
Unintended Consequences: Generic Competition in the Prescription Drug Market

Erwin A. Blackstone, PhD and Joseph P. Fuhr, Jr, PhD

The difficulty in maintaining the appropriate balance between innovation and imitation is probably no better illustrated than in the pharmaceutical industry. The Hatch-Waxman (H-W) Act encourages innovation by extending patent terms, but also stimulates imitation and competition by reducing the requirements for generic entry in the drug market.

This paper examines how the H-W Act has worked by evaluating a number of issues. While brand name manufacturers have the economic incentive to forestall generic competition, at issue is whether they have done so illegally. These issues include:

- The automatic 30-month stay for generic Abbreviated New Drug Applications (ANDAs);
- The 180-day exclusivity period granted to the generic drug that first challenges a patent with an ANDA;
- Brand name manufacturers' multiple listings of patents in the *Orange Book*;
- Settlement agreements between generic companies and brand name manufacturers; and
- Agreements between generic competitors.

Our analysis will illustrate the familiar law of unintended consequences, namely, that the solution often leads to other unforeseen problems. Recognizing some of its

flaws, Congress has recently amended the H-W Act. As such, we will evaluate some of these amendments and make public recommendations to improve social welfare.

Importance of Generic Competition

The cost of health care in the United States is increasing faster than the inflation rate. Presently, 15% of the Gross Domestic Product (GDP) is being expended on health care, and this percentage has been increasing significantly over time. An important public policy issue is how to decrease, or at least slow down, the price and resource allocation of medical services.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (commonly referred to as the Medicare Modernization Act, or the MMA) will, for the first time, provide prescription drug benefits to Medicare recipients through implementation of Medicare Part D.

As a result, the demand and usage of prescription drugs will increase. In 2003, \$216.4 billion was spent on prescription drugs.¹ The cost of this program to the federal government has been estimated to be approximately \$400 billion over the next 10 years. An important determinant of the cost of Medicare Part D is the price that the government will pay for prescription drugs. In 2001, the average price of a branded drug prescription was \$72.70, whereas the average price of a generic drug prescription was \$16.85.² Thus, because generic drugs are generally priced considerably lower than branded drugs, the entry of generics into the market can significantly decrease the price of prescription drugs and government expenditures for these drugs. However, the entry of generic drugs presents a trade-off in the drug market. Competition from generic companies results in lower returns to brand name pharmaceutical manufacturers on their patented drugs. The H-W Act recognizes the importance and cost of developing these drugs. Thus, public policy must be careful not to achieve a short-term goal (lower drug prices) at the expense of a long-term goal (incentives to develop new and better drugs).

History of the Hatch-Waxman Act

Prior to the passage of the H-W Act in 1984 (also known as the Drug Price Competition and Patent Restoration Act), generic drugs had a difficult time gaining approval from the Food and Drug Administration (FDA). A potential generic producer was required to conduct its own studies to demonstrate their drug's safety and effectiveness. Given the time and cost to do so and the threat that other generic drugs would also be trying to enter the market, few companies even attempted to seek FDA approval of their generic products. In the 1962 to 1984 period, there were 150 brand name drugs that lost patent protection without a single generic entry.³ Further, a generic company was not allowed to conduct tests to establish the safety and effectiveness of its generic product until the relevant patent had expired. This meant that a brand name manufacturer would typically enjoy an extra 2 years of protection until the FDA could approve the generic competitor.³ On the other hand, brand name manufacturers often found that FDA approval of their drugs took so much time that the period of patent protection was reduced from the nominal 17 years to a shorter period of time. The effective patent life in the mid-1990s was estimated to be approximately 11 to 12 years.⁴

The H-W Act tried to address both problems and thus achieve a compromise between the competing interests of the innovator and imitator companies. Under the H-W Act, the FDA can extend patent protection for up to 5 years if the

In the 1962 to 1984 period, there were 150 brand name drugs that lost patent protection without a single generic entry.

drug approval process takes an inordinate length of time, but the overall period of protection after restoration cannot exceed 14 years.

The H-W Act also tried to provide generic producers with reduced costs of market entry and the ability to challenge patents they believe are not effective or relevant. Specifically, the H-W Act allowed generic producers to develop their drugs even during the period of patent protection without the threat of patent infringement (the Bolar Exemption).⁵ More importantly, generic applicants for FDA approval could now file an ANDA. Such an application could be filed before the innovator's patent expired and had to show only bioequivalence to the branded drug. This considerably reduced the cost of a generic market entry. Thus, from the moment the innovator's patent expired, a generic drug could be approved and enter the market at a substantially reduced price. Nevertheless, approval was still a cumbersome process, taking an average of 25 months, 15 days.⁶

As part of the ANDA, the H-W Act also allowed a generic company to certify that its product did not infringe on a valid patent. Procedurally, the FDA required the in-

novating drug manufacturer to provide information about any relevant patents covering the new drug in its New Drug Application (NDA). The information, relating approved drugs and their claimed patents, was compiled in the *Orange Book*, or *Approved Drug Products with Therapeutic Equivalence Evaluations*.⁷

As part of its ANDA, the generic applicant must make 1 of 4 certifications for each patent listed in the *Orange Book*⁷:

- 1) No patent is listed,
- 2) The patent has expired,
- 3) The patent will expire on a certain date, or
- 4) The patent is invalid or, if valid, will not be infringed by the applicant drug.

The most contentious certification is number 4, often referred to as Paragraph 4 certification. If an ANDA makes such a certification, it must notify the innovator of its claim and provide a detailed explanation for its determination that the patent is invalid or will otherwise not be infringed.⁸ The innovator has 45 days to decide whether to contest the claim. During this period, the ANDA cannot be approved.

If the innovator chooses to sue during the 45-day period, it then gains an automatic 30-month stay before the generic company's ANDA can be approved unless a court decision invalidating the patent or declaring it not infringed is made in the interim. This stay is automatic upon a suit and occurs regardless of the merits of the suit.⁸ Since infringement suits typically take more than 2 years to be resolved, the patent holder obtains

eneric drug companies' gains from the H-W Act included lower costs and faster entry to the market.

at least an additional 2 years of protection on what could be an invalid or irrelevant patent.⁸

To encourage generic drug companies to challenge invalid or irrelevant patents, the H-W Act provides a 180-day exclusivity period for the first generic that files a Paragraph 4 certification. This 180-day exclusivity period does not start until the applicant markets the product. Even with the questionable importance of the first mover advantage in the generic market, such a 180-day exclusivity period can be quite significant. This issue will be addressed in more detail later in this article.

In summary, the H-W Act was intended to provide benefits to both innovators and imitators. Pioneer drug manufacturers could receive patent protection extensions when the delay in FDA approval process was inordinately long. Clinical trials and other work to obtain approval to market a new drug takes approximately 7 years beyond the 3 years it takes to obtain the patent. Ten years of protection typically remain to recover the \$500 million to \$800 million drug development costs.^{3,9} Drug manufacturers contend that 12 to 19 years of protection are generally required to recoup their investment.⁹ Thus, the intent of patent restoration is to provide incentives for pioneer drug manufacturers to engage in the costly process of developing new drugs.

However, generic drug companies also gained from the H-W Act. Their gains included lower costs and faster entry to the market once a branded drug's patent expired, was declared invalid, or was not relevant. Even within the

patent challenge procedures, the H-W Act had a balance of competing interests. It encouraged patent challenges, but provided an automatic 30-month stay of entry.

Interestingly, one commentator claimed that the H-W Act benefits generic drug companies more than brand name manufacturers.⁹ She noted that as of 1988, 40 drugs had their patents extended for an average of 1.8 years, even though the regulatory review period averaged 8.2 years.⁹

Public Policy Issues

On the surface, the H-W Act seems to have achieved its dual objectives of both increasing protection for the brand name manufacturers, which spend enormous sums of money on research and development, while encouraging generic competition. The brand name manufacturers are doing relatively well financially, with annual returns on equity that exceed the returns in other industries.¹⁰ Yet considerable competition has arisen in the drug market due to the growing importance of generic drugs. For example, according to the Congressional Budget Office, 19% of the prescription drugs sold in 1984 were generic, whereas in 2001, 45% of prescription drugs sold were generic. It is estimated that the purchase of generic in-

stead of branded drugs saved consumers between \$8 billion and \$10 billion in 1994. Innovation is also being spurred by federally funded health-related research, which exceeds \$10 billion each year and is moving rapidly toward \$20 billion annually.¹⁰

However, the cases we examined raise a number of important issues and show that unintended consequences often occur. In particular, the cases demonstrated how vulnerable brand name manufacturers are to the loss of patent protection. It is not unusual that such drugs account for as much as 20% of a brand name firm's revenue. Accordingly, these brand name manufacturers have strong incentives to manipulate any laws that can extend patent protection.

Two provisions of the H-W Act have caused similar unintended consequences.¹⁰ They are:

- 1) A statutory, 30-month, nonadjudicated preliminary injunction for any pharmaceutical patent listed in the *Orange Book*, and
- 2) A 180-day period of exclusivity for the first ANDA applicant to challenge any listed patent.

The first provision essentially gave the brand name manufacturer the incentive to sue for patent infringement in all ANDA Paragraph 4 certifications, no matter how small the probability of successfully defending the patent. Also, there was an economic incentive for these firms to attempt to list more than 1 patent for a given drug in the *Orange Book*, especially after the ANDA had been applied for, because this allowed multiple 30-month stays. There

were no limits to the number of 30-month stays that brand name manufacturers could obtain. The Federal Trade Commission (FTC) found that the additional time gained from the multiple stays ranged from 4 to 40 months.⁶ The only cost to the brand name manufacturer was the cost of litigation, which was generally much less than the monopoly profits gained by keeping a competitor off the market for an additional 30 months.

In contrast, the cost to the brand name manufacturer of permitting a generic entry was high. For example, within weeks of the patent expiration covering Prozac[®] (fluoxetine), generic competitors captured 80% of the prescriptions for that drug.¹¹

The legal system also gives the brand name manufacturer an advantage. Under the H-W Act, the brand name manufacturer receives an automatic 30-month injunction against the entry of a generic competitor. However, if it is found that the generic drug did not infringe on the branded drug patent, there is no remuneration from the brand name manufacturer to the generic company. If, after the 30-month stay, the generic drug enters the market and later a court determines that the generic did infringe on the brand name manufacturer's patent, the generic company owes damages to the brand name manufacturer. The damages owed are usually greater than the profit earned by the generic company from market entry. Thus, there is a disincentive for the generic company to enter the market because the cost could be much greater than the benefit. Compromises

The profit that the generic drug generates is usually less than the profit lost by the brand name manufacturer.

that allow the generic drugs to enter the market before the branded drug's patent expired may be best for consumers. However, as the courts recognize, reducing the profits that innovators earn can also reduce innovation.

In any event, because the generic drug enters the market at a considerably lower price than the branded drug, the profit that the generic drug generates is usually less than the profit lost by the brand name manufacturer. Thus, there is incentive for both parties to collude and share the larger profits instead of competing and sharing a smaller total profit. However, brand name manufacturers have considerable incentives to prevent competition, both legally and illegally. The H-W Act provides the brand name manufacturer the legal means to forestall competition, but also allows what the FTC considers illegal means to circumvent the intent of the H-W Act.

The brand name manufacturer gains simply by suing the first generic drug company to challenge its patent. Not only does it receive the automatic 30-month stay, but even if it ultimately loses its infringement lawsuit, it gains from having to confront only 1 generic competitor for 6 months.¹² If it did not sue the first generic drug company to challenge its patent, nu-

merous generic drugs could immediately enter the market. Because 1 generic drug's price tends to be 85% of the brand name drug's price as opposed to 75% with 2 generic drugs,¹² there is some advantage to keeping out additional competitors, even if only for the first 6 months. Barr Laboratories, for example, enjoyed a 180-day period of exclusivity from August 2000 to February 2001 in its successful challenge to Prozac[®].¹¹ Barr gained from its generic monopoly, while Eli Lilly faced only 1 competitor since it confronted only 1 generic drug for the 6 months of exclusivity.

The second provision of the 180-day period of exclusivity for the first generic is intended to provide an incentive for the generic drug company to challenge questionable patents. Under the H-W Act, the generic company has a 180-day period of exclusivity from the day it markets the product. In some cases, generic drug companies have entered into agreements with brand name manufacturers to not enter the market. Thus, the 180-day period of exclusivity does not start and all other generics are prohibited from market entry. When a settlement includes a payment not to enter the market and the generic drug company does not give up the exclusivity period, a warning flag should immediately be raised. Such a prohibition seems to have great potential for restricting competition, and will be discussed in more detail later in this article.

The Cost of Pharmaceuticals
Much of the costs associated with a particular drug is fixed, namely,

its research and development costs, which in 2001 were estimated to be about \$800 million.¹² The actual production cost for many drugs is quite low, often a small fraction of their eventual price. However, only 1 in every 5000 chemicals tested on animals results in a marketable drug.⁴ For example, within months of their patent expirations, generic versions of Zantac[®] (ranitidine), an antiulcer drug, and Capoten[®] (captopril), a heart medicine, were priced at 10% to 20% of the branded versions.¹¹ In general, the average variable cost for brand name manufacturers approximated 30% of their average revenues.¹³ Further, marginal cost is likely to be below the average variable cost because of the start-up costs of production. Competition among generics could quickly drive their prices to marginal cost and reduce the market shares and profits of the brand name manufacturers. Examples of such price savings have been seen for Cardizem[®] (diltiazem) with a price of \$1.45 per pill versus the generic version at 22 cents per pill, Vasotec[®] (enalapril) with a price of \$1.08 per pill versus the generic version at 45 cents per pill, and Prozac[®] with a price of \$2.61 per pill versus its equivalent generic at a price of \$1.41 per pill.¹⁴ The potential cost savings from generic competition are substantial. For example, 3 months after Naprosyn[®] (naproxen) went off patent, its manufacturer, Syntex, lost 75% of its market share to the generic competitor.¹⁵

The H-W Act had a large effect on the development of generic drugs and the creation of the generic drug segment. From only

The top 5 generic companies accounted for more than 50% of the generic segment's sales in 2002.

19% of prescriptions in 1984, the share of prescriptions for generic drugs grew to 45% by 2001.^{12,16} Even with so large a share of prescriptions, the generic share of the \$121.8 billion drug industry revenue in 2001 was only 8%, reflective of the much lower generic prices.¹⁶

Between 2002 and 2006, several brand name drugs with annual sales of \$40 billion lost patent protection or can be anticipated to have their patents expire in the near future.¹¹ The 2002 and 2003 period alone saw Prilosec[®], an antiulcer drug from AstraZeneca with \$3.7 billion in US sales in 2001, lose its patent protection. Patent protection during this period also expired for Schering-Plough's nonsedating allergy drug Claritin[®] (loratadine), with annual sales of \$2.5 billion. Other drugs that have lost or soon will lose their patent protection include Glucophage[®] (metformin), Augmentin[®] (amoxicillin/clavulanate), Paxil[®] (paroxetine), and Cipro[®] (ciprofloxacin), with total combined annual sales of \$6.9 billion.

The loss of patent protection on a company's drugs without new drugs ready for market entry can be a serious problem. For example, between 2001 and 2002, Bristol-Myers Squibb witnessed an 8% decline in global sales revenues, at-

tributed to patent protection losses without major new drugs reaching the market, while the other 10 leading prescription drug companies experienced global sales increases of 6% to 15%. Bristol-Myers Squibb fell from the sixth to eighth largest drug company as determined by global sales, according to rankings from IMS Health Inc., a health information provider.¹⁷

The Generic Market

The generic market itself exhibits the impact of increasing concentration and the presence of monopoly elements. As some firms exit, the generic market is becoming more concentrated.¹⁸ The top 5 generic companies accounted for more than 50% of the generic segment's sales in 2002. It is noteworthy that some brand name manufacturers have their own generic divisions or subsidiaries. For example, Geneva Pharmaceuticals is a wholly owned subsidiary of Novartis.

A recent merger in which Baxter International acquired the generic injectable drug business of Wyeth Corporation highlighted the concentrated nature of the market.¹⁹ In 2002, propofol, a general anesthetic and sedative, had only 2 generic producers and entry was difficult because a patented preservative is required to produce the product. Production of pancuronium, a fast- and long-acting muscle-paralyzing agent, is also highly concentrated. Prior to the merger, the Herfindahl-Hirschman Index (HHI) for the generic pancuronium market was 3656, which means that the industry essentially had the equivalent of 2.7 equal-

size firms. Baxter entered into a consent decree with the FTC that, among other conditions, called for the divestiture of all Wyeth's assets related to propofol.²⁰ High concentration also existed for other generic products involved in the merger.

Generic prices during a 1-year period ending in 2002 increased by 15% compared to only 8.8% for branded drugs, perhaps reflective of the fact that the generic market is becoming more concentrated. Some generic companies have raised prices far more than the average increases. For example, in 2002, Watson Pharmaceuticals raised the price of its generic tranquilizer meprobamate from 12 cents per dose to 99 cents per dose. Likewise, Geneva Pharmaceuticals increased the per dose price of its generic antihistamine from 3 cents to 31 cents. Despite such increases, the generic prices remained far below the prices for the branded products. For example, the wholesale price of Geneva's generic promethazine was still 55% lower than that of the branded version.

Generic drugs are still constrained by the buying power they face from large wholesalers and large retail pharmacy chains. For example, the top 4 buyers accounted for 59% of the sales of Watson Pharmaceuticals in 2002.²¹ Further, there is evidence that buyer concentration is continuing to increase.²¹ In addition, under Medicaid, some states are combining their purchases to obtain greater bargaining power and lower prices.²² Finally, Medicare Part D will make the US government the leading purchaser of pharmaceuti-

The first generic drug in a therapeutic class may be able to take substantial business away from the brand name drug by obtaining advantageous insurance company reimbursement.

icals, and it may use its market power in the future.

Is There a First Mover Advantage in the Generic Drug Segment?

The successful generic challenger under Paragraph 4 of the H-W Act gains a 6-month period of exclusivity as the only generic drug on the market for a particular therapeutic class. During that period of exclusivity, the price of the generic drug may be high, but still below that of the branded drug. One study found that a single generic competitor meant that its price would be 59% of the branded drug, while 3 generic competitors would reduce the generic price to 50% of the branded drug and 10 generic competitors would reduce the generic price to 29% of the branded drug.²³

A first mover advantage typically exists when brand name recognition is important or "learning by doing" plays a significant role in an industry. In both cases, the first firm in the market is able to establish a position that is difficult for

other firms to overcome.

In the generic drug segment, price is the primary competitive weapon. The first generic drug in a therapeutic class may be able to take substantial business away from the brand name drug by obtaining advantageous insurance company reimbursement. However, it is still vulnerable to displacement by subsequent generic drugs offering lower prices. Supporting this is the experience of the generic division of Schering-Plough, which entered the market after the 6-month exclusivity period had expired.²⁴ A retail pharmacy is unlikely to want to inventory more than 1 generic drug in a therapeutic class. Accordingly, the 6-month exclusivity period will have few, if any, carry-over benefits.²⁵

On the other hand, the increasing concentration in the generic segment may foretell a greater profit over a longer period as rivalry is attenuated. In such a situation, the first mover advantage may become more important. Further, the closer the generic drug price is to the brand name drug price, the greater the gains to risking an infringement finding. Indeed, part of the reason generic companies may have been reluctant to enter and challenge brand name manufacturers is because low generic prices meant that they were undertaking great risk. Obviously, generic prices would still have to be substantially below brand name prices to obtain much business.

Bolar Exemption

In October 1983, the District Court in *Roche Products, Inc. v. Bolar Pharmaceutical Co.* "embraced the notion that the activi-

ties involved in seeking FDA approval to market a patented drug did no economic harm to the patent owner during the life of patent.”⁵ However, in 1984, in *Roche Products, Inc. v. Bolar Pharmaceutical Co.*, “the Court of Appeals for the Federal Circuit decided that the manufacture, use, or sale of a patented invention during the term of the patent constituted an act of infringement, even if it was for the sole purpose of conducting tests and developing information necessary to apply for regulatory approval.”⁵ Thus, the Appeals Court reversed the District Court and held that the development of the data to support an ANDA could not begin until a patent expired.⁵ The H-W Act exempts generic companies from Bolar and allows these companies to market a product the day a valid patent expires or is found not to be infringed. Without this so-called “safe harbor exemption,” generic drug companies would not be able to apply for an ANDA until the day of patent expiration. The approval of an ANDA usually takes between 18 and 24 months. Thus, without the Bolar exemption, generic competition would not occur until at least 18 months after the patent expired.

Alfred Engleberg, an expert in this field, claims that: “Patent term extension and the Bolar exemption are self-canceling provisions which, taken together, have no net effect on the length of the exclusive marketing period of most new drugs. The patent certification procedures are being abused by both sides and produce no benefit that would not otherwise occur.”¹⁰

The FDA’s role in maintaining the *Orange Book* is simply ministerial.

The *Orange Book* and the 30-Month Stay

Under the H-W Act, brand name manufacturers are expected to list patents that cover approved drugs in the FDA’s *Orange Book*. Listed patents are to be confined to those protecting ingredients, composition, formulation, and method of use.⁸ However, the FDA’s role in maintaining the *Orange Book* is simply ministerial, without any requirement under its regulations to exercise legal or discretionary judgment on the accuracy of patent listings.²⁵ This was confirmed by the US Court of Appeals for the District of Columbia in *Bioscience v. Thompson*, in which the court noted that: “The FDA has a long-standing policy not to get involved in patent disputes. It administers the Hatch-Waxman Amendments in a ministerial fashion, simply following the intent of the parties that list patents.”²⁶

Engelberg states that:

“Unfortunately, the Act naively presumed good faith on the part of patent holders in selecting the patents that would be listed. Therefore, it provided no guidance whatsoever as to what patents should or should not be listed and no mechanism for determining if a patent was properly or improperly listed. Moreover, the drafters of the

Act failed to recognize that the automatic 30-month injunction inadvertently created a powerful incentive for the holder of an NDA to list any and every patent related to a drug product irrespective of whether such patent was a significant barrier to legitimate competition. Thus, the ’84 Act automatically enables a patent owner to prevent competition irrespective of the merits of the patent being asserted and without any meaningful penalty for a wrongful assertion save for the possible award of the opposing party’s legal fees. These fees are nominal as compared to the hundreds of millions of dollars in monopoly profits that can be earned during the 30 months a competitor is held off the market.”¹⁰

Thus, there is an incentive for brand name manufacturers to list numerous patents and be able to file for the automatic 30-month stay. Further, these companies have an incentive to add patents to the list after the original stay has been obtained in order to file for an additional 30-month stay before the first stay expires. Noteworthy is the increase in patents per “blockbuster” drug from 2 before 1984 to 10 after the H-W Act.¹⁶ In the case of BuSpar® (buspirone), an antianxiety drug, a patent was added to the *Orange Book* only 12 hours before the generic competitor was to enter the market. The generic company had already manufactured the drug and was shipping it to sellers the next day.

Out-of-Court Settlements

Much of the litigation between generic companies and brand name manufacturers concerning certificate 4 issues has been settled out of court. Litigants settling out of court avoid the cost of litigation, achieve a quicker resolution to the issues, as well as reduce their risk by obtaining the certainty of the result. However, in some of these settlements, anticompetitive issues and harm to consumers have been alleged.

The settlement can be illegal only if the patent is not valid or infringed. If the patent was valid or infringed upon, there would be no generic entry until after the patent's expiration. Thus, any settlement that allows entry before the patent expires cannot be anticompetitive if the patent is valid. Some settlements provide payments to generic companies that delay their entry. Such settlements may actually enhance competition by giving the generic competitor revenues to better compete with the branded firms in the future.²⁶

However, if the patents are invalid or not infringed upon, the settlement can be anticompetitive. Without litigation on the validity of the patent, no one knows with certainty the legality of the settlement.

The H-W Act has created perverse incentives that undercut the objectives of the Act. The FTC investigated these settlements and contended that some were anticompetitive. In some cases, the FTC entered into consent decrees that prevented the parties to the settlement from continuing the alleged anticompetitive practices. In one case, the company agreed to pay \$670 million to settle a class

Litigants settling out of court avoid the cost of litigation, achieve a quicker resolution, and reduce their risk by obtaining the certainty of the result.

action suit brought by state attorneys general.²⁷ In this article, we will examine this and other cases.

Hoechst Marion Roussel/Andrx

In May 2001, the FTC entered into a consent order with Hoechst Marion Roussel (now sanofi-aventis) and Andrx concerning alleged anticompetitive violations in the hypertension and angina markets (a consent order is not an admission of wrong-doing; it is simply an agreement to do or not do something). Cardizem[®] CD (diltiazem controlled delivery) is a drug used for the treatment of hypertension and angina and the prevention of heart attacks and stroke. Total 2000 US sales of once-a-day diltiazem products were approximately \$1 billion, with Hoechst sales of Cardizem[®] CD accounting for over \$700 million.²⁸ The FTC complaint alleged that Hoechst and Andrx entered into an agreement in which Andrx was paid millions of dollars to delay bringing a competitive generic alternative to Cardizem[®] CD to market.

On September 22, 1995, Andrx

filed an ANDA with the FDA to manufacture and distribute a generic version of Cardizem[®] CD. As the first to file under Paragraph 4, Andrx was eligible to receive the 180-day exclusivity right. Hoechst sued Andrx for patent infringement and received an automatic 30-month stay.

Among other patents, Hoechst's original patent on Cardizem[®] CD expired in November 1992. However, in November 1995, Carderm Capital, L.P. received a patent (number 5,470,584), which covered Cardizem[®] CD's dissolution of 0% to 45% of diltiazem within 18 hours.²⁸ Hoescht received a license to the '584 patent and in January 1996, Hoescht and Carderm sued Andrx for infringing this patent. The suit gave Hoescht the automatic 30-month stay on Andrx's ANDA, which would expire in July 1998. Andrx then made claims of unfair competition against Hoescht and amended its ANDA to specify that at least 55% of its product's total diltiazem would be released within 18 hours as opposed to Hoescht's maximum release of 45%. Andrx also indicated to the patent court its intention to enter the market once its ANDA was granted.

The FDA tentatively approved Andrx's ANDA on September 15, 1997, with final approval to be given once the 30-month stay expired in July 1998 or earlier upon a favorable court ruling. On September 24, 1997, Hoescht and Andrx agreed, among other things, that Andrx would not market its generic drug until it received a favorable and unappealable court decision concerning patent infringement and would not relin-

quish or otherwise transfer its 180-day exclusivity provision.

Beginning in July 1998, Hoechst paid \$10 million on a quarterly basis to Andrx. July 1998 was when the 30-month stay would no longer be in effect and thus Andrx would be able to market the generic version of Cardizem[®] CD. In addition, both companies agreed that if Hoechst lost the lawsuit, Hoechst would pay Andrx an additional \$60 million annually beginning in July 1998. Thus, Andrx had the potential of earning \$100 million annually by not marketing its generic version of Cardizem[®] CD. It was estimated that a generic version of Cardizem[®] CD would have been sold at 70% of the brand name drug price and would have taken approximately 40% of the Cardizem[®] CD market share within the first year.²⁸ Using these estimates, Andrx would have enjoyed revenues of about \$200 million. However, if Andrx had lost the infringement case, it would have had to pay Hoescht much more than \$200 million in damages, making its market entry quite risky. While it was receiving the quarterly payments, Andrx supplemented its ANDA in September 1998 to include a reformulated generic version of Cardizem[®] CD, and on February 3, 1999, it certified to Hoescht that its reformulated version did not infringe the '584 patent. The FDA approved Andrx's reformulated product on June 9, 1999. On that day, Hoescht and Andrx terminated their agreement, with Hoescht paying a final sum of \$50.7 million, making the total payments of \$89.83 million to Andrx. Andrx



Often the real question of a litigation agreement is whether the agreement is a legitimate temporary settlement of a patent dispute or, conversely, a sharing of monopoly.

began selling its generic Cartia[®] XT (diltiazem extended-release capsules) on June 13, 1999 at a much lower price than Cardizem[®] CD and gained substantial market share. The 180-day exclusivity period also began on June 13, 1999.

Evaluation of the Agreement

The real question is whether the agreement was a legitimate temporary settlement of a patent dispute or, conversely, a sharing of monopoly profits by paying a lower-priced competitor not to enter the market. The agreement did not benefit society and seemed to benefit only 2 parties (Andrx and Hoechst). The temporary settlement did not avoid court costs or decrease uncertainty concerning the result of the patent litigation, the 2 efficiency reasons for settlement. Without the temporary settlement when the 30-month stay period ended and Andrx received an ANDA, it had to decide to either enter the market or postpone entry until the litigation concerning patent validity was finally resolved. If Andrx entered the market and the patent was valid or infringed upon, it would have

owed damages far exceeding its profit from market entry. If the patent was not valid or infringed upon, Hoescht would have lost its monopoly profits. Thus, the temporary agreement was simply a sharing of monopoly profits in the Cardizem[®] CD market.

The size of the payments, the nontransferability of the 180-day exclusivity period, and the seeming differential claims in the patent dispute all suggest a sharing of monopoly profits. Indeed, in rejecting a summary dismissal of the private plaintiff's claims, the Appellate Court noted "there is simply no escaping the conclusion that the agreement, all of its other conditions, and provisions notwithstanding, was at its core a horizontal agreement to eliminate competition for Cardizem[®] CD throughout the entire United States, a classic example of a per se illegal restraint of trade."²⁹ Earlier, the District Court was concerned that the provisions of the agreement were overly restrictive. It noted that even noninfringing or potentially noninfringing versions were prevented from competing.²⁹ Private plaintiffs alleged that the dissolution profile was sufficiently different that continuation of the patent dispute itself was designed to maintain Hoescht's monopoly position.²⁹ As mentioned, the \$89 million payment may itself have indicated a weak position for Hoescht. The strong incentive for the agreement and the above evidence are highly suggestive of the suspicious nature of the agreement. Further, whether the agreement was itself terminated because of a possible FTC investigation is unclear. Nevertheless, given the

eneric drug companies' gains from the H-W Act included lower costs and faster entry to the market.

uncertainties of patent litigation, it is quite possible that a legitimate dispute was at issue. A hearing before an FTC Administrative Law Judge (ALJ) to resolve such issues, as is done for mergers, would have been appropriate. The Consent Decree was entered into after the generic drug entered the market and thus the challenged agreement was no longer in existence. The decree required both Hoechst and Andrx to notify the FTC in writing 30 days before entering into such agreements for the next 10 years. In 2005, in a private class action suit, the branded drug companies agreed to pay over \$30 million in an out-of-court settlement.³⁰

Abbott Laboratories/Geneva Pharmaceuticals

In May 2000, the FTC entered into a consent decree with Abbott Laboratories and Geneva Pharmaceuticals concerning alleged anticompetitive activities in the hypertension and benign prostatic hyperplasia markets. Hytrin[®] (terazosin) is used for the treatment of hypertension and benign prostatic hyperplasia. Total US sales of Hytrin[®] by Abbott were \$542 million for 1998 and \$292 million in the first 6 months of 1999. This represented over 20% of the net sales of Abbott's pharmaceutical division.³¹ Ninety percent of the Hytrin[®] sales were in capsule form and the remaining 10% were tablets.³¹ The complaint alleged that Abbott paid Geneva \$4.5 million per month to delay bringing a generic alternative to Abbott's brand name drug Hytrin[®] to market.

In January 1993, Geneva filed

an ANDA with the FDA for the generic version of Hytrin[®] in tablet form, and in December 1995, in capsule form. Thus, Geneva was the first filer in both cases. In June 1996, Abbott sued Geneva for patent infringement in the tablet form, but for some unknown reason, probably due to an oversight, did not file an infringement suit for the capsule form. Therefore, Abbott received a 30-month stay for Hytrin[®] tablets, but not for Hytrin[®] capsules.

The FTC alleged that when Geneva received FDA approval for the capsule form, it contacted Abbott and claimed it would launch its generic drug unless Abbott paid them not to enter the market. Abbott agreed to pay \$4.5 million per month until the District Court ruled on the patent infringement case concerning the tablet form, and put \$4.5 million per month in escrow until the final resolution of the litigation, with the prevailing party in the litigation receiving the escrow monies.³¹

Geneva agreed not to bring a generic into the market until the final resolution of the patent infringement lawsuit involving the generic tablet product (including possible review by the Supreme Court) or entry into the market of another generic tera-

zosin product. Geneva also agreed not to transfer, assign, or relinquish its 180-day exclusivity right to market its generic product.³²

Pursuant to the agreement, Geneva did not introduce its generic capsules in April 1998, even though the FDA approved its ANDA, in September 1998 when the district granted it summary judgment, or in July 1999 when the Court of Appeals affirmed the decision invalidating Abbott's patent. Geneva finally entered its generic drug to the market on August 13, 1999 when, aware of the FTC's investigation, it cancelled its agreement with Abbott.³² The Supreme Court denied Certiorari or review of the case on January 10, 2000.³¹

Abbott had estimated that entry of a generic version of Hytrin[®] would have eliminated over \$185 million in sales in just 6 months, or roughly 70% of the market share for Hytrin[®]. Since Hytrin[®] was highly profitable, Abbott was willing to pay Geneva a substantial "premium" over Geneva's probable revenues of \$1 million to 1.5 million per month.³¹

A District Court characterized the Abbott Laboratories agreements as a per se illegal geographic market allocation between competitors. The US Court of Appeals for the Eleventh Circuit reversed in *Valley Drug Co. v. Geneva Pharmaceuticals, Inc.*,³² noting that Abbott had patent protection (1 of which was later found invalid), so that it had the legal right to exclude others, including generic producers. It held that a reasonable settlement of patent litigation

involving payments to potential competitors does not by itself invoke antitrust liability. It added that invoking antitrust liability could diminish the disclosure incentives behind patents.³³

Evaluation of the Abbott Laboratories and Geneva Pharmaceuticals Agreement

Again, similar to the Hoescht/Andrx agreement, the temporary agreement and continuation of lawsuits between parties was simply a way to share monopoly profits and foreclose entry by other generics. Society did not benefit from this agreement, and the only beneficiaries were Abbott and Geneva. In addition, the agreement had several troublesome aspects. Geneva could not enter the market until all appeals (including appeals to the Supreme Court) were exhausted. The agreement prevented Geneva from relinquishing its 180-day exclusivity rights and developing or marketing noninfringing generic products.³⁴ These aspects would appear to go beyond normal settlement provisions, since Abbott had failed to contest the capsule ANDA and thus Geneva was free to enter the capsule market, which represented 90% of the Hytrin[®] market, although it would still have to bear the risk of a possible infringement finding. The amended H-W Act requires that patent agreements between competitors be brought before the FTC or Department of Justice (DOJ) to determine whether they are in the public interest or at least are not attempts to prevent competition.

Bristol-Myers Squibb

In April 2003, the FTC entered in-

The amended H-W Act requires that patent agreements be brought before the FTC or DOJ to determine whether they are in the public interest or at least are not attempts to prevent competition.

to a consent order with Bristol-Myers Squibb concerning alleged anticompetitive behavior with respect to BuSpar[®], Taxol[®] (paclitaxel), and Platinol[®] (cisplatin). The State Attorney Generals had also filed an antitrust class action suit concerning BuSpar[®] and Taxol[®], which was settled on January 7, 2003 when Bristol-Myers Squibb agreed to pay a total of \$670 million (\$535 for BuSpar and \$135 for Taxol).³⁵

According to the FTC complaint, the pattern of illegal activity involved misusing regulations instituted by Congress to hasten the approval of generic drugs, misleading the FDA and the PTO in order to protect patents on these branded drugs, and filing baseless patent infringement lawsuits against would-be generic competitors.³⁶

BuSpar[®], used to treat persistent anxiety, had total US sales of over \$600 million in 2000. Taxol[®], used to treat ovarian, breast, and lung cancers, as well as AIDS-related Kaposi's sarcoma, had total US sales of over \$1 billion in 2000. Platinol[®] and Platinol-AQ[®]

(cisplatin injection), used to treat various forms of cancer, had total US sales of \$100 million in 1999.

BuSpar[®]

The FTC alleged that Bristol-Myers Squibb was paying a would-be generic competitor \$72.5 million to settle patent litigation, thereby preventing the introduction of a generic version of BuSpar[®]; filing false information with the FDA in order to list a patent in the *Orange Book*, thereby automatically obtaining additional 30-month stays; and filing baseless patent infringement suits against potential generic competitors.³⁶ Bristol-Myers Squibb's BuSpar[®] was approved by the FDA on September 29, 1986. At the time, Bristol-Myers Squibb enjoyed patent protection from patents 3,976,776 and 4,182,763. The '776 patent covering buspirone's tranquilizing effects for the treatment of anxiety expired in August 1993. The '763 patent claimed the use of buspirone for treating anxiety.³⁷

In 1992, Schein Pharmaceuticals was the first to file an ANDA with the FDA for a generic version of BuSpar[®]. Bristol-Myers Squibb sued Schein for patent infringement and received a 30-month stay that was to expire in early 1995.³⁸ In December 1994, Bristol-Myers Squibb entered into an agreement under which it would pay Schein \$72.5 million over 4 years if Schein agreed not to market its generic version of BuSpar[®] until the '763 patent expired in November 2000. The FTC alleged that Bristol-Myers Squibb faced a strong likelihood that the '763 patent would be declared invalid since it arguably was anticipated

by the '776 patent.³⁷ As part of the agreement, Schein had to affirm the validity of the '763 patent.

To protect itself further against the entry of generics, in 1999, Bristol-Myers Squibb filed for a new '365 patent with the PTO involving the use of buspirone. The PTO repeatedly rejected Bristol-Myers Squibb efforts because "Bristol-Myers Squibb had been making and selling BuSpar[®] to treat anxiety in the United States for nearly 14 years."³⁸ Bristol-Myers Squibb was finally successful when it requested a patent that claimed solely the use of the metabolite of buspirone and received patent '365 only hours before patent '763 was due to expire. It then listed patent '365 in the *Orange Book* and received an additional 30-month stay.³⁸ For technical reasons, the FTC claimed that the '365 patent did not meet the statutory requirement for a listing in the *Orange Book*. Bristol-Myers Squibb also was accused of intentionally making false and misleading statements. Nonetheless, consistent with its ministerial approach to *Orange Book* listings, the FDA accepted Bristol-Myers Squibb's statements and listed patent '365 in the *Orange Book*. Bristol-Myers Squibb thus received another 30-month stay, delaying generic entry. BuSpar[®] did not face generic competition until March 2001 when the District Court in *Mylan v. Thompson* ordered Bristol-Myers Squibb to delist patent '365 from the *Orange Book*.³⁹ This decision was reversed by the Appeals Court when it decided that a private action had no right to delist. However, the reversal did not affect competition in this market.

Taxol[®]

The State Attorney Generals claimed that Bristol-Myers Squibb fraudulently secured patents on Taxol[®] to extend its monopoly. The FTC claimed that Bristol-Myers Squibb improperly listed 3 patents in the *Orange Book*, filed misrepresentative statements with the FDA, and entered into an unlawful agreement with a generic competitor in order to obtain an additional 30-month stay on FDA approval of a generic version of Taxol[®].

In 1991, the National Cancer Institute (NCI) gave Bristol-Myers Squibb the exclusive right to use existing and future data for FDA approval of paclitaxel, and Bristol-Myers Squibb obtained FDA approval to market Taxol[®] exclusively in 1992. Because the NCI funded the discovery and initial development of paclitaxel as an anti-cancer drug,⁴⁰ much of the research relating to Taxol[®] was in the public domain so that the research results were unpatentable. To obtain a patent, Bristol-Myers Squibb had to demonstrate to the PTO that its claimed method of administering Taxol[®] differed from the methods used in the prior studies.

In an attempt to secure a patent, Bristol-Myers Squibb allegedly told the PTO that certain studies did not provide evidence of safety and efficacy, which contradicted the statements made to the FDA when the company obtained FDA approval. However, Bristol-Myers Squibb needed to do this to receive the patent. Bristol-Myers Squibb was successful in securing 2 patents, '537 and '803, and listed them in the *Orange Book*. The FTC claimed that the patents were

obtained by "inequitable conduct," which should have meant that they could not be listed in the *Orange Book*.³⁷ After several generic companies applied for an ANDA, Bristol-Myers Squibb filed infringement suits and successfully received an automatic 30-month stay. The company obtained a third patent, '331, from American Bioscience Inc. (ABI) and listed it in the *Orange Book* to obtain another automatic 30-month stay. The agreement provided that ABI receive royalties on a significant percentage of Bristol-Myers Squibb's sales of Taxol[®]. The FTC alleged that the '331 patent's relevant claims were invalidated by prior actions.³⁷ As a result of a District Court decision, Bristol-Myers Squibb requested that patent '331 be delisted. The FDA then permitted the generic producer IVAX to market its generic version of Taxol[®]. IVAX enjoyed a 180-day exclusivity period, as it was able to mount a Paragraph 4 challenge because of the alleged improperly listed patents.

Platinol[®]

The FTC complaint alleged that Bristol-Myers Squibb wrongfully submitted a patent for listing in the *Orange Book* to obtain an unwarranted 30-month stay on FDA approval of competing generic products.³⁸ In December 1996, Bristol-Myers Squibb's patent protection for its Platinol[®] products expired, and 4 generic companies were ready to enter the market. However, in October 1996, the PTO gave Bristol-Myers Squibb a new patent, '925, based on an amendment to an application that it had initially filed in 1970. Bristol-Myers Squibb listed patent

'925 in the *Orange Book* and filed patent infringement suits against the generic companies and obtained a 30-month stay. In October 1999, a District Court found by clear and convincing evidence that patent '925 was invalid for double patenting, a ruling that the Federal Circuit Court upheld. This judicial and regulatory maneuvering allowed Bristol-Myers Squibb to maintain its monopoly on Platinol® and the associated profits at little cost to the drug company. Bristol-Myers Squibb incurred only the cost of litigation and regulatory procedures.

Evaluation of the Bristol-Myers Squibb Cases

The Bristol-Myers Squibb experience shows the possible dangers created by the H-W Act's 30-month stay provision. Absent the H-W Act, Bristol-Myers Squibb would have had to obtain an injunction to prevent generic competition. To avoid the anticompetitive manipulation of the H-W Act, there should be some coordination and sharing of information among the various agencies involved. The FDA, PTO, and FTC each should be apprised of information that a company is supplying to the other agencies. In the case of BuSpar®, Bristol-Myers Squibb enjoyed a 14-year monopoly and for Taxol® an 8-year monopoly. Although the appropriate period of protection cannot be precisely determined, both products enjoyed substantial periods of protection. Finally, the experience of Bristol-Myers Squibb shows how rapid entry of generic drugs in the current market environment greatly reduces the innovator's market share and profits.

The consent decree included the following provisions:

Bristol-Myers Squibb is prohibited from late listing patents after competitors have filed applications with the FDA for generic entry. The order also contains prohibitions relating specifically to the listing and enforcement of patents relating to Taxol® and BuSpar®, including listing any patent in the Orange Book relating to products with the same active ingredient, or taking any action that would trigger an additional 30-month statutory stay on final FDA approval of a generic form of Taxol® or BuSpar® (the order does not provide specific relief for Platinol® because a court held the only unexpired patent on Platinol® was invalid).³⁶

Some of these provisions have been included in the revisions to the H-W Act.

Biovail Corporation

In October 2002, the FTC entered into a consent decree with the Biovail Corporation concerning alleged anticompetitive activities in the high blood pressure and chronic chest pain markets. Tiazac® is a once-a-day diltiazem-based prescription drug used for the treatment of high blood pressure and chronic chest pain. In 2000, total US sales of Tiazac® were almost \$200 million, which represented about 38% of Biovail's revenue.⁴¹ Biovail forecasted that a generic version of Tiazac® would capture 40% of the market in the first year.⁴¹ The FTC complaint charged that:

Biovail illegally acquired the exclusive license to a drug patent in order to prevent generic competition from ending its monopoly of the antihypertension drug Tiazac®. Biovail then wrongfully listed the acquired patent as claiming Tiazac® in the FDA's Orange Book in order to maintain its monopoly. As a result of the Orange Book listing and other conduct, including making a misleading statement to the FDA during the regulatory process, the complaint alleged that Biovail sought to illegally delay the entry of generic Tiazac® by gaining a second 30-month stay on generic entry through patent infringement litigation.³⁶

In June 1998, Andrx was the first to file an ANDA for the generic version of Tiazac®. Biovail then filed a patent infringement suit and received a 30-month stay, which was to expire on February 26, 2001. In March 2000, the US District Court found that Biovail's Tiazac® was not infringed. In September 2000, the FDA tentatively approved Andrx's ANDA. Andrx would receive final approval if the Federal Court of Appeals upheld the District Court's decision. In February 2001, the Federal Circuit Court affirmed the District Court's ruling of noninfringement on Biovail's patent '791.

However, a month earlier, Biovail listed a second patent, '463, for Tiazac®, which was obtained through an exclusive patent license from DOV Pharmaceuticals, Inc. Given this new patent, Andrx had to file again, claiming no

patent infringement. Biovail once again filed a patent infringement suit and received another 30-month stay.

According to the [FTC] complaint, however, Biovail was aware that the '463 patent did not claim the formulation of Tiazac[®] that it had been marketing. The product described in the '463 patent contains at least 1% of uncoated or "free" immediate-release diltiazem, in addition to extended-release diltiazem in the form of coated beads. Accordingly, Biovail did not need the '463 patent in order to make or sell its existing FDA-approved formulation of Tiazac[®]. This suggests that the '463 patent could not simultaneously be valid and properly listed in the Orange Book for Tiazac[®].³⁶

If patent '463 claimed the formulation of Tiazac[®] that it was marketing, patent '463 would seemingly have infringed on Biovail's patent '791. Therefore, instead of paying DOV Pharmaceuticals for the patent rights, it could be argued that Biovail should have contested the issuance of patent '463.

Andrx attempted to have patent '463 delisted from the *Orange Book* and sued in Federal Court.

The FDA learned that Biovail's position was that the '463 patent covered a new formulation of Tiazac[®] that Biovail had developed only after it acquired and listed the '463 patent, rather than the version of Tiazac[®] that the FDA had approved and

that Biovail had been marketing. The FDA notified Biovail on March 20, 2001, that its new formulation of Tiazac[®] was not approved by the FDA under the Tiazac[®] NDA. Accordingly, the FDA would de-list the '463 patent from the Orange Book unless Biovail amended its certification to indicate that the patent claimed the version of Tiazac[®] the FDA had approved.³⁶

The FTC complaint also alleged that:

This declaration was misleading because it did not clarify whether the term "Tiazac[®]," as used by Biovail, meant the form of Tiazac[®] the FDA had approved for marketing (as the FDA intended) or Biovail's revised form of the product.³⁶

As a result of the Consent Decree, Biovail was required to divest part of its exclusive rights to the acquired patent to DOV Pharmaceuticals, the original owner. The decree also prohibited Biovail from causing a statutory stay on any generic versions of Tiazac[®]. In addition, Biovail was prohibited from wrongfully listing patents in the *Orange Book* and was required to notify the FTC prior to acquiring any patents that would be listed in the *Orange Book*.⁴² This case illustrates the strong incentive that a brand name manufacturer has to utilize patents, whether applicable or not, to try to maintain its monopoly.

Biovail/Elan

In August 2002, the FTC entered into a consent decree with Biovail and Elan concerning alleged anti-competitive behavior in the hypertension market. Adalat[®] CC (nifedipine extended-release) is used for the treatment of hypertension. Prior to the entry of generic drugs in 2000, Bayer, the patent holder for Adalat[®] CC, had sales of over \$270 million.

Unlike the previous cases, the defendants were 2 generic companies that were being sued for anti-competitive behavior, whereas the brand name manufacturer, Bayer, was not part of the suit. The complaint charges that:

Biovail and Elan agreed not to compete in violation of the FTC Act. The complaint alleges that the companies' agreement substantially reduces their incentives to introduce competing 30-mg and 60-mg generic Adalat[®] products, and that the agreement lacks any countervailing efficiencies.⁴³

Elan was the first to file an ANDA for the 30-mg generic version of Adalat[®], and Biovail was the first to file for the 60-mg version of the drug. As first filer, each was entitled to a 180-day exclusivity period for the 30- and 60-mg formulations, respectively. Each was the second firm to file an ANDA for the dosage for which the other was first filer.

In October 1999, Biovail and Elan agreed not to compete with each other in the Adalat[®] market. Under the agreement, Biovail would pay Elan for the exclusive agreement to distribute Elan's 30-

and 60-mg generic Adalat® products. The agreement also provided for Teva Pharmaceuticals, a distributor of Biovail, to sub-distribute Elan's 30-mg generic Adalat® and either Teva or another firm to sub-distribute Elan's 60-mg product. The agreement was to last a minimum of 15 years. In March 2000, the FDA gave final approval to Elan's 30-mg product, and Biovail began to market it. In December 2000, the FDA approved Biovail's 60-mg generic Adalat®, and Biovail entered the market. Also in December 2000, the FDA gave final approval to Biovail's 30-mg product and in October 2001, the FDA gave final approval to Elan's 60-mg product. Neither company launched these products and thus there was only 1 entrant in the generic market for each dosage.

Evaluation of the Biovail/Elan Agreement

As of September 2001, Biovail had paid approximately \$45 million in royalties to Elan. Entry of a second generic competitor at each dosage level would cause lower prices because any first mover advantage for the first generic producer would force the second and subsequent producers to cut prices substantially. Accordingly, an agreement that yields a monopoly to a generic can be quite profitable. In this case, generic competitors entered into an agreement to suppress competition and share the excess profits. The consent order required Biovail and Elan to terminate their agreement immediately, but did not call for any fines. Thus, the companies were able to keep the monopoly profits that they earned during the agreement.

Schering-Plough Corporation

In March 2001, the FTC filed a complaint against Schering-Plough Corporation, Upsher-Smith Laboratories, and American Home Products (AHP) Corporation concerning alleged anticompetitive behavior in the market to treat potassium depletion in coronary artery disease patients. The product involved was K-DUR® 20 (potassium chloride). The FTC alleged that Schering, Upsher-Smith, and AHP entered into anticompetitive agreements in which Schering paid Upsher-Smith and AHP millions of dollars to forgo launching a competitive generic alternative to K-DUR® 20.³⁶

In August 1995, Upsher-Smith was the first to file an ANDA to market Klor Con® M20, a generic version of Schering's K-DUR® 20. In December 1995, Schering sued Upsher-Smith for infringement of patent '743. In December 1995, ESI Lederle, Inc., a division of AHP, submitted an ANDA to market a generic version of K-DUR® 20. In February 1996, Schering sued ESI for infringement of patent '743.

In June 1997, Schering and Upsher-Smith settled the patent litigation, with Schering paying \$60 million to Upsher-Smith for agreeing not to enter the market, either with the infringing generic or any other generic version of K-DUR® 20 until September 2001. They agreed to dismiss the litigation without prejudice, and Schering received licenses to market 5 Upsher-Smith products. The FTC claimed that the value of the licenses had little relation to the \$60 million payment.⁴⁴

AHP agreed that its ESI divi-

sion would not market any generic version of Schering's K-DUR® 20 until January 2004, would not market more than 1 generic version of Schering's K-DUR® 20 between 2004 and September 2006, and would not support any study of the bioequivalence or therapeutic equivalence of a product to K-DUR® until September 5, 2006.⁴⁵

The FTC complaint alleged that Schering paid Upsher-Smith and AHP millions of dollars to delay their launch of a generic version of K-DUR® 20.

In April 2002, the FTC entered into a consent decree with AHP. In June 2002, in his initial decision in the Upsher-Smith case, ALJ D. Michael Chappell dismissed all allegations of anticompetitive behavior. The ALJ also found that the FTC did not "prove or properly define the relevant market, and Schering did not have monopoly power in the relevant product market as properly and more broadly defined."⁴⁴

The ALJ believed that:

For Complaint Counsel to prove that the agreements to settle the patent litigation between Schering and Upsher-Smith and between Schering and ESI were anticompetitive requires a presumption that the '743 patent was not valid or that Upsher-Smith's and ESI's products did not infringe the '743 patent.⁴⁵

In December 2003, the FTC overturned the initial decision holding that:

*...there was a direct nexus between Schering's payment and Upsher's agreement to delay its competitive entry, and that this payment substantially exceeded Schering's reasonable expectation of the value of the Upsher licenses.*⁴⁵

On March 8, 2005, the Eleventh Circuit Court set aside the Commission decision, and vacated the cease and desist order. The Eleventh Circuit Court held the FTC did not establish that the challenged agreements restricted competition beyond the exclusionary effects of Schering's patent. The FTC then filed a petition for rehearing en banc on April 22, 2005, which it lost. The FTC is currently appealing the ruling to the Supreme Court.

Schering-Plough Settlement Issues

The Schering-Plough settlement raises several issues. Simply paying the generic challenger is suggestive of payment to delay market entry. However, as the ALJ found, that conclusion was not warranted. The ALJ ruled that the antitrust impact of the agreement cannot be determined until the validity of the patent is determined. If the patent is valid and/or infringed upon, there is clearly no antitrust violation. The settlement did permit generic entry before the 2006 expiration of the contested patent. Therefore, it is possible that the settlement increased generic competition before it otherwise would have. One witness noted that because of such high risks, generic drugs would not enter the market as long as there was a disputed

patent, even after the 30-month stay had ended, whereas another expert noted that the outcome of intellectual property disputes is especially difficult to predict. Further, the Federal Circuit Court, which hears patent disputes, has a 50% reversal rate, suggesting the great difficulty in trying to determine patent validity and infringement issues.⁴⁵ On the other hand, the FTC concluded that the evidence, including post-settlement behavior, indicated that Schering-Plough paid to delay the entry of generic products and that licenses Schering-Plough received from Upsher-Smith were not sufficiently valuable to justify the \$60 million payments. Given the complexity of the issues involved, proposed patent settlements are now reviewed by the FTC and DOJ as part of the amended H-W Act.

Recent Developments

The swirling controversy over the H-W Act has already prompted some changes. By executive order, President Bush has modified some provisions of FDA policy with respect to generic companies and brand name manufacturers. Specifically, as of August 18, 2003, brand name manufacturers have been limited to one 30-month stay when a generic company makes a Paragraph 4 challenge. Further, only patents covering the actual product can be filed; patents on packaging of the product are no longer permitted. Finally, false statements made to obtain patents are now treated as criminal violations.⁴⁶ The FDA estimated that these and other changes will save consumers \$35 billion over 10 years.⁴⁷

These changes address some of the problems of the H-W Act, but critics contend that gaming the system will still be possible. For example, brand name manufacturers could choose not to list patents in the *Orange Book*, a situation that could make generic entry risky. The brand name manufacturer could sue on nonlisted patents after the generic company has produced its product, posing a substantial liability risk for the generic company. It is unlikely that generic drug companies would risk market entry without some assurance that they would not be exposed to substantial liability at a later date. Others suggest that generic companies can attempt to bring declaratory judgments to determine that the brand name manufacturers do not have valid patents.

Congress also made amendments to the H-W Act, in part to codify by legislation some of President Bush's executive order. The law limits companies to one 30-month stay.⁴⁸ Also, patents used for the 30-month stay must have been listed for at least 1 day prior to the ANDA application. To handle the issue of a patent holder choosing not to take advantage of the 30-month stay and suing later, the law permits a generic applicant to obtain a declaratory judgment of noninfringement so that its risk of entry would be reduced. Normally, such a declaratory judgment requires an "actual controversy." In any event, problems with the current situation have led to policy changes and additional proposals.

In October 2004, the Supreme Court left standing the per se illegality ruling in the Sixth Circuit

Court with regards to Cardizem® CD and the Eleventh Circuit Court decision with regards to Hytrin®, overturning a similar *per se* ruling.⁴⁹ Thus, no legal standard is set as it applies to interim patent infringement settlements. However, in private class action suits that were settled out of court, the companies agreed to pay the plaintiffs.

Analysis of Change and Public Policy Recommendations

The cases we examined in this article show how some parts of the H-W Act have been used to circumvent the law in anticompetitive ways. Thus, some revisions to the H-W Act were necessary and have been enacted. According to a Congressional Budget Office study, the amendments to the H-W Act will increase competition and reduce total US drug spending by \$7 billion between 2004 and 2013. Also, savings for existing mandatory federal programs would be \$750 million over this 10-year period.⁵⁰

H-W Act Revisions

1) Before an out-of-court settlement is approved, the settlement is reviewed by the FTC or DOJ to determine whether such an agreement may have anti-competitive effects. This is similar to the Hart-Rodino Act, in which the FTC or DOJ examines the competitive effects of proposed mergers. Although an important first step, it does not address the important issue of patent validity or infringement and, as seen by the Schering-Plough case, it can lead to even more litigation.

Controversy over the H-W Act has already prompted some changes. President Bush has modified some provisions of FDA policy with respect to generic companies and brand name manufacturers.

- 2) Under the amended H-W Act, brand name manufacturers are limited to one 30-month stay. Also, these companies are not allowed to add patents to the *Orange Book* after the initial ANDA is requested. All patents that are allegedly infringed upon or are valid are to be listed and contested in the 45-day period provided by the H-W Act, and this is the only window of opportunity for brand name manufacturers to allege patent infringement. However, the amended H-W Act does not address the issue that if there is more than 1 patent in question, the same court and trial should examine these patent issues.
- 3) The first generic company to file an ANDA is given a 180-day exclusivity period. This has created the problem that if the first generic filer decides not to

enter the market for any reason, no other generic competitor can enter the market during that period. How does one ensure that other generic firms are not blocked from entry? One possibility is to allow the generic company only a limited number of days to enter the market once its ANDA has been approved and the 30-month stay has elapsed. The amended H-W Act does this by having the 180-day exclusivity period forfeited if, under certain conditions, the applicant fails to enter the market within 75 days.⁵¹ However, if the courts at that time have not decided on the validity of the infringement suit, the generic company may be reluctant to enter because the profits it would gain from market entry might well be less than the profits lost by the brand name manufacturer. If the courts decided later that the patent was infringed, the generic company must pay damages far greater than the profit earned by market entry. Thus, one should not force the generic company to enter the market or take away the 180-day exclusivity period if the generic firm has a valid reason for not entering.

There are valid reasons for keeping the 180-day exclusivity clause. The 180-day exclusivity clause was instituted to give generic companies the incentive to challenge existing patents and avoid the free-rider problem of 1 company paying the cost of litigation, while other generic companies, which did not incur the cost of litigation,

Take-Away Message

- Generic drug use is a cornerstone in Medicare's and Medicaid's plan to provide coverage of prescription drugs in the most cost-effective manner possible.
- Because of the low rate of discovery (1 in every 5000 chemicals tested) and high cost of development (\$800M) protections are required to assure continued innovation of branded pharmaceuticals.
- The Hatch-Waxman (H-W) Act encourages innovation by extending patent terms, while stimulating imitation and competition by reducing the requirements for generic entry in the drug market.
- Under the MMA, pharmacies are required to inform enrollees of any differential between the price of a covered Part D drug and the cost of the lowest-priced generic version of that drug available under the Part D plan at that pharmacy.

ROI

- From a prescribing standpoint, it is important to realize that not all generic drugs are equivalent because of bioavailability and standardization of dosage differences exist—these are most evident in products such as Coumadin®, Synthroid®, and Megace® ES.
- This year, several billion dollars of revenue generated by branded products will be lost to generic manufacturers, having a tremendous impact on the profitability and therefore stock prices of those companies affected.

can enter their products at the same time. The amended H-W Act allows for the forfeiture of the 180-day exclusivity period under various conditions. However, the issue we want to address is when “the first applicant enters into an agreement with another ANDA applicant, the NDA holder or a patent holder, and the FTC or a District Court has found that the agreement violates the antitrust laws.”⁵² This is too restrictive in that the violation of antitrust laws should not be a necessary condition for forfeiture. The original law intended that the first ANDA filer benefits from taking the risk of being the first to file. A generic company should give up its exclusivity rights if it enters into a settlement agreement with 1 of the above-mentioned firms. The settlement rewards the generic company and thus there is no reason to further reward it with

a 180-day exclusivity period, especially given the possible anti-competitive effects of the 180-day exclusivity.

- 4) Presently, brand name manufacturers incur little cost, but enjoy great potential gains when they challenge an ANDA. One way to decrease the incentive to challenge an ANDA and thus avoid frivolous suits is to make the cost greater for the brand name manufacturer. This can be achieved by requiring patent holders seeking to invoke the 30-month stay to post a bond, which is often the case for those seeking an injunction relief. The amount of the bond would be determined by the potential profits that the generic company (or possibly even the profits of the brand name manufacturer) would have foregone by the delay in entry and would be given to the generic company if it is successful in court. Although

their risk of market entry without a final court determination is still substantial, generic companies have prevailed in 73% of patent infringement cases through June 1, 2002.⁵² Given the importance of generic competition in helping control health care costs, litigation concerning patent validity and/or infringement cases should be decided quickly. However, the FTC and DOJ are not experts on patent cases. Thus, the federal government should establish some method to fast-track these litigations.

These recommendations and the revisions to the H-W Act should improve the workings of the H-W Act and thus make its dual goals more attainable. It is appropriate to reward innovation, but only during the statutory period of patent protection. Agreements between innovator and generic firms that benefit them at the expense of society should not be permitted. Given the newly passed Medicare Part D, which provides prescription drug benefits for Medicare patients, the proper workings of the H-W Act take on added importance. However, one must be careful not to trade lower drug prices today for a reduction of innovation in the future. Finally, given the importance of innovation, doubts and issues should be resolved in ways that encourage and promote innovations. MPM

Erwin A. Blackstone, PhD, is a Professor of Economics at Temple University, Fox School of Business, located in Philadelphia, PA.
Joseph P. Fuhr, Jr, PhD, is a Professor of

Economics at Widener University, School of Business Administration, located in Chester, PA. He is also a researcher for the Department of Health Policy Research at Jefferson Medical College in Philadelphia, PA.

References

1. Rx drugs sales up 11.5 percent in 2003. *Health Care Daily*. February 19, 2004, p. 1.
2. Suszynski M. Generic remedy. *Best's Review*. 2002; 108:86.
3. Behrendt KE. The Hatch-Waxman Act: balancing competing interests or survival of the fittest? *Food Drug Law*. 2002;57.
4. Eurek S. Hatch-Waxman reform and accelerated market entry of generic drugs: is faster necessarily better? *Duke Law Technol Rev*. August 13, 2003. Available at: <http://www.law.duke.edu/journals/dltr/articles/2003dltr0018.html>. Accessed February 11, 2006.
5. Roche Products Inc. v. Bolar Pharmaceutical Co., 733 F.2d 858 (Fed Cir. 04/23/1984). Available at: http://biotech.law.lsu.edu/cases/IP/patent/roche_v_bolar.htm. Accessed February 11, 2006.
6. Federal Trade Commission. *Generic Drug Entry Prior to Patent Expiration: An FTC Study*. July 2002, p. 11. Available at: <http://www.ftc.gov/os/2002/07/generic-drugstudy.pdf>. Accessed February 11, 2006.
7. Morse MH. Settlement of intellectual property disputes in the pharmaceutical and medical devices industries: antitrust rules. *George Mason Law Rev*. 2002;10:359-401.
8. Hollis A. *Closing the FDA's Orange Book*. Regulation. 2001;24(winter). Available at: <http://www.cato.org/pubs/regulation/regv24n4/regv24n4.html>. Accessed February 11, 2006.
9. Miller JL. Drug Price Competitions and Patent Term Restoration Act: the elimination of competition between drug manufacturers. *DePaul J Health Care Law*. 2002; 5(summer).
10. Engelberg AB. Special patent provisions for pharmaceuticals. Have they outlived their usefulness? *J Law Technol*. 1999;39:389-426. Available at: http://www.idea.piercelaw.edu/articles/39/39_3/11.Engelberg.pdf. Accessed February 11, 2006.
11. Standard and Poor's. *Healthcare: Pharmaceuticals Industry Survey*. December 12, 2002.
12. Berndt ER. Pharmaceuticals in U.S. health care: determinants of quantity and price. *J Econ Perspect*. 2002;16:45-66.
13. Comanor WS, Schweitzer SO. Pharmaceuticals. In: Adams W, Brock J, eds. *The Structure of American Industry*, 9th ed. Englewood Cliffs, NJ: Prentice Hall, 1995, p. 185.
14. US Senate. *Committee on Commerce, Science and Transportation Hearings on Generic Pharmaceuticals, Marketplace Access, and Consumer Issues*. April 23, 2002, p. 2.
15. Mossinghoff GJ. Overview of the Hatch-Waxman Act and its impact on the drug development process. *Food Drug Law J*. 1999;54:187-194. Available at: http://www.fdlj.org/pubs/Journal%20Online/jour_toc/vol54_2.htm#art2. Accessed February 11, 2006.
16. US Senate. *Testimony of Kathleen Jaeger Before the Committee on Commerce, Science and Transportation Hearings on Generic Pharmaceuticals, Marketplace Access, and Consumer Issues*. April 23, 2002.
17. Pfizer increases its lead in drug sales. *Philadelphia Inquirer*. May 24, 2003, pp. C1 and C3.
18. Frudenheim M. As patents on popular drugs end, cost of generics show a surge. *New York Times*. December 27, 2002, Section A, p.1.
19. Baxter International Inc., and Wyeth, FTC File No. 021-0171, Docket No. C-4068. Analysis of agreement containing consent orders to aid public comment. Available at: <http://www.apecp.org.tw/doc/USA/Case/usacase01.htm>. Accessed February 9, 2006.
20. FTC requires spin-offs for Baxter's purchase of Wyeth's generic injectable drug business. *Antitrust Fund Trade Regulation*, January 10, 2003. In: Baxter International Inc., and Wyeth, FTC File No. 021-0171, Docket No. C-4068. Analysis of agreement containing consent orders to aid public comment. Available at: <http://www.apecp.org.tw/doc/USA/Case/usacase01.htm>. Accessed February 9, 2006.
21. *Watson Pharmaceuticals, 10-K Report for Fiscal Year Ended December 31, 2002*.
22. Pear R. Washington approves 5-state pool to buy drugs for 900,000 Medicaid. *New York Times*. April 23, 2004, p. A20.
23. Deutsch LL. *Industry Studies*, 3rd ed. Armonk, NY: ME Sharpe; 1998, p.118.
24. *Schering-Plough, Upsher-Smith, and American Home Products, Docket #9297, Initial Decision*. Available at: <http://www.apecp.org.tw/doc/USA/Case/usacase01.htm>. Accessed February 9, 2006.
25. Countering delays in introduction of generic drugs. *Lancet*. 2002;359:181.
26. Piatt SE. Regaining the Balance of Hatch-Waxman in the FDA Generic Approval Process: An Equitable Remedy to the Thirty-Month Stay. *NYU Ann Surv Am Law*. 2003;59:202-203.
27. Leary TB. Antitrust issues in the settlement of pharmaceutical patent disputes. Presented at the Sixth Annual Health Care Antitrust Forum, Northwestern School of Law, Chicago, Illinois, November 3, 2000.
28. *Hoechst Marion Roussel, Inc., Carderm Capital L.P., and Andrx Corporation, FTC Docket No. 9290, Complaint*, March 16, 2000. Available at: <http://www.apecp.org.tw/doc/USA/Case/usacase01.htm>. Accessed February 9, 2006.
29. *Cardizem CD Antitrust Litigation. Louisiana Wholesale Drug Company et al. v. Hoechst Marion Roussel, Inc. and Andrx Pharmaceuticals, Inc.*, U.S. Court of Appeals for the Sixth Circuit, 2003 U.S. App. Available at: <http://caselaw.lp.findlaw.com/scripts/getcase.pl?court=6th&navby=case&no=03a0195p>. Accessed February 9, 2006.
30. Indirect Purchaser Settlements in Drug Overcharge Case Get Approval. *Antitrust and Trade Regulation*. August 5, 2005.
31. *Abbott Laboratories and Geneva Pharmaceuticals Inc., FTC Docket No. 3945, Complaint*. Available at: <http://www.apecp.org.tw/doc/USA/Case/usacase01.htm>. Accessed February 9, 2006.
32. *Valley Drug Co. v. Geneva Pharmaceuticals, Inc., 11th Circuit, No. 02-12091*. September 15, 2003. Available at: <http://www.ca11.uscourts.gov/opinions/ops/200212091.pdf>. Accessed February 9, 2006.
33. Per se condemnation of agreements with generic drug makers is overturned. *Antitrust and Trade Regulation Report*. September 26, 2003;85:340-342.
34. *Abbott Laboratories, Docket No. C-3945 (May 22, 2000) (consent order)*. Available at: <http://www.ftc.gov/os/2000/05/c3945complaint.htm>; *Geneva Pharmaceuticals, Inc., Docket No. C-3946 (May 22, 2000) (consent order)*. Available at: <http://www.ftc.gov/os/2000/05/c3946complaint.htm>. Accessed February 9, 2006.
35. Bristol-Myers will pay \$670 million to settle BuSpar, Taxol antitrust suit with state AGs, BNA's. *Health Law Reporter*. January 9, 2003;12:53.
36. FTC Bureau of Competition. *FTC antitrust actions in health care services and product*. June 2005.
37. *Bristol-Myers Squibb Company, Docket No. C-4076 Complaint, April 14, 2003*. Available at: <http://www.apecp.org.tw/doc/USA/Case/usacase01.htm>. Accessed February 9, 2006.
38. *FTC Analysis to Aid Public Comment in the Matter of Bristol-Myer Squibb Company, File Nos. 001 0221 011 0046, and 021 0181*.
39. *Mylan v. Thompson, No. 01-1492*. Available at: <http://www.usdoj.gov/osg/briefs/2001/0responses/2001-1492.resp.html>. Accessed February 9, 2006.
40. A General Accounting office study reported that the U.S. government spent \$484 million on Taxol research between 1977 and 2002; Bristol-Myers Squibb earned \$9 million in Taxol sales and paid the government \$35 million of royalties. See "GAO questions federal deal with Bristol-Myers Squibb." *The Philadelphia Inquirer*. June 7, 2002.
41. *FTC Analysis to Aid Public Comment in the Matter of Biovail Corporation, Docket No. C-4060*.
42. Wrongful 'Orange Book' listing raises red flag with FTC; leads to consent order with Biovail Corp. concerning its drug Tiazac. *FTC News Release*. April 23, 2002.
43. Consent order resolves charges that Biovail and Elan agreement unreasonably restrained competition in market for generic anti-hypertension drug. *FTC News Release*. June 27, 2002.
44. Administrative Law Judge dismisses FTC allegations of anticompetitive conduct by Schering-Plough and Upsher-Smith. *FTC News Release*. July 2, 2002.
45. *Schering-Plough Corporation, Upsher-Smith Laboratories, and American Home Products Corporation, Docket No. 9297*. Available at: <http://www.apecp.org.tw/doc/USA/Case/usacase01.htm>. Accessed February 9, 2006.
46. Final patent rule brings significant change to brand, generic competition. *The Food and Drug Letter*. August 1, 2003.
47. *FDA Generic Drugs Final Rule: Questions and Answers*. June 12, 2003. Available at <http://www.fda.gov/oc/initiatives/generics/QNA.htm>. Accessed February 9, 2006.
48. Testimony of Kathleen Jaeger before the Senate Committee on the Judiciary on Legislative and Regulatory Responses to the FTC study on barriers to entry in the pharmaceutical marketplace. *Federal News Service*. June 17, 2003.
49. Supreme Court delays setting standard for settlements curbing entry by generics. *Antitrust and Trade Regulation*. October 15, 2004.
50. Congressional Budget Office. *Analysis of Changes to Hatch-Waxman Act*. August 27, 2003.
51. Lietzan EK. A brief history of 180-day exclusivity under the Hatch-Waxman Amendments of the Food, Drug and Cosmetic Act. *Food Drug Law J*. 2004;59. Available at: http://www.fdlj.org/pubs/Journal%20Online/jour_toc/vol59_2.html. Accessed February 9, 2006.
52. For a discussion of this and other related issues, see Federal Trade Commission. *Generic Drug Entry Prior to Patent Expiration: An FTC Study*. July 2002. Available at: <http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf>. Accessed February 11, 2006.