Process

In order to encourage greater access to lower-priced drug products, Hatch-Waxman sought to shorten the time it took for generics to reach the market. The act created the ANDA process, which eliminated lengthy and expensive clinical trials. This new “abbreviated” approval process breathed new life into the fledgling generic drug industry.

According to the FDA, a generic drug is “identical, or bioequivalent to a brand name drug in dosage form, safety, strength, route of administration, quality, performance characteristics and intended use.”¹⁰ In short, generic drugs are chemically identical to their branded counterparts. Even if a generic has a different color, a different taste, or comes in a different shape¹¹ or package, the FDA considers the product to be equivalent if it meets the same standards for strength, quality, purity and identity as the branded product.

When patents or other periods of exclusivity (see section below) expire, manufacturers can apply to the FDA to sell generic versions of the innovator products. Drug companies must submit an ANDA to the FDA’s Office of Generic Drugs in the Center for Drug Evaluation and Research for approval to market a generic product. To gain FDA approval, a generic drug must meet the following criteria:

- Contain the same active ingredient(s) as the innovator drug (inactive ingredients may vary).
- Be identical in strength, dosage form, and route of administration.
- Have the same use indications.
- Be bioequivalent (performs in the same manner as the innovator drug).
- Meet the same batch requirements for identity, strength, purity, and quality.
- Be manufactured under the same strict standards of the FDA’s good manufacturing practice regulations required for innovator products.

Once approved by the FDA, all products, both innovator as well as generic, are listed in the FDA’s *Approved Drug Products with Therapeutic Equivalence Evaluations*, also known as the “Orange Book.”

For drugs first marketed after 1962, the ANDA process does not require the drug sponsor to repeat costly animal (preclinical) and human (clinical) research on ingredients or dosage forms already approved for safety and effectiveness. Hence the term “abbreviated.” Instead of repeating these expensive and time-consuming efforts, generic applicants, unlike the innovator sponsor, need only demonstrate bioequivalence. “One way

scientists demonstrate bioequivalence is to measure the time it takes the generic drug to reach the bloodstream in 24 to 36 healthy volunteers. This gives the rate of absorption, or bioavailability, of the generic drug, which they can then compare to that of the innovator drug. The generic version must deliver the same amount of active ingredients into a patient's bloodstream in the same amount of time as the innovator drug."¹²

Generic Drug Competition Provisions

Several important—and hotly debated—provisions that relate directly to the generic competition portion of Hatch-Waxman are highlighted below:

Paragraph IV Certification — As a result of Hatch-Waxman, the Food Drug and Cosmetics Act requires that, among other things, one of the following four certifications be made when filing an ANDA:

- The drug has not been patented.
- The patent has already expired.
- The generic drug will not go on the market until the patent expiration date passes.
- The patent is not infringed or is invalid.

These certifications are referred to as the paragraphs I, II, III, and IV certifications. Paragraph IV certifications, which are essentially generic drug patent challenge notifications, became a major issue during the drafting of Hatch-Waxman. It continues to generate considerable attention today and is the focus of both congressional and regulatory attention. At issue is the automatic 30-month postponements or ANDA stays.

ANDA and the 30-Month Stay Period — To begin the FDA approval process, a generic applicant must do two things: (a) certify in its ANDA that the patent in question is invalid or is not infringed by the generic product (the “paragraph IV certification”) and (b) notify the patent holder of the submission of the ANDA. If the patent holder files an infringement suit against the generic applicant within 45 days of the ANDA notification, FDA approval to market the generic version is automatically postponed for 30 months (unless, before that time, the patent expires or is judged to be invalid or not infringed). This 30-month postponement allows the patent holder time to assert its patent rights in court before the generic competitor is permitted to enter the market. The 30-month stay is meant to allow time for the patent holder to litigate, although the litigation may in fact take longer.

It is important to note that if a generic were to come to market before successfully completing a challenge, its manufacturer would be subject to treble damages based upon the brand manufacturer's profits. Some analysts point out that going to court has no real downside for the brand manufacturers because the 30-month stay is automatic and worth far more in profits than the cost of litigation. Much of the recent attention, (discussed further in the “Reforming Hatch-Waxman: Closing the Gaps”

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section below), has centered on what many see as the exploitative initiation of 30-month postponements by innovator companies. Multiple 30-month stays can further delay any generic entry.

The 180-Day Exclusivity Period — Under Hatch-Waxman, an applicant can seek FDA approval to market a generic drug before the expiration of the patent of the branded product upon which the generic is based. The first company to submit a paragraph IV certification ANDA to the FDA has the exclusive right to market the generic drug for 180 days. This 180-day exclusivity period was included in the legislation to encourage generic companies to invest in the required product testing and to cover expensive legal challenges to pioneer (innovator) products. The generic drug industry has itself become competitive since the enactment of Hatch-Waxman. Over time, this 180-day exclusivity period has created some contention and confusion as to when the 180-day period begins and which generic firm is first. In addition, this provision continues to generate concern and calls for reform, largely because of the incentive it creates for brand and generic companies to enter into anticompetitive arrangements under which, for example, the generic manufacturer accepts payment from a brand name company not to market the generic product, thus effectively blocking all other generics from entering the market.

Data Exclusivity — Another important element of the generic competition component of Hatch-Waxman involves what has been referred to as “data exclusivity.” The act protects an innovator’s proprietary clinical research data from use or reference by others for five years. This provision precludes generic applications from submission to the FDA until five years after the FDA has approved the innovator drug for marketing. PhRMA notes in its “2002 Pharmaceutical Industry Profile”: “In contrast, members of the European Union provide between five and 10 years of protection, during which time marketing approval will not be provided to competitors that seek to rely directly or indirectly on the data generated by the innovator of the product.”¹³

Patent Term Restoration Provisions

The section of the code that pertains to patent term restoration is long and complicated. The provisions cover numerous situations and run the gamut from due diligence petitions to multiple investigational new drugs (INDs) to criteria for determining whether a patent for a human drug product is eligible for patent extension.

A pioneer product can receive an extension term—the patent term restoration—that is equal to one-half of the time of the IND period (the point at which human clinical trials begin) and the new drug application (NDA) period (that is, when the NDA is reviewed by the FDA). A human drug product patent is deemed to be eligible for a patent extension if it satisfies the following six conditions:

- The applicant must show that the patent has not expired.
- The applicant must establish that the patent has not previously been extended.
- The patent owner or its agent must submit an application for patent term restoration that includes details about the patent and the activities undertaken to secure FDA approval.
- The applicant must establish that the product was subject to a regulatory review period before its commercial marketing or use.
- The applicant must show that the product either represents the first permitted commercial marketing or use of the product after the regulatory review period.
- The applicant must submit the application for patent term restoration to the PTO within 60 days of FDA approval of the commercial marketing application.¹⁴

Hatch-Waxman mandates that a maximum of five years can be restored to the patent and that the total patent life (that is, period of market exclusivity) with the patent extension cannot exceed 14 years. If the patent life of the product after approval has 14 or more years left, the product would not be eligible for patent extension.

According to the FDA, "FDA's primary responsibility is to assist the PTO in determining a product's eligibility for patent term restoration and to provide information to PTO regarding a product's regulatory review period....FDA also has the responsibility for due diligence petitions and due diligence hearings. PTO is responsible for determining the period of patent extension. FDA defers to PTO on all matters involving the construction and validity of patent claims."¹⁵

This is a particularly critical issue, especially for generic drug companies. While the PTO has responsibility for patent approval and the FDA has the authority to approve drug products for marketing, no agency has oversight of the Orange Book or, therefore, of the validity of the patents listed within it. This lack of accountability is problematic for generic companies, who argue that the FDA should play a larger role in determining the validity of patents prior to listing them in the Orange Book. The FDA, in turn, would argue that review of patents is the job of the PTO and that the FDA's role does not include Orange Book oversight. The dispute is important because of the relationship between an Orange Book listing and the 30-month stay.

Hatch-Waxman also contains a provision whereby the manufacturer of the innovator product must exercise due diligence in order to achieve patent term restoration. In fact, the Hatch-Waxman Act overruled a U.S. Court of Appeals decision in the famous *Roche Products v. Bolar Pharmaceuticals* case, in which the court held that a generic company could not manufacture and test a medicine before the patent expires even if its only purpose was to prepare a marketing application. Under Hatch-Waxman,

While the PTO has responsibility for patent approval and the FDA has the authority to approve drug products for marketing, no agency has oversight of the Orange Book.

generic manufacturers are allowed to use pioneer medicines still under patent to obtain bioequivalency data for their FDA applications. This provision enables generic products to be dispensed to patients the day after the innovator's patent becomes ineffective or expires.

Analysts are bracing for a bull market in generics as more than \$20 billion worth of brand-name drug products reach the end of their patent terms over the next several years. With a significant number of top-selling prescription drugs involved, many brand-name research pharmaceutical companies are seeking ways to extend their patent protection.

In their zeal to remain competitive, a number of companies have attempted to expand this protection. Recently, a number of cases revealing serious and significant abuses have come to light. A number of the methods that have been employed by some drug companies (both brand and generic) have raised the ire and concern of members of Congress, consumer groups, health insurers, state attorneys general, and the Federal Trade Commission (FTC).¹⁶ These concerns have led to suits, charges, and efforts by some to modernize Hatch-Waxman.

REFORMING HATCH-WAXMAN: CLOSING THE GAPS

With every patent that is set to expire, an enormous amount of money is at stake for innovator companies, generic firms, consumers, and attorneys. Many of the tactics that have been called into question recently are directed at both the brand-name and the generic companies. While not all licenses and agreements used to resolve patent disputes between innovator and generic companies are inherently anticompetitive and violate antitrust laws, the FTC has been particularly concerned about the possible anticompetitive activities of pioneer pharmaceutical companies in using the 30-month stay and the 180-day marketing exclusivity provisions of the Hatch-Waxman Act. The FTC has also kept its attention focused on generic firms exhibiting anticompetitive behavior.

Questionable Practices

The types of practices that have been brought to the attention of the FTC,¹⁷ other regulatory agencies, and the courts include the following:

Evergreening — A practice whereby a company, as its product is about to go “off-patent” will begin to patent additional features of the product or introduce a slightly modified version of the existing drug form. Companies may, for example, introduce a new dosage formulation or an over-the-counter version of the product. Sometimes these changes

| Major Patent Expirations 2002–2005 | |
|------------------------------------|---|
| 2002 | Augmentin (<i>antibiotic</i>) |
| 2003 | Biaxin (<i>antibiotic</i>) Flonase/Flovent (<i>allergy</i>) |
| 2004 | Claritin (<i>allergy</i>) Diflucan (<i>antifungal</i>) |
| 2005 | Epogen/Procrit (<i>anemia</i>) Pravachol (<i>statin</i>) Zocor (<i>statin</i>) Zithromax (<i>antibiotic</i>) |

provide superior therapeutic advances. But exclusivity has been granted to brand companies for minor product and labeling changes that many have argued present little or no therapeutic benefit. While this practice is not necessarily illegal, it causes concern because it ultimately postpones generic market entry.

Staggered Orange Book Listings — Before a generic comes to market, its manufacturer must certify to each and every patent listed in the Orange Book, thus creating the incentive for brand name manufacturers to delay listing some of their patents in the Orange Book. If a brand name company chooses to file a lawsuit, the 30-month stay is automatic, regardless of the merits of the new patent. Each stay triggers the automatic delay in generic approvals (until the stay expires or the court resolves the dispute.) By staggering their Orange Book patent listings, innovator companies can extend their market exclusivity indefinitely. It is the alleged use of strategic Orange Book listings to achieve multiple 30-month stays that has drawn attention. Some have argued that Congress never intended that there be more than one 30-month stay on a given drug. The FTC is investigating the existence of invalid patents.

Brand Migration — One of several patent and exclusivity strategies designed to extend product life cycles and thereby delay competition. Towards the end of a drug's exclusivity period, some companies have focused on marketing efforts to "convert" or direct patients to the company's other product, such as a new branded product that is heavily promoted to both patients and physicians (for example, AstraZeneca's attempt to move patients currently on Prilosec, which is nearing its patent expiration, to its patented successor product, Nexium).

Anticompetitive Agreements between Brand and Generic Companies — Under these agreements manufacturers of brand-name products have colluded with generic manufacturers to delay or eliminate specific generic drugs from entering the market (for example, an April 2001 FTC press release announced a consent agreement with Hoechst Marion Roussel [HMR], now Aventis, and Andrx Corporation to resolve an allegedly illegal agreement between the companies that affected the \$750 million-a-year market for Cardizem CD, a widely prescribed drug used to treat hypertension and angina. The FTC's complaint alleged that HMR, the manufacturer of Cardizem CD, agreed to pay Andrx millions of dollars to delay bringing its generic version of the drug to market. There have been several examples of companies entering into such anticompetitive agreements: Abbott/Geneva, Schering-Plough/Upsher-Smith/ESI Lederle, and most recently, Bristol-Myers Squibb, which illegally kept generic versions of the cancer drug Taxol off the market for three years.) It is also worth noting that several state attorneys general have also filed suit in these cases.

Anticompetitive Agreements between Generic Companies — The FTC is also concerned with maintaining competition among generic firms. In

FTC v. Mylan Laboratories, Inc., the FTC and several states sued Mylan, charging “Mylan and other companies with monopolization, attempted monopolization, and conspiracy in connection with agreements to eliminate much of Mylan’s competition by tying up supplies of the key ingredients for two widely-prescribed anxiety drugs—lorazepam and clorazepate.”¹⁸

FTC Study

Given the heightened awareness of possible impropriety and the complexity that exists within the patent legislation arena, the FTC has undertaken a study of pharmaceutical practices related to the Hatch-Waxman Act. By focusing on four areas, the study’s findings should yield valuable information as Congress continues to consider possible reforms to Hatch-Waxman. The study is examining the following:

- The extent to which agreements between brand-name pharmaceutical manufacturers and generic drug firms may have delayed generic competition.
- The operation of provisions in Hatch-Waxman that award a 180-day period of market exclusivity to a generic firm.
- The impact of (a) provisions in the act on the listing of patents by brand-name pharmaceutical companies in the FDA Orange Book and (b) provisions that trigger a stay on FDA approval of a proposed generic drug.
- The use of the FDA’s Citizen Petition process by brand-name drug companies to oppose potential generic entrants.

The study, begun in October 2000 and due out in the fall of 2001, has not yet been completed. According to FTC, the study is expected to be released in the summer of 2002.¹⁹

Proposed Solutions

In their effort to close what they see as gaps that currently exist in Hatch-Waxman, Sens. Charles E. Schumer (D-N.Y.) and John McCain (R-Ariz.) have introduced S. 812, the “Greater Access to Affordable Pharmaceuticals Act of 2001,” also known as the GAAP Act. A companion bill in the House, H.R. 1862, is sponsored by Reps. Sherrod Brown (D-Ohio) and Jo Anne Emerson (R-Mo.). Among other things, these bills would

- Eliminate the automatic 30-month stay brand companies receive when filing suit against a generic challenger.
- Reform the 180-day rule by providing a “rolling exclusivity” to generic drug applicants.
- Stop the filing of citizen petitions (usually by competitor companies, brand or generic) with the FDA.
- Require the FTC to assess the impact of the GAAP Act.

The GAAP Act has enjoyed a ground swell of support, particularly as the 2002 election looms closer and the hope of enacting a Medicare prescription drug benefit drifts farther away. Nevertheless, two powerful opponents have weighed in—PhRMA, the trade association representing the brand-name drug industry and Sen. Orrin Hatch (R-Utah), one of the two original sponsors of the 1984 Hatch-Waxman legislation.

PhRMA claims the GAAP Act would “cripple effective remedies for patent infringement, permit generic drugs that do not duplicate their reference drugs, inhibit the submission of citizen petitions, and revise generic exclusivity to keep more rival generics off the market for six months and permit unnecessary litigation.”²⁰ However, Hatch, testifying before the Senate Committee on Health, Education, Labor, and Pensions on May 8, 2002, stated that “no law as complex as the 1984 Act is so perfect that it cannot be improved as it faces the tests of time and changing conditions. In my view, there have been several unintended and unanticipated consequences of the 1984 law and other changes in the pharmaceutical sector that bear attention by Congress.” Nevertheless, Hatch stated that he opposed adoption of the bill in its current form. “Without additional facts, my preliminary view at this point is that the provisions of McCain-Schumer related to the 30-month stay may overcorrect a problem that may, in fact, be somewhat overstated in the first place.” The senator also took issue with the bill’s reform of the 180-day rule. Despite this particular opposition, there is still much support not only for the proposed legislation but also for the general notion of reforming Hatch-Waxman and increasing access to more affordable drugs.

OTHER PERIODS OF EXCLUSIVITY

It is worth noting that, in addition to patents, other means can confer prescription drug products with periods of market exclusivity. Two of these are provided through the Orphan Drug Act of 1983 and the FDA Modernization Act of 1997.

■ The Orphan Drug Act was passed in 1983 to encourage the development of what is referred to as orphan drugs, that is, drugs used to treat diseases that affect fewer than 200,000 people. It has been estimated that 10 to 20 million Americans suffer from approximately 5,000 orphan diseases for which no effective cure or treatment exists. In order to make it commercially feasible to develop orphan drugs, the law provides a 50 percent tax credit for certain clinical research expenses, in addition to a seven-year period of market exclusivity (following approval by the FDA).

■ As part of the FDA Modernization Act of 1997, or FDAMA, Congress provided pharmaceutical manufacturers with a research incentive—six months of additional marketing exclusivity for pharmaceutical companies to conduct FDA-requested studies of drugs commonly used to treat children. This provision was reauthorized in 2001 for six more years.

The Orphan Drug Act of 1983 and the FDA Modernization Act of 1997 provide two means of conferring prescription drug products with periods of market exclusivity.

ADDITIONAL POLICY AND REGULATORY CONSIDERATIONS AT HOME AND ABROAD

Patents, market exclusivity, and innovation are affected by a host of factors, including tax policy, technology transfer, and international trade.

Domestic Policy and Regulatory Considerations

Patents alone are not enough inducement or protection for drug researchers and manufacturers to take on the daunting work of discovery and development. Many argue that to conquer diseases for which cures do not exist, to continue to transfer knowledge and technology from federal laboratories to the private sector for commercialization, and to continue to chip away at the untapped marvels of science will take a commitment and a level of resources that can only be met through a public-private partnership. To that end, several initiatives have been established, including the passage of landmark legislation such as the Patent and Trademark Law Amendments Act of 1980 (more commonly referred to as the Bayh-Dole Act) that provides strong incentives for public-private research collaborations. The R&D tax credit, which is set to expire in 2004, has also provided a significant incentive for companies, including pharmaceutical companies, to increase their investment in U.S.-based research and development.

Questions have been raised, however, as to what constitutes the right balance between taxpayer-supported research and the private sector's right to set prices, hold patents, and reap the benefits of its commercialized products. While the issue is beyond the scope of this paper, the question is relevant in that breakthrough innovation in medical science involves striking a balance between risk, resources, and incentives to commercialize what some consider a public good.

International Trade and Patent Protection

The U.S. pharmaceutical industry is a world leader in the research and development of new products. But while pharmaceutical companies (several of which are multinational) are busy protecting their domestic patents, patent piracy costs the industry hundreds of millions of dollars every year, despite various provisions agreed to in NAFTA (the North American Free Trade Agreement) and GATT (the General Agreement on Tariffs and Trade). Patent protection has become an important part of the World Trade Organization's (WTO's) trade rules. During the WTO Uruguay Round of agreements, for example, the WTO brought intellectual property into the global trading system through the Agreement of Trade-Related Aspects of Intellectual Property Rights (TRIPS), outlining policies for such controversial matters as compulsory licensing.

In light of recent international trade negotiations, some analysts have questioned whether companies end up with greater patent protection

Patent piracy costs the industry hundreds of millions of dollars each year.

than they otherwise would receive under U.S. law. Given the huge variety of patent laws that differ from country to country and the patent violations that occur overseas, the ultimate effects on both the U.S. brand and generic pharmaceutical industries are not yet clear.

CONCLUSION

The compromise Congress hammered out 20 years ago in an effort to balance additional effective patent life with quicker access to generic drugs was controversial then and continues to stir debate today. While some have called for the reform of Hatch-Waxman to address perceived shortcomings and gaps, others maintain that the original bill should remain intact, until such time as additional evidence of abuse or circumstances warrant change.

ENDNOTES

1. Other changes, such as the proliferation of biologics—that is, drugs derived from living material such as plants, animals, or microorganisms—do not fall under the loophole umbrella. Rather, these products were simply not contemplated when Hatch-Waxman was enacted. While biologics, like other drugs, are covered by patents, there is currently no process in place for the development of generic biologics. Although some argue that Hatch-Waxman reform should include a specific method for ensuring access to generic alternatives to biologics, this is still the subject of much debate and beyond the scope of this paper.
2. U.S. Code, Title 35, Sec. II, Chap. 10, Sec. 101.
3. Others, however, point out that the nature of such competition is different from the unique competitive dynamic that arises between a branded drug and its generic counterpart. The existence of other drugs in the same therapeutic category does not mean that exclusion of a generic version of one of those drugs does not harm competition or extend monopoly power in an economic sense.
4. Sometimes, financial incentives influence physician prescribing, for example, prescribing or overprescribing drug products with inflated prices. See Dawn M. Gencarelli, "Average Wholesale Price for Prescription Drugs: Is There a More Appropriate Pricing Mechanism?" Issue Brief No. 775, National Health Policy Forum, June 17, 2002; accessed June 20, 2002, at [http://www.nhpf.org/pdfs/8-775+\(web\).pdf](http://www.nhpf.org/pdfs/8-775+(web).pdf).
5. Alfred B. Engelberg, "Patent Term Extension: An Overreaching Solution to a Nonexistent Problem," *Health Affairs*, 1, no. 2 (Spring 1982), 42.
6. Congressional Budget Office, "How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry," U.S. Congress, Washington, D.C., July 1998.
7. General Motors, "Generic Drug Study," comments filed in response to a request for public comment on a proposed Federal Trade Commission information request to firms in the pharmaceutical industry (FTC File No. V000014), received by the FTC December 18, 2000; accessed May 29, 2002, at <http://www.ftc.gov/os/comments/genericdrugstudy/>.
8. Kathleen D. Jaeger, Generic Pharmaceutical Association, "Drug Pricing and Consumer Costs," testimony before the Committee on Commerce, Science, and Transportation, U.S. Senate, April 23, 2002, 3; accessed June 17, 2002, at <http://commerce.senate.gov/hearings/042302jaegar.pdf>.
9. Gerald J. Mossinghoff, "Overview of the Hatch-waxman Act and its Impact on the Drug Development Process," *Food and Drug Law Journal*, 54, no 2: 187–194; accessed June 20, 2002, at <http://www.oblon.com/Pub/seeker.php3?hatchwax.html>.

10. Information accessed on May 29, 2002 from the FDA's Office of Generic Drugs Web site at <http://www.fda.gov/cder/ogd/>.
11. Sometimes, it is not true that a generic can be a different shape. A tablet, for example, is not the same as a capsule.
12. Center for Drug Evaluation and Research, "Drug Applications: Abbreviated New Drug Application (ANDA) Process for Generic Drugs," U.S. Food and Drug Administration; accessed May 29, 2002, at <http://www.fda.gov/cder/regulatory/applications/ANDA.htm> on.
13. Pharmaceutical Research and Manufacturers of America, "2002 Pharmaceutical Industry Profile"; accessed June 20, 2002, at <http://www.phrma.org/publications/publications/profile00/>.
14. Center for Drug Evaluation and Research (CDER), "Small Business Assistance: Frequently Asked Questions on the Patent Term Restoration Program," U.S. Food and Drug Administration; accessed May 29, 2002, at http://www.fda.gov/cder/about/smallbiz/patent_term.htm.
15. CDER, "Small Business."
16. It is important to note that not all FTC concerns center on brand-name drug companies. The agency also focuses on deals between generic firms that it suspects could be keeping prices high or colluding with brand-name companies. While the FTC has been investigating such agreements between brand-name drug products for the past five years, this recent focus on generic products is new. *USA Today* reported on June 7, 2002, that the FTC is negotiating a settlement with drugmakers Biovail and Elan, the first in the agency's new focus on questionable generic deals.
17. The FTC's primary focus has been on patent settlement agreements and allegedly improper Orange Book listings (looking at, for example, whether Bristol-Meyers Squibb Co. may have "misrepresented" the patent on the company's anti-anxiety drug BuSpar to the FDA or the U.S. PTO; the validity of Biovail's patent for the heart drug Tiazac, which the FDA said should not have appeared in the Orange Book; an effort by Bristol-Meyers to "protect its market" for the company's breast cancer drug Taxol, which lost patent protection in 2001; and whether GlaxoSmithKlein may have listed a patent for the company's antidepressant drug Paxil that "didn't apply to the drug as approved by the FDA"); see Henry J. Kaiser Family Foundation, *Daily Health Policy Report*, January 8, 2002.
18. Molly Boast, "Competition in the Pharmaceutical Marketplace: Antitrust Implications of Patent Settlements," testimony before the Committee on the Judiciary, U.S. Senate, May 24, 2001, 15-16.
19. Timothy J. Muris, "Prepared Statement of the Federal Trade Commission," testimony before the Committee on Commerce, Science, and Transportation, U.S. Senate, April 23, 2002; accessed June 20, 2002, at <http://www.ftc.gov/os/2002/04/pharmtestimony.htm>. This testimony also provides a summary of the FTC's law enforcement focus.
20. Pharmaceutical Research and Manufacturers of America, "A Bad Way to Hurry the Approval of Generic Drugs," press release; accessed May 29, 2002, at <http://www.phrma.org/press/print.phtml?article=398.html>.