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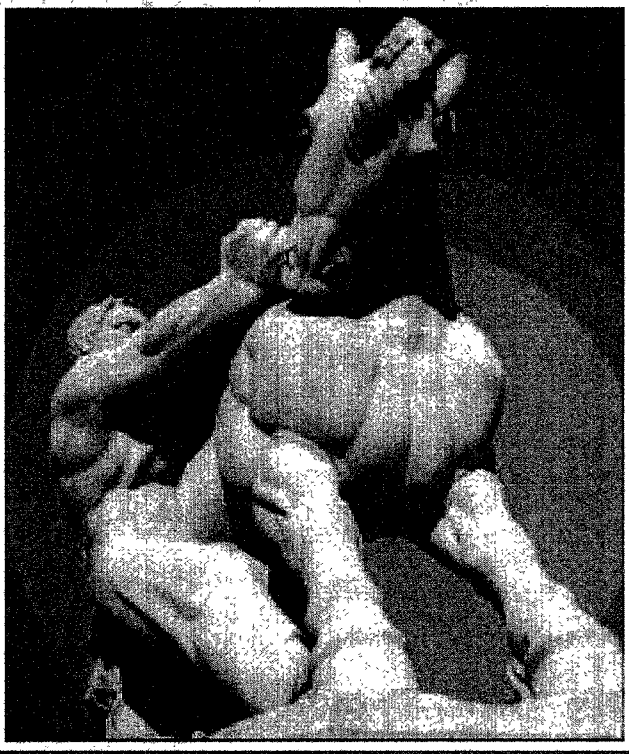
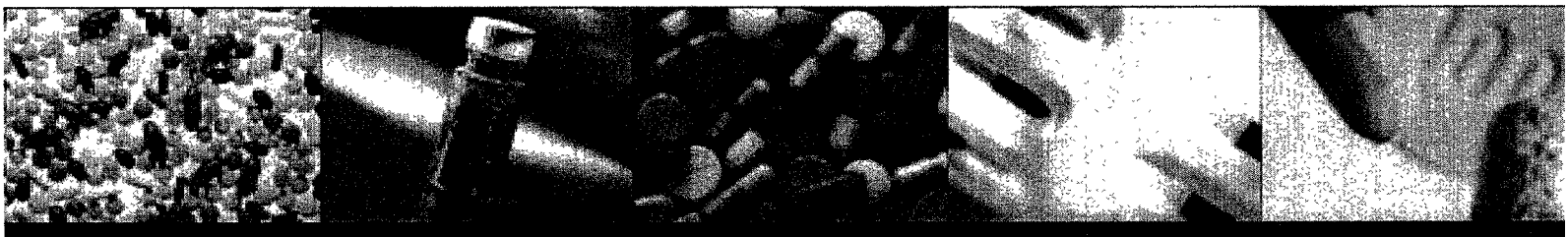


Generic Drug Entry Prior to Patent Expiration:

An FTC Study

Federal Trade Commission

July 2002



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GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY

Executive Summary and Legislative Recommendations

Pharmaceutical drug products have become increasingly important to providing consumers with a myriad of treatments and cures that increase life expectancy and enhance lives. It is critical to maintain appropriate incentives for the development of new drug products, because the necessary research and development is risky and costly. Innovation in the pharmaceutical industry, spurred in part by competitive market forces, continues to bring enormous benefits to Americans.

At the same time, expenditures on pharmaceutical products continue to grow and often outpace expenditures for other consumer products. Pharmaceutical expenditures concern not only consumers, but government payers, private health plans, and employers as well. Generic drugs offer opportunities for significant cost savings over brand-name drug products.

The Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act have shaped substantially the current legal environment governing Food and Drug Administration (FDA) approval of generic drug products. Hatch-Waxman established a regulatory framework that sought to balance incentives for continued innovation by research-based pharmaceutical companies and opportunities for market entry by generic drug manufacturers. The Amendments compensate brand-name companies, in certain circumstances, for a lengthy drug approval process, which can shorten the effective life of patent protection for drug products. The Amendments also streamline the procedures for bringing generic drug products to the market.

Beyond any doubt, Hatch-Waxman has increased generic drug entry. Generic drugs now comprise more than 47 percent of the prescriptions filled for pharmaceutical products – up from 19 percent in 1984, when Hatch-Waxman was enacted.

In spite of this record of success, two of the provisions governing generic drug approval prior to patent expiration (the 180-day exclusivity and the 30-month stay provisions) are susceptible to strategies that, in some cases, may have prevented the availability of more generic drugs. These provisions continue to have the potential for abuse.

The Commission has taken antitrust law enforcement actions against certain brand-name and generic drug companies whose allegedly anticompetitive agreements took advantage of one or the other of these provisions. Through vigorous enforcement of the antitrust laws, the FTC has taken an active role in ensuring that consumers benefit from competition in the pharmaceutical industry.

This study examines whether the conduct that the FTC challenged represented isolated instances or is more typical, and whether the 180-day exclusivity and the 30-month stay provisions of the Hatch-Waxman Amendments are susceptible to strategies to

delay or deter consumer access to generic alternatives to brand-name drug products. The study focuses solely on the procedures used to facilitate generic drug market entry *prior to* expiration of the patent(s) that protect the brand-name drug product. The study does not address other procedures for generic entry, and it does not address the patent restoration features of Hatch-Waxman.

To accomplish the study, the Commission subpoenaed documents and information from brand-name and generic drug manufacturers, and examined instances since 1992 in which generic applicants filed an application with FDA seeking to enter the market with a generic version of a drug product prior to expiration of the brand-name drug products' patents.[1] An increasing number of generic applicants have sought entry prior to patent expiration. During the 1980s, only 2 percent of generic applications sought entry this way, but from 1998 to 2000, approximately 20 percent of the generic applications sought entry prior to patent expiration.

The brand-name drug products included in the study represent some of the largest drug products as measured by annual sales. They include "blockbuster" drugs[2] such as Capoten, Cardizem CD, Cipro, Claritin, Lupron, Neurontin, Paxil, Pepcid, Pravachol, Prilosec, Procardia XL, Prozac, Vasotec, Xanax, Zantac, Zocor, Zoloft, and Zyprexa.

Based on the data obtained through the study, we make two primary recommendations concerning the 30-month stay provision and the 180-day exclusivity to mitigate the possibility of abuse that deters more generic drugs from becoming available.[3]

Recommendation 1: Permit only one automatic 30-month stay per drug product per ANDA to resolve infringement disputes over patents listed in the Orange Book prior to the filing date of the generic applicant's ANDA.

The Current 30-Month Stay Provision: A 30-month stay of FDA approval of a generic applicant[4] is invoked if a brand-name company receives notice of a generic applicant's paragraph IV certification and files suit for patent infringement within 45 days of that notice. Filing of the lawsuit stays FDA's approval of the ANDA until the earliest of: (1) the date the patents expire; (2) a determination of non-infringement or patent invalidity by a court in the patent litigation; or (3) the expiration of 30 months from the receipt of notice of the paragraph IV certification.

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[1] These applications are technically referred to as Abbreviated New Drug Applications (ANDAs) containing a paragraph IV certification.

[2] As used herein, "blockbuster" is defined as a drug product that appears in the top 20 drug products (as ranked publicly by annual gross sales) during one of the years covered by this study.

[3] The study did not provide data on whether, or how, the suggested recommendations might affect brand-name companies' and generic applicant's incentives to enter the market with new brand-name or generic drug products.

[4] For ease of discussion purposes, the term "generic applicant" means those applicants who have filed an ANDA containing a paragraph IV certification. *See* Appendix A for a glossary of frequently used terms.

Key Facts From the Study:

To What Extent Does 30 Months Approximate the Time Typically Required for FDA Review of a Generic's ANDA or for Resolution of the Contemplated Patent Infringement Litigation?

Thirty months historically has approximated the time required for FDA review and approval of the paragraph IV ANDAs of generic applicants that were not sued, and for district and appellate court resolutions of ANDA-related patent infringement litigation. On average, the time required for FDA review and approval was 25 months and 15 days from the application filing date in those cases where generic applicants filing a paragraph IV certification were not sued (and thus could begin commercial marketing once they had FDA approval). On average, the time between the filing of a patent infringement lawsuit and a district court decision in the case was 25 months and 13 days. On average, the time between the filing of a patent infringement lawsuit and a court of appeals decision in the case was 37 months and 20 days.

In the future, patent infringement litigation brought by brand-name companies against generic applicants that have filed ANDAs with paragraph IV certifications may take longer to resolve. The data suggest that cases involving multiple patents take longer than those involving fewer patents. As of June 1, 2002, for 6 out of the 7 cases that have been pending for more than 30 months before a decision from a district court, the brand-name company has alleged infringement of 3 or more patents.

Prior to 1998, for only 1 out of the 9 "blockbuster" drug products in which the brand-name company sued the first generic applicant did the brand-name company allege infringement of 3 patents. Since 1998, for 5 of the 8 "blockbuster" drug products where the brand-name company filed suit against the first generic applicant, the brand-name company alleged infringement of 3 or more patents. Thus, future 30-month stays may expire more frequently *before* the parties obtain a decision of a court in the patent infringement litigation.

Has the Study Identified Any Circumstances That Can Prevent FDA Approval of Generic ANDAs Beyond 30 Months?

Yes. If a brand-name company lists an additional patent in the Orange Book *after* the generic applicant has filed its ANDA, more than one 30-month stay may be generated. The generic applicant is required to re-certify to this later-listed patent, and if, upon notice of the generic's re-certification, the brand-name company sues within 45 days, then FDA approval of the generic's previously filed ANDA is stayed for *an additional* 30-months from the notice date or until a court decision in the newly instituted patent litigation.

From 1992 through 2000, brand-name companies have listed patents in the Orange Book after an ANDA has been filed for the drug product in 8 instances; 6 of these 8 instances occurred since 1998. For the 8 drug products, the additional delay of FDA approval caused by the additional 30-month stay (beyond the first 30-month stay) ranged from 4 to 40 months. In all 4 of the

cases so far with a court decision on the validity or infringement of a later-issued patent, the patent has been found either invalid or not infringed by the ANDA.

Arguments exist that the later-issued patents, which have provided the basis for additional 30-month stays, do not meet FDA's requirements for listing patents in the Orange Book. (These arguments are discussed in detail in Appendix H to the Report.) Under current court rulings and FDA procedures, however, it is very difficult for generic applicants to test these arguments. Recent court opinions have held that Hatch-Waxman does not provide a private right of action through which generic applicants may challenge a patent listing in the Orange Book. The FDA has stated that it lacks the resources and the expertise to review patents to determine whether they are properly listed.

Reasons for the Recommendation:

One 30-month period historically has approximated the time necessary for FDA review and approval of the generic's ANDA. Thus, it does not appear that the 30-month stay provision, as applied once to each ANDA for patents listed in the Orange Book prior to the ANDA's filing date, has a significant potential to delay generic entry beyond the time already necessary for FDA approval of the generic's ANDA. The data also do not indicate that court decisions in ANDA-related patent litigation typically are reached much earlier than 30 months from notice of the generic's ANDA.

The expiration of the 30-month stay may have more significance in the future, if ANDA-related patent litigation begins to last longer than was the case from 1992-2000. Generic applicants may rely on expiration of the 30-month stay more frequently as the first point at which they may decide whether to enter the market, rather than to wait for a court decision on ANDA-related patent litigation that may take longer than 30 months.

The history thus far of multiple 30-month stays caused by the filing of later-issued patents appears problematic, however. The 4 courts that have ruled so far on the patents causing more than one 30-month stay each have found the relevant patent to be invalid or not infringed. The other 4 drug products with multiple 30-month stays involved patents whose listing in the Orange Book could have been the subject of non-frivolous challenges by the generic applicant, had either FDA review of listability or a private right of action to challenge listability under Hatch-Waxman been available.

Multiple 30-month stays prevented FDA approval of the generic applicants' ANDAs for 4 to 40 months *beyond* the initial 30-month period. FDA approval may have occurred more quickly in the absence of the multiple 30-month stays, because the data indicate that FDA approval has occurred, on average, within 25 months and 15 days for generic applicants with paragraph IV certifications that were not sued.

Even without an additional 30-month stay, later-listed patents still receive the usual protections of patent infringement litigation. The brand-name company may sue for patent infringement with respect to any of its patents that it believes may be

infringed by a generic applicant's ANDA, and may seek a preliminary injunction, just as other patent holders do against alleged infringers.[5]

One minor change to the patent statute, which would clarify when brand-name companies can sue generic applicants for patent infringement, would ensure that brand-name companies have recourse to the courts to protect their rights under later-issued patents. Congress may wish to overrule a recent district court decision, *Allergan, Inc. v. Alcon Labs, Inc.*, 200 F. Supp. 2d 1219 (C.D. Cal. 2002), which questions the rights of brand-name companies to sue for patent infringement regarding patents obtained or listed after an ANDA with a paragraph IV has been filed. Under the plain language of 35 U.S.C. § 271(e)(2), however, *all* ANDAs constitute acts of infringement sufficient to establish the existence of a case or controversy with respect to *all* patents that claim any drug or any method of using the drug that may be infringed by generic marketing under an ANDA – regardless of whether the patent has been listed in the Orange Book or has been the subject of a paragraph IV ANDA (as opposed to a different kind of ANDA).

To permit only one 30-month stay per drug product per ANDA[6] should eliminate most of the potential for improper Orange Book listings to generate unwarranted 30-month stays. However, it should be noted that, currently, the FDA does not review the propriety of patents listed in the Orange Book, and courts have ruled that generic applicants have no private right of action to challenge those listings. As a result, there is no mechanism to delist an improperly listed patent from the Orange Book. The lack of such a mechanism may have real world consequences in that the Commission is aware of at least a few instances in which a 30-month stay was generated solely by a patent that raised legitimate listability questions.

There have been various suggestions to address this situation, each with its own pros and cons. One proposal has been to establish an administrative procedure through which generic applicants could obtain substantive FDA review of listability. The FDA, however, has taken the position that it lacks the expertise and resources necessary to perform such a review, and its solely ministerial review of Orange Book listings has been upheld by the courts. At a minimum, it appears useful for the FDA to clarify its listing requirements (*see* Appendix H).

Another remedy that may warrant consideration would permit a generic applicant to raise listability issues as a counterclaim in the context of patent infringement litigation already initiated by the brand-name company in response to a paragraph IV notice from the generic applicant. This would permit resolution of the issue in the same district court proceeding in which other aspects of the relevant patents were at issue. It remains unclear how frequently such a provision

[5] Thus, the usual patent protections would remain for brand-name companies whose patents may be listed in the Orange Book after the filing of a generic applicant's ANDA solely because it took a long time for the Patent Office to issue the patent.

[6] This would be applied only to resolve infringement disputes over patents listed in the Orange Book prior to the filing date of the generic applicant's ANDA.

would be used.

Recommendation 2: Pass legislation to require brand-name companies and first generic applicants to provide copies of certain agreements to the Federal Trade Commission.

The Current 180-Day Marketing Exclusivity Provision: The first generic applicant to file an ANDA containing a paragraph IV certification is awarded 180 days of marketing exclusivity, during which the FDA may not approve a subsequent generic applicant's ANDA for the same drug product. The 180-day exclusivity period is calculated from either the date of the first commercial marketing of the generic drug product or the date of a court decision declaring the patent invalid or not infringed, whichever is sooner. Through this 180-day provision, Hatch-Waxman provides an incentive for companies to challenge patent validity and to "design around" patents to find alternative, non-infringing forms of patented drugs. The 180-day marketing exclusivity provision was intended to increase the economic incentives for a generic company to be the first to file an ANDA containing a paragraph IV certification and get to market.

Key Facts From the Study:

How Frequently Has FDA Granted 180-Day Exclusivity?

The regulatory landscape implementing 180-day exclusivity has shifted over the last several years. Before 1992 (a time period not included in this study), the FDA granted 180-day exclusivity to 3 generic applicants. From 1992 until 1998, the FDA did not grant 180-day exclusivity to any generic applicant. Since 1998, when the FDA changed its regulations in response to a court ruling, and more ANDAs containing paragraph IV certifications have been filed, the FDA has granted 180-day exclusivity to the first generic applicant for 31 drug products. Thus, the 180-day exclusivity has been granted for 31 out of the 104 drug products for which a first generic applicant filed an ANDA containing a paragraph IV certification from 1992 through 2000.

Has the 180-Days Exclusivity Been Triggered Most Often by a Court Decision or by the First Generic's Commercial Marketing?

For 19 of the 31 drug products, commercial marketing triggered the running of the first generic applicant's 180-day exclusivity.[7] For the other 12 drug products, a court decision favorable to the generic applicant triggered the 180-day exclusivity.

How Have Generic Applicants Fared in Patent Infringement Litigation?

Generic applicants have prevailed in 73 percent of the cases in which a court has resolved the patent dispute.[8] The rate at

[7] The data further indicate that, when not sued, first generic applicants begin commercial marketing, after receiving FDA approval, in a timely manner that triggers the running of the 180 days and thus would allow FDA approval of subsequent eligible generic applicants once the 180 days has run.

[8] These statistics include other cases in addition to those involving the 12 drug products where a court decision triggered the 180-day exclusivity. For example, during a time when FDA did not consider a *district court* decision sufficient to trigger the 180-day exclusivity, some generic applicants began commercial marketing following

which the U.S. Court of Appeals for the Federal Circuit reversed district court decisions of patent invalidity and non-infringement for drug products in this study was 8 percent.

When Did Generic Applicants Enter the Market?

In most instances, generic applicants have waited to enter the market until at least a district court has held that the patent covering the brand-name company's drug product was invalid or not infringed by the generic applicant's ANDA.

Are There Circumstances in which the 180-Day Exclusivity Has Been "Parked" For Some Period of Time, So That the First Generic Applicant Does Not Trigger It, and FDA Approval of Any Subsequent Eligible Generic Applicant Would Be Precluded?

Yes. During the time period of the study, there were 20 final settlements of ANDA-related patent litigation. Fourteen of the 20,[9] at the time they were executed, had the potential to delay the start of the first generic applicant's 180-day exclusivity.[10] If the 180-day exclusivity for the first generic applicant does not run, then the FDA may not approve any subsequent eligible generic applicants. Once the 180-day exclusivity runs, the FDA may approve any additional generic ANDAs that have been filed and meet regulatory requirements.

Under 2 of these 14 settlement agreements, the first generic applicant did begin commercial marketing, but each generic was marketing the brand-name company's product as a generic – neither was marketing under its own ANDA. As discussed in more detail below, it is unclear whether this type of "commercial marketing" is sufficient to trigger the running of the 180-day exclusivity.

In addition to the 20 final settlement agreements, there were 4 interim settlement agreements pursuant to which the patent litigation continued, but the parties agreed upon certain conditions in the meantime. The Commission has challenged interim settlements for 3 drug products.[11] In those agreements, the Commission alleged that the brand-name drug company paid the first generic applicant not to enter the market, thereby retaining its (unused) 180-day marketing exclusivity and precluding FDA from approving any eligible subsequent generic applicants.

Have Such Agreements Continued Following FTC Enforcement Action in this Area?

Between April 1999 (shortly after FTC investigations in this area became

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expiration of the 30-month stay and a favorable decision of a district court. In each of these instances, the generic applicant ultimately prevailed in the appellate court, but commercial marketing, not the district court decision, triggered the 180-day exclusivity.

[9] Ten brand-name companies and 10 generic companies used these types of agreements with respect to14 drug products.

[10] In some cases, this delay did not occur due to subsequent events.

[11] *See Abbott Laboratories*, No. C-3945 (May 22, 2000) (consent order), *available at* <http://www.ftc.gov/os/2000/03/abbott.do.htm> (this consent order related to 2 drug products: Hytrin tablets and Hytrin capsules). *Hoechst Marion Roussel, Inc.*, No. 9293 (May 8, 2001) (consent order), *available at* <http://www.ftc.gov/os/2001/05/hoechstdo.pdf>.

public) and the end of the period covered by this study, brand-name companies and first generic applicants have not entered agreements similar to the interim agreements challenged by the FTC.

Reasons for the Recommendation:

The data in the study suggest that the generic applicants have brought appropriate patent challenges: generic applicants prevailed in nearly 75% of the patent litigation ultimately resolved by a court decision.[12] Moreover, most generic applicants have waited to enter the market until at least a district court has held that the patent covering the brand-name company's drug product was invalid or not infringed by the ANDA. This may reflect the fact that a generic applicant's potential liability for lost profits on the brand-name drug usually will vastly exceed its own potential profits after market entry.

The data also indicate that, when not sued, first generic applicants, upon receiving FDA approval, begin commercial marketing in a timely manner that triggers the running of the 180 days and allows FDA approval of any subsequent eligible generic applicant once the 180 days has run. Thus, the data suggest that, in and of itself, the 180-day exclusivity provision generally has not created a bottleneck to prevent FDA approval of subsequent eligible generic applicants.

[12] The data do not establish, however, whether even more appropriate patent challenges might have been brought if the period of generic market exclusivity was longer than 180 days.

Require Brand-Name Companies and First Generic Applicants to Provide Copies of Certain Agreements to the Federal Trade Commission

Issues that merit antitrust scrutiny, however, may arise when brand-name companies and first generic applicants reach agreements that have the potential to "park" the first generic applicant's 180-day exclusivity for some period of time. Fourteen of the 20 final settlement agreements obtained through the study had this potential as of the time they were executed. Such agreements may be procompetitive or competitively neutral. But they also may raise antitrust issues, as was alleged to be the case in the interim settlement agreements the FTC challenged.

Given this history, we believe that notification of such agreements to the Federal Trade Commission and the U.S. Department of Justice is warranted. We support the Drug Competition Act of 2001 (S. 754) introduced by Senator Leahy, as reported by the Committee on the Judiciary, which would require that if a brand-name company and a generic applicant enter into an agreement that relates in any way to the 180-day exclusivity or which concerns the manufacture, marketing, or sale of either the brand name drug or its generic equivalent, then both companies must file a copy of the agreement (or a complete written summary of any oral agreement), along with copies of any other related agreements, with the Commission and the Department of Justice.

Minor Recommendations to the 180-Day Exclusivity Provision:

It is unclear whether a few types of

factual circumstances trigger the running the 180-day exclusivity. Three minor changes would clarify that these circumstances should trigger the 180-day exclusivity and thus reduce any potential for the 180-day marketing exclusivity provision to function as a bottleneck to subsequent generic entry.

Minor Recommendation 1: Clarify that "commercial marketing" includes the first generic applicant's marketing of the brand-name product.

The data revealed 2 instances when the brand-name company and the first generic applicant settled the patent infringement lawsuit with a supply agreement, and 3 other instances in which an optional supply agreement was one part of a patent settlement. In all instances, the agreements contemplated that the brand-name company would supply the generic applicant with the brand-name drug product, so that the generic applicant could market it as a generic version. Currently, it is somewhat unclear whether marketing of the brand-name product by the first generic applicant constitutes "commercial marketing" sufficient to trigger the 180-day exclusivity.[13]

To avoid situations in which the running of the 180 days is not triggered because of this uncertainty, it would be desirable to clarify that "commercial marketing" includes *any* marketing by the first generic applicant, even under a supply agreement with the brand-name company. In some circumstances, such commercial marketing may be the only event that can trigger the running of the 180-day exclusivity. For example, if there is a second generic applicant, but it is not sued by the brand-name company, then there will not be a court decision to trigger the 180 days, and only the first generic applicant's commercial marketing under the supply agreement could start the running of the 180 days and thus, after 180 days, free the FDA to approve any eligible subsequent generic applicants.

Minor Recommendation 2: Codify that the decision of any court on the same patent being litigated by the first generic applicant constitutes a "court decision" sufficient to start the running of the 180-day exclusivity.

There is some question as to *which* court's decision is sufficient to activate the "court decision" trigger of the 180-day exclusivity. Two courts of appeal have held,[14] and the FDA has issued guidance, [15] that *any* court's decision on whether the

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[13] In response to a citizen petition involving the 30 mg strength of Procardia XL, the FDA determined that the first generic applicant was ineligible for 180-day exclusivity, because the generic applicant and the brand-name company had settled their patent litigation and effectively changed the generic applicant's certification from a paragraph IV to a paragraph III. In addition, and under alternative reasoning, the FDA determined that even if the first generic applicant was eligible for the 180-day exclusivity, that exclusivity already had been triggered by the generic applicant's marketing under a supply agreement with the brand-name company. *See* FDA Letter to Deborah A. Jaskot, Docket No. OPP-1446/CP1 (Feb. 6, 2001). This letter leaves somewhat unclear whether a supply agreement alone would be sufficient to satisfy the commercial marketing trigger for the 180-day exclusivity. *See, also, Mylan Pharmaceuticals, Inc. v. Tommy G. Thompson*, 2001 U.S. Dist. LEXIS 24234 (N.D. WV Apr. 18, 2001).

[14] *See Teva Pharmaceuticals, USA, Inc. v. FDA*, 182 F.3d 1003 (D. C. Cir 1999), *Granutec, Inc. v. Shalala*, 139 F.3d 889 (4th Cir. 1998).

[15] *See* FDA Guidance for Industry: 180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug and Cosmetic Act (Jun. 1998). *See also Teva Pharmaceuticals, USA, Inv. v. FDA*, 182 F.3d 1003, 1005 (D.C. Cir. 1999).

patent at issue is invalid or not infringed is sufficient to trigger the running of the first generic applicant's 180-day exclusivity.

On balance, we believe this is the correct result, but there are pros and cons. On the one hand, the rule would make it less likely that agreements between brand-name and generic companies that had the effect of "parking" the 180-day exclusivity for some period of time could forestall FDA approval of a subsequent eligible generic applicant. This is because, if the brand-name company sues the second (or later) generic applicant, and that generic applicant won its patent litigation, then the 180-day exclusivity of the first generic applicant would begin to run from the date of the later generic applicant's favorable court decision. Such circumstances may arise; the data showed that brand-name companies sued later generic applicants in nearly 85% of the cases. The rule would be consistent with the mandate in the legislative history of Hatch-Waxman to "make available more low-cost drugs,"[16] because the rule would assist in eliminating potential bottlenecks to FDA approval of subsequent eligible generic applicants.

Such a rule also could speed generic entry when the second generic applicant's lawsuit is resolved prior to that of the first applicant. This appears to be appropriate given the low reversal rate of district court opinions of patent invalidity and non-infringement. For example, under this rule, if both the first and second generic applicants are sued, but the court hearing the second generic applicant's case is the first to arrive at a decision, then that court's decision would trigger the running of the first generic applicant's 180-day exclusivity, regardless of whether the first generic applicant had received FDA approval. The data revealed 1 such case.

On the other hand, as illustrated in the preceding paragraph, the operation of this rule could deprive the first generic applicant of its ability to market under the 180-days exclusivity, even though the first generic applicant had been diligently pursuing resolution of its patent litigation. This result could dampen the incentive to become the first generic applicant.[17] Moreover, if the later court issues a non-infringement decision, the reasoning underlying the holding may not apply to the first generic applicant's ANDA, depending upon the facts of the case.

Minor Recommendation 3: Clarify that a court decision dismissing a declaratory judgment action for lack of subject matter jurisdiction constitutes a "court decision" sufficient to trigger the 180-day exclusivity.

One court of appeals has held that a dismissal of a declaratory judgment action for lack of a case or controversy is a "court decision" of non-infringement sufficient to trigger the 180-day exclusivity.[18] We believe that the court's reasoning is persuasive and should be adopted.

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[16] H.R.Rep. No. 98-857, pt. 1, 98th Cong., 2d Sess., at 14 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2647.

[17] By contrast, the absence of such a rule also could dampen the incentive for later generic applicants to develop eligible ANDAs containing paragraph IV certifications.

[18] *Teva Pharmaceuticals, USA, Inc. v. FDA*, 182 F.3d 1003 (D. C. Cir 1999).

The U.S. Court of Appeals for the District of Columbia confronted a situation in which the brand-name company did not sue any of the generic applicants for patent infringement, presumably because the brand-name company's patents were not infringed by the ANDA. To trigger the first generic applicant's 180-day exclusivity (because it had not yet been approved by the FDA), the second generic applicant sought a declaratory judgment that its ANDA did not infringe the brand-name product's patents. The district court hearing the case dismissed the lawsuit for lack of subject matter jurisdiction, because the brand-name company indicated that it would not sue the second generic applicant for patent infringement, thus eliminating its reasonable apprehension of a patent infringement suit and the existence of a case or controversy. This dismissal also estopped the brand-name company from suing the generic applicant in the future.

The Court of Appeals determined that the dismissal for lack of case or controversy was, in fact, a court decision, because the brand-name company indicated that the second generic applicant's ANDA did not infringe the relevant patent. As a result, the dismissal activated the court decision trigger. Such a rule eliminates the potential for a bottleneck created by a first generic applicant that does not exercise its commercial marketing rights.

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Chapter 1 Introduction and Background

Introduction

In April 2001, the Commission began an industry-wide study focused on certain aspects of generic drug competition under the Hatch-Waxman Amendments.[1] The Amendments provide certain methods by which generic drug manufacturers can obtain approval to market a generic version of a brand-name product. The study's purpose was to provide a more complete picture of how generic drug competition has developed under one method the Amendments established: generic entry *prior to* expiration of the brand-name company's patents on the relevant drug product.[2] This report sets forth the results of the study.[3]

The study was prompted, in part, by the Commission's enforcement actions against alleged anticompetitive agreements that relied on certain Hatch-Waxman provisions.[4] The study was designed to determine whether such agreements are isolated instances or more typical, and whether particular provisions of the Hatch-Waxman Amendments are susceptible to strategies to delay or deter consumer access to low-cost generic alternatives to brand-name drug products.

The study also was requested by Representative Henry Waxman, one of the co-sponsors of Hatch-Waxman, who asked the FTC to "investigate and produce a study on the use of agreements between and among pharmaceutical companies and potential generic competitors and any other strategies that may delay generic drug competition throughout the U.S." Other members of Congress have proposed legislation to amend various portions of Hatch-Waxman, including the sections that

[1] Drug Price Competition and Patent Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended 21 U.S.C. § 355 (1994)).

[2] The study did not examine how generic competition has developed under the other methods the Amendments established. Nor did the study examine whether Hatch-Waxman provisions have achieved another purpose of the Amendments: to compensate brand-name companies for lost patent life due to the time needed for FDA's safety and efficacy review process.

[3] Appendix A contains a glossary of frequently used terms and their meanings under Hatch-Waxman.

[4] *See, e.g.*, *Abbott Laboratories*, No. C-3945 (May 22, 2000) (consent order), *available at* <http://www.ftc.gov/os/2000/03/abbott.do.htm>. *Hoechst Marion Roussel, Inc.*, No. 9293 (May 8, 2001) (consent order), *available* <http://www.ftc.gov/os/2001/05/hoechstdo.pdf>. The same issues are raised by another case in which the Commission settled similar allegations, *see* American Home Products, Docket No. 9297 (Feb. 19, 2002) (decision and order) *available at* <http://www.ftc.gov/os/2002/02/ahpdo.pdf>. *See also* *Schering-Plough Corp., et al.*, Docket No. 9297, Initial Decision (Jul. 2, 2002), *available at* <http://www.ftc.gov/os/2002/07/scheringinitialdecisionp1.pdf>. The Commission also has accepted for public comment a consent order settling charges that Biovail illegally acquired an exclusive patent license and wrongfully listed that patent pursuant to another provision of the FDA's regulations implementing Hatch-Waxman. *Biovail Corp.*, File No. 011-0094, Agreement Containing Consent Order, (Apr. 19, 2002), *available at* <http://www.ftc.gov/os/2002/04/biovaildecision.htm>. Moreover, the Commission has accepted for public comment a consent order settling charges that Elan and Biovail entered into a supply and distribution agreement for a generic drug product that may have unreasonably restrained their incentives to compete against each other. *See* FTC, *Biovail Corp. and Elan Corp.*, File No. 011 0132, Agreement Containing Consent Order (Jun. 27, 2002), *available at* <http://www.ftc.gov/os/2002/06/biovailelanagreement.pdf>.

are the subject of the Commission's study.[5]

Finally, the study was motivated, in part, by the prospect of a substantial sales volume of brand-name drug products coming off patent in the next several years.[6] This represents an enormous opportunity for the generic drug industry and, conceivably, a commensurate threat to the brand-name pharmaceutical industry. Brand-name pharmaceutical drug manufacturers seeking to protect the sales of brand-name drugs may have an incentive and ability to enter into agreements with would-be generic competitors, or engage in other types of activities, that would slow or thwart the entry of competing generic drug products.

The Commission has developed significant expertise regarding competition in the pharmaceutical industry. The Commission has, for example, brought antitrust enforcement actions affecting both brand-name and generic drug manufacturers.[7] Commission staff have conducted empirical analyses of competition in the pharmaceutical industry, including in-depth studies by the staff of the Bureau of Economics.[8] The Commission has provided testimony before Congress,[9] and Commission staff have filed comments with the Food and Drug Administration ("FDA") regarding competitive aspects of Hatch-Waxman implementation.[10] In addition, individual Commissioners have addressed the subject of pharmaceutical competition before a variety of audiences, both to solicit input from affected parties and to promote dialogue regarding practical solutions.[11]

[5] *See, e.g.*, S. 812, 107th Cong. (2001) (introduced by Sens. Schumer and McCain); S. 2677, 107th Cong. (2002) (introduced by Sen. Rockefeller); S. 754, 107th Cong. (2001) (introduced by Sen. Leahy).

[6] National Institute for Health Care Management, "Prescription Drugs and Intellectual Property Protection" (Aug. 2000) at 3.

[7] *See, e.g., FTC v. Mylan Laboratories, Inc. et al.*, 62 F. Supp. 2d 25 (D.D.C. 1999); *Roche Holding Ltd.*, 125 F.T.C. 919 (1998) (consent order); *Ciba-Geigy Ltd.*, 123 F.T.C. 842 (1997) (consent order).

[8] Bureau of Economics Staff Report, Federal Trade Commission, *The Pharmaceutical Industry: A Discussion of Competitive and Antitrust Issues in an Environment of Change* (Mar. 1999) *available at* <http://www.ftc.gov/reports/pharmaceutical/drugrep.pdf>; David Reiffen and Michael R. Ward, *Generic Drug Industry Dynamics*, Bureau of Economics Working Paper No. 248 (Feb. 2002) ("Reiffen and Ward"), *available at* <http://www.ftc.gov/be/econwork.htm>

[9] Testimony of Federal Trade Commission before the Committee on Commerce, Science and Transportation, United States Senate (April 23, 2002) *available at* <http://www.ftc.gov/os/2002/04/pharmtestimony.htm>; Testimony of the Federal Trade Commission before the Committee on the Judiciary, United States Senate, *Competition in the Pharmaceutical Marketplace: Antitrust Implications of Patent Settlements* (May 24, 2001) *available at* <http://www.ftc.gov/os/2001/05/pharmtstmy.htm>.

[10] *FDA: Citizen Petition*, Comment of the Staff of the Bureau of Competition and of Policy Planning of the Federal Trade Commission Before the Food and Drug Administration (Mar. 2, 2000) *available at* <http://www.ftc.gov/be/v000005.pdf> (recommending modifications to the FDA's Proposed Rule on citizen petitions intended to discourage anticompetitive abuses of the FDA's regulatory processes); *FDA: 180-Day Marketing Exclusivity for Generic Drugs*, Comment of the Staff of the Bureau of Competition and of Policy Planning of the Federal Trade Commission Before the Food and Drug Administration (Nov. 4, 1999) (AMarketing Exclusivity Comment@) *available at* <http://www.ftc.gov/be/v990016.htm> (recommending that the FDA's Proposed Rule on 180-day marketing exclusivity be modified to limit exclusivity to the first ANDA filer and to require filing of patent litigation settlement agreements).

[11] *See, e.g.*, Sheila F. Anthony, *Riddles and Lessons from the Prescription Drug Wars: Antitrust Implications of Certain Types of Agreements Involving Intellectual Property* (June 1, 2000) *available at* <http://www.ftc.gov/speeches/anthony/sfip000601.htm>; Thomas B. Leary, *Antitrust Issues in Settlement of Pharmaceutical Patent Disputes* (Nov. 3, 2000) *available at* <http://www.ftc.gov/speeches/leary/learypharma.htm>; Thomas B. Leary, *Antitrust Issues in the Settlement of Pharmaceutical Patent Disputes, Part II* (May 17, 2001) *available at* <http://www.ftc.gov/speeches/leary/learypharmaceutical settlement.htm>; Timothy J. Muris, *Competition and*

In October 2000, the Commission began the formal process of obtaining authorization to conduct this study. As required by the Paperwork Reduction Act and implementing regulations of the Office of Management and Budget,[12] the Commission published a Federal Register notice[13] that included, among other things, the special orders under Section 6(b) of the Federal Trade Commission Act[14] that the Commission planned to serve on brand-name pharmaceutical companies and generic drug manufacturers.

In response to the public comments received following this Federal Register notice, the Commission clarified the proposed information requests as suggested by several parties and published in March 2001 a second notice requesting public comments.[15] On April 6, 2001, the Commission obtained OMB approval to conduct the study, and on April 25, 2001, the Commission began service of the special orders on 28 brand-name companies and over 50 generic drug companies.[16] By December 31, 2001, the Commission had received substantial compliance with the special orders.

Overview of the Hatch-Waxman Act and the FDA's Implementing Regulations

Before describing the scope of the study, it is important to understand the historical context in which Hatch-Waxman arose. Moreover, the generic approval process Hatch-Waxman implemented demands an understanding of the interaction of the patent system and the regulatory structure governing the approval of brand-name drugs.

Pre-Hatch-Waxman Regulatory Environment

In 1962, amendments to the Federal Food, Drug, and Cosmetic Act added a proof-of-efficacy requirement to new drug approvals; before that time, the FDA approved drugs for safety only. As a result of the amendments, brand-name companies are required to prove that new drugs are safe and effective prior to FDA approval. To prove safety and efficacy, brand-name companies are required to conduct tests on humans ("clinical trials") and to submit those results to the FDA with their new drug application (NDA).

Those seeking to market a generic version of an existing post-1962 brand-name drug also had to perform their own safety and efficacy studies, much like the brand-name companies had to demonstrate the safety and efficacy of the brand-name drug.[17] The FDA did not have a streamlined

Intellectual Property Policy: The Way Ahead, at 5-6 (Nov. 15, 2001) *available at* <http://www.ftc.gov/speeches/muris/intellectual.htm>.

[12] The Commission was required to obtain OMB clearance before it could begin the study because the number of special orders to be sent triggered the requirements of the Paperwork Reduction Act of 1995, 44 U.S.C. Ch. 35, as amended.

[13] *See* 65 Fed. Reg. 61334 (Oct. 17, 2000).

[14] 15 U.S.C. § 46(b).

[15] *See* 66 Fed. Reg. 12512 (Feb. 27, 2001).

[16] Several brand-name drug companies have equity interests in generic subsidiaries and, thus, were requested to answer questions relating to both brand-name products and generic products.

[17] The FDA considered "such retesting to be unnecessary and wasteful because the drug [had] already been determined to be safe and effective. Moreover, such

procedure by which to approve generic versions of brand-name drug products whose patents had expired.[18] By 1984, the FDA estimated that there were approximately 150 brand-name drugs whose patents had expired for which there was no generic equivalent.[19]

Another factor complicating generic drug approval concerned the timing of when generic companies could perform their clinical tests. Before Hatch-Waxman was enacted, a generic company could not begin the required FDA approval process until *after* patents on the relevant brand-name product had expired; to begin earlier would typically have infringed the brand-name company's patents.[20] Thus, at that time, patent law coupled with the FDA generic approval process, in effect, extended the term of the brand-name company's patent protection and delayed market entry by generic versions of brand-name pharmaceutical drug products.

Brand-name pharmaceutical companies also confronted problems. The discovery and development of new drug products are expensive and time-consuming.[21] To spur this investment, as well as to recoup investments made, brand-name companies obtain patent protection to exclude others from making, using, or selling an invention for a number of years. Often, however, the brand-name companies obtained patents prior to FDA approval of the drug product. Thus, the effective terms of many patents were shortened due to the time required for the FDA to ensure the safety and efficacy of the brand-name company's drug product.

The Hatch-Waxman Amendments

Congress passed the Hatch-Waxman Amendments to address both issues.[22] To enable earlier generic entry, the Amendments provided that certain conduct related to obtaining FDA approval that would otherwise constitute patent infringement would be exempt from infringement liability under the patent laws. In addition, generic applicants were permitted to rely on the brand-name company's trade secret data demonstrating the safety and efficacy of the brand-name drug product. To restore patent protection to brand-name companies to compensate them for the time used to obtain FDA approval, the Amendments contained provisions to extend patent terms in certain circumstances.

Thus, Hatch-Waxman balanced an expedited FDA approval process to speed generic entry with patent term restoration to

retesting is unethical because it requires that some sick patients take placebos and be denied treatment known to be effective." *See* H.R. Rep. No. 98-857, Part I at 16 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2649.

[18] The FDA did establish, however, a procedure to determine the effectiveness of all drugs approved prior to 1962, and it established a policy of permitting the approval of a generic equivalent to a safe and effective pre-1962 brand-name drug. This generic approval procedure, however, did not apply to drugs approved after 1962. *Id.*

[19] *Id.* at 17.

[20] *Roche Products, Inc. v. Bolar Pharmaceutical Co.*, 733 F.2d 858 (Fed. Cir. 1984).

[21] *See* Pharmaceutical Research and Manufacturers of America, "Delivering on the Promise of Pharmaceutical Innovation: The Need to Maintain Strong and Predictable Intellectual Property Rights, White Paper," *submitted to* Federal Trade Commission and the Department of Justice – Antitrust Division (Apr. 22, 2002) at 7-10, *available at* <http://www.ftc.gov/os/comments/intelpropertycomments/phrma020422.pdf>.

[22] Appendix B contains the Hatch-Waxman Amendments, as codified at 21 U.S.C. 355 et seq.

ensure continuing innovation. As one federal appellate judge explained, the Amendments "emerged from Congress's efforts to balance two conflicting policy objectives: to induce brand-name pharmaceutical firms to make the investments necessary to research and develop new drug products, while simultaneously enabling competitors to bring cheaper, generic copies of those drugs to market."[23]

Pursuant to the Federal Food, Drug, and Cosmetic Act, a brand-name company seeking to market a new drug product must first obtain FDA approval by filing a New Drug Application (NDA). The NDA ultimately must include a variety of information that is extremely expensive and time-consuming to develop, including clinical trial data.

When the NDA is filed, the NDA filer also must provide the FDA with certain categories of information regarding the patents that cover the drug that is the subject of its NDA.[24] Upon approval of the NDA, the FDA lists the patents in an agency publication entitled "Approved Drug Products with Therapeutic Equivalence," commonly known as the "Orange Book."[25] In addition to patents on the active ingredient in a drug product, patents on specific formulations (*i.e.*, a tablet form) or methods of use (*i.e.*, used to treat heartburn in mammals) of the drug product are also listed in the Orange Book.

Rather than requiring a generic manufacturer to repeat the costly and time-consuming NDA process, the Amendments permit the company to file an Abbreviated New Drug Application ("ANDA"). The object of the ANDA process is to demonstrate that the generic drug product has the same active ingredient, route of administration, dosage form and strength, and proposed labeling as the brand-name drug. The ANDA also must contain sufficient information to demonstrate that the generic drug is "bioequivalent" to the relevant brand-name product.[26] As a result of providing this information, the generic applicant is allowed to rely on the FDA's previous findings of safety and effectiveness for the referenced brand-name drug, and thus the applicant does not have to provide its own clinical studies to demonstrate the generic drug product's safety and effectiveness. This reliance on the innovator's safety and efficacy data allows generic applicants to save very substantial amounts of money in development costs.

An ANDA also must contain a certification regarding each patent listed in the Orange Book that relates to the relevant NDA for which the generic applicant is seeking to make a generic version. The statute provides ANDA applicants with four certification options: they may certify (I) that the required patent information has not been filed; (II) that the patent has expired; (III) that the patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (IV) that the patent is invalid or will not be infringed by the generic drug for which the ANDA

[23] *Abbott Labs. v. Young*, 920 F.2d 984, 991 (D.C. Cir. 1990) (Edwards, J., dissenting on other grounds) (citations omitted).

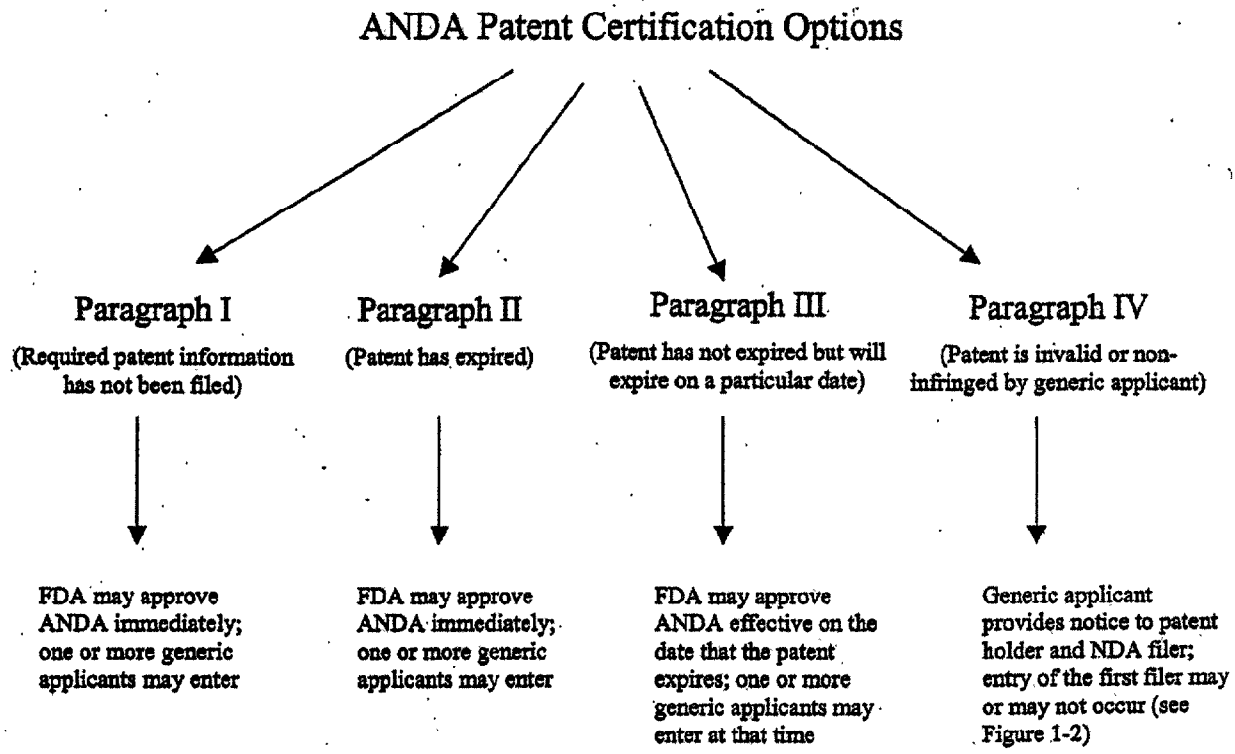
[24] 21 U.S.C. § 355(b)(1).

[25] *Id.* at § 355(j)(7)(A).

[26] *Id.* at § 355(j)(2)(A)(iv). Bioequivalence means that the rate and extent of absorption of the generic drug is not significantly different from the rate and extent of absorption of the listed drug when administered at the same dosage.

applicant seeks approval. For ease of discussion throughout this study, these certifications will be referred to as paragraph I, II, III and IV certifications, respectively. Figure 1-1 depicts graphically the FDA approval process depending upon which certifications the generic applicant makes.

Figure 1-1 ANDA Patent Certifications



If the applicant makes a certification under paragraphs I or II, the FDA may approve the ANDA immediately, provided other requirements are met.[27] If the applicant makes a paragraph III certification, the FDA may approve the ANDA effective on the date that the patent expires.[28]

Paragraph IV Certifications

When an applicant makes a paragraph IV certification, two additional provisions of Hatch-Waxman are implicated. These two provisions are at the heart of the FTC's study.

The first is the automatic "30-month stay" protection afforded brand-name companies. An ANDA filer that makes a paragraph IV certification must provide a notice to both the patent holder and the

[27] *Id.* at § 355(j)(5)(B)(ii).

[28] *Id.*

NDA filer[29] with a detailed statement of the factual and legal basis for the ANDA filer's assertion that the patent is invalid or not infringed. Once the ANDA filer has provided such notice, a patent holder (usually the brand-name company) must bring an infringement suit within 45 days to take advantage of the statutory stay provision.[30] If the patent holder does not bring suit within 45 days, the FDA approval process may proceed, and the FDA may approve an ANDA as soon as regulatory requirements are fulfilled.[31] A 30-month stay of FDA approval of an ANDA applicant is invoked when a brand-name company receives notice of a generic applicant's paragraph IV certification and files suit for patent infringement within 45 days of that notice.[32] Filing of the lawsuit stays the FDA's approval of the ANDA until the earliest of: (1) the date the patent(s) expire; (2) a final determination of non-infringement or patent invalidity by a court in the patent litigation; or (3) the expiration of 30 months from the receipt of notice of the paragraph IV certification.

The second provision is the "180-day period of exclusivity." The first generic applicant to file an ANDA containing a paragraph IV certification is eligible for 180 days of marketing exclusivity, during which the FDA may not approve subsequent ANDAs for the same drug product.[33] The 180-day exclusivity period thus increases the economic incentives for a generic company to be the first to file an ANDA containing a paragraph IV certification. Through this 180-day provision, the Amendments also provide an incentive for generic companies to litigate patents that may be invalid and to "design around" patents to find alternative, non-infringing forms of patented drugs.[34] The 180-day exclusivity period is calculated from either the date of the first commercial marketing of the generic drug product or the date of a court decision declaring the patent invalid or not infringed, whichever is sooner.[35] After the 180 days, other generic products can enter the market, provided they obtain the FDA regulatory approval. Subsequent eligible generic applicants must wait until the first generic applicant's 180 days have run before the FDA can approve the subsequent ANDA.

Figure 1-2 describes graphically how the 30-month stay and 180-day exclusivity provisions affect FDA approval of a generic applicant's ANDA.

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[29] *Id.* at § 355(j)(2)(B). Although the patent holder and the NDA filer are often the same person, this is not always the case. The Hatch-Waxman Amendments require that all patents that claim the drug described in an NDA must be listed in the Orange Book. Occasionally, this requires an NDA filer to list a patent that it does not own.

[30] *Id.* at § 355(j)(5)(B)(iii).

[31] *Id.* For example, the statute requires the ANDA applicant to establish bioequivalence.

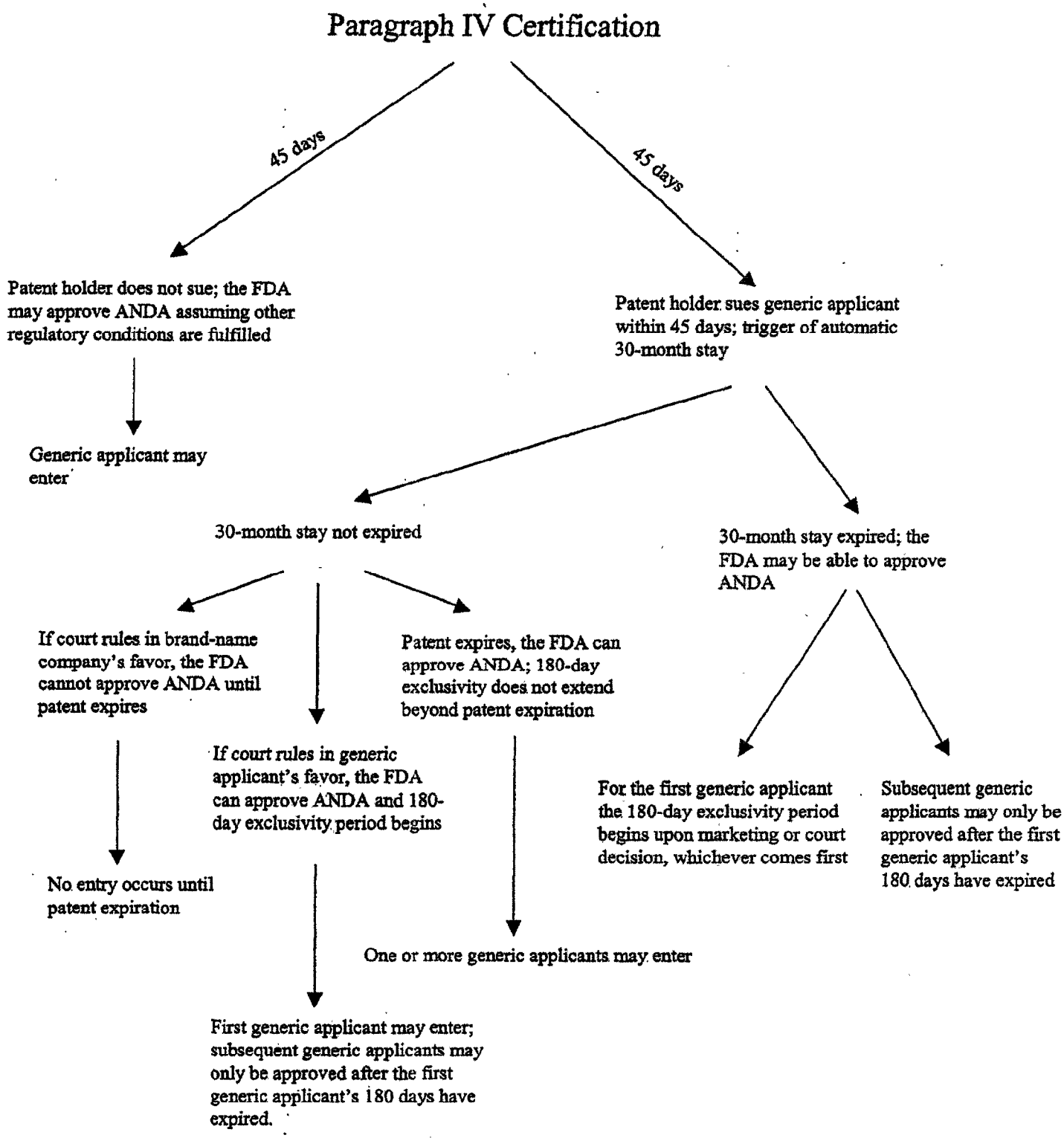
[32] 21 U.S.C. at § 355(j)(5)(B)(iii).

[33] *Id.* at § 355(j)(5)(B)(iv).

[34] *See Granutec, Inc. v. Shalala*, 139 F.3d 889, 891 (4th Cir. 1998).

[35] 21 U.S.C. § 355(j)(5)(B)(iv).

Figure 1-2 Paragraph IV Certifications



Price Effect of Generic Entry

Because generic drugs are typically far less expensive than their corresponding brand-name versions, competition from generic drugs can deliver large savings to consumers. A Congressional Budget Office (CBO) study attempted to quantify the magnitude of this effect by analyzing retail pharmacy data from 1993 and 1994. The study found that, for drugs that are available in both generic and brand-name versions, the average price of a generic prescription was approximately half of the average price of a brand-name prescription.[36] The CBO estimated that, in 1994, the availability of generic drugs saved purchasers between $8 billion and $10 billion.[37]

The broader empirical economics literature also points to a number of competitive effects associated with the introduction of generic drugs. Early research using small data samples with information on brand name and generic prescription drug prices and sales found that (1) brand name drug prices rose slightly, but that average drug prices declined some 20 percent within approximately two years of generic entry,[38] and (2) generic entry produces slight reductions in brand name drug prices and declines in generic prices as the number of generic rivals increases.[39]

A more recent study of 32 drugs that lost patent protection around the time of the passage of the Hatch-Waxman Amendments found that generic entry results in somewhat higher prices for brand-name prescription drugs (in light of factors such as inelastic demand among users of brand-name products), but large decreases in the prices of corresponding generic drugs.[40] Another recent study of 32 drugs that lost patent protection after passage of the Hatch-Waxman found that generic drug prices fell until at least the fifth generic firm enters, and that falling prices from increased competition can continue with the entry of additional generic competitors.[41] It is also noteworthy that elements of this literature indicate that generic entrants gain significant market share at the expense of their rival brand name drug companies after their entry. Overall, this literature points to significant short-run competitive impacts of generic entry that can lead to substantial benefits for consumers of prescription drugs.

Scope of the Study

This study focuses solely on the competitive circumstances surrounding

[36] Congressional Budget Office, *How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry* (July 1998) ("CBO Study") at 28, *available at* <http://www.cbo.gov/showdoc.cfm?index`655&sequence'0>.

[37] *Id.* at 31.

[38] Henry Grabowski & John M. Vernon, "Brand Loyalty, Entry and Price Competition In Pharmaceuticals After the 1984 Drug Act," 35 J. of Law & Econ. 331-50 (Oct. 1992).

[39] Richard E. Caves, et al., "Patent Expiration, Entry, and Competition in the U.S. Pharmaceutical Industry" (Brookings Papers on Economic Activity, Microeconomics, Martin Neil Baily & Clifford Winston, eds., Brookings Institution, Washington, DC 1991).

[40] Richard G. Frank & David S. Salkever, "Generic Entry and the Pricing of Pharmaceuticals," 6 J. of Econ. & Mgmt Strategy, 75-90 (Spring 1997) (Generic entry will induce those buyers who are highly sensitive to price to switch to low-price generics; price-insensitive buyers continue to purchase branded products. This segmentation of the market means that the branded drug often will face a less elastic demand curve, which can induce the profit-maximizing branded producer to raise its price.).

[41] Reiffen and Ward, *supra* n. 8.

generic competition for those brand-name drug products (1) subject to an ANDA notice containing a paragraph IV certification (2) that brand-name companies received after January 1, 1992 and prior to January 1, 2001. By focusing on these brand-name drug products, the study could examine how the 180-day marketing exclusivity and the 30-month stay provisions have influenced the development of generic drug competition.

The study does not address how generic competition has developed under paragraph I, II, or III certifications. The study also does not address the patent restoration features of Hatch-Waxman.

ANDAs Under Hatch-Waxman

According to the FDA, from the time Hatch-Waxman became effective in 1984 through December 31, 2000, 8,019 ANDAs were filed with the FDA.[42] Of these applications, 7,536 (94 percent) raised no patent issues (*i.e.*, the ANDAs did not contain a paragraph IV certification). A substantial portion of the total number of ANDAs, however, relate to the same brand-name product or NDA. Thus, the total number of ANDAs does not represent 8,019 unique brand-name drug products, and it is unclear as to how many unique brand-name drug products the total 8,019 ANDAs related.

Four hundred eighty-three (483) (or six percent of the total number of ANDAs filed) contained Paragraph IV certifications. The 483 ANDAs relate to 130 unique brand-name drug products as measured by unique NDAs. The share of ANDAs with paragraph IV certifications – compared to all ANDAs filed (those with paragraph I-IV certifications) -- has increased significantly since Hatch-Waxman was enacted. According to the data provided by the FDA, during the 1980s (1984-89), only 2 percent of ANDAs contained paragraph IV certifications. This share increased to approximately 12 percent for the 1990s, and it has increased substantially in the last few years: from 1998-2000, approximately 20 percent of ANDAs contained paragraph IV certifications.

The brand-name drug products this study covered include any drug product for which the brand-name company received notification of an ANDA containing a paragraph IV certification after January 1, 1992 and prior to January 1, 2001.[43] This selection criteria resulted in 104 drug products, as represented by New Drug Applications (NDAs) filed with the FDA, within the scope of the study. As noted previously, from 1984 to January 2001, 130 unique NDAs were subject to at least one ANDA with a paragraph IV certification. The most recent 104 brand-name drug products (of the 130 total) are included within the scope of the study.

Appendix C contains a list of the NDAs within the scope of the study. The drug products included in the study represent some of the largest drug products as measured by annual sales, including so-called "blockbuster" drugs such as Capoten, Cardizem CD, Cipro, Claritin, Lupron Depot, Neurontin, Paxil, Pepcid, Pravachol,

[42] FDA staff provided this information to the FTC staff.

[43] If any later-filed generic applicant filed its ANDA with the requisite certification after January 1, 1992, even if the first generic applicant for a particular drug product filed its application prior to January 1, 1992, the drug product was included within the scope of the study.

Prilosec, Procardia XL, Prozac, Vasotec, Xanax, Zantac, Zocor, Zoloft, and Zyprexa.

The FDA provided the Commission with the identity of the generic companies that have filed ANDAs containing paragraph IV certifications since enactment of Hatch-Waxman in 1984. Using this information, FTC staff identified which brand-name companies had received notice of the filing of an ANDA containing a paragraph IV certification. The list of brand-name companies and generic companies are attached as Appendix D. Special orders were served on all identified brand-name companies who received notice of, and on the first three generic drug companies who had filed, the ANDA.[44]

The FTC's special orders required the brand-name companies to produce agreements with generic applicants that relate to the ANDA filing, results of ANDA patent infringement litigation with generic applicants, listing of patents in the FDA's Orange Book, sales information, and the use of citizen petitions. Generic applicants were required to produce agreements relating to the innovator's drug products for which they had filed an ANDA containing a paragraph IV certification, and to respond to questions about the results of patent infringement litigation with the brand-name company, sharing of litigation expenses with other generic applicants, allegations of improper Orange Book listings, and sales information.

Organization of the Report

Chapter 2 of the Report reviews the frequency and outcome of patent infringement lawsuits in connection with paragraph IV certifications. Chapter 3 discusses the agreements that litigants have used to settle patent infringement litigation under Hatch-Waxman. Chapters 4 and 5 examine in more detail how certain Hatch-Waxman provisions, the 30-month stay and the 180-day exclusivity provisions respectively, affect generic entry. Chapter 6 discusses the use of citizen petitions by brand-name companies for drug products included in the study.

Appendix A contains a glossary of terms used most frequently. Appendix B contains the text of Hatch-Waxman. Appendix C lists the NDAs within the scope of the study. Appendix D lists the brand-name companies and generic companies that received special orders. Copies of the questions in the special orders are contained in Appendix E. Appendix F contains a copy of the FTC Staff's Citizen Petition on the listability of certain patents in the Orange Book. Appendix G describes the drug products where the brand-name company has filed a patent in the Orange Book after being notified of the ANDA, which, in turn, generated an additional 30-month stay upon suit. Appendix H analyzes certain categories of patents that raise Orange Book listability issues.

[44] In many instances, only one generic applicant had filed an ANDA containing a paragraph IV certification for a particular drug product. In these cases, special orders were served only on the first generic applicant.

Chapter 2 Outcomes of Patent Infringement Lawsuits Under the Hatch-Waxman Amendments

Introduction

The application of both the 180-day exclusivity and 30-month stay provisions depends, at least in part, upon whether the brand-name company initiates patent infringement litigation against a generic applicant.[1] As noted earlier, the 180-day exclusivity provision grants, under certain circumstances, 180 days of exclusive marketing to the first generic applicant that files an ANDA containing a paragraph IV certification. A 30-month stay of FDA approval of a potential generic competitor is invoked if a brand-name company receives notice of a generic applicant's paragraph IV certification and files suit for patent infringement within 45 days of that notice.

Filing of the lawsuit stays the FDA's approval of the ANDA until the earliest of: (1) the date the patents expire; (2) a final determination of non-infringement or patent invalidity by a court in the patent litigation; or (3) the expiration of 30 months from the receipt of notice of the paragraph IV certification. This chapter reviews the frequency and outcome of these patent infringement lawsuits.

For nearly 75 percent of drug products this study covered, brand-name companies initiated patent infringement litigation against the *first* generic applicant. In the other 25 percent, there was no suit, and the FDA has approved most of the generic products, thus allowing generic entry to occur. FDA approval of ANDAs submitted by first generic applicants who were not sued by the brand-name company took, on average, 24 months and 2 weeks from the ANDA filing date.

In 70 percent of the cases in which the brand-name company sued the *first* generic applicant, there has been either a court decision, or the parties have agreed to a final settlement. Of these lawsuits, involving 53 drug products, 20 settled without a court decision on the merits of the patent infringement lawsuit. These settlement agreements are discussed in detail in Chapter 3. In the other 30 percent of the cases, a district court had not yet ruled as of June 1, 2002.

Of all the patent infringement cases (including first and subsequent generic applicants) in which there has been a decision of a court as of June 1, 2002, generic applicants prevailed in 73 percent of the cases, and brand-name companies prevailed in 27 percent. Of the decisions favoring the generic applicant, there were slightly more non-infringement decisions (14) than patent invalidity decisions (11). The rate at which the U.S. Court of Appeals for the Federal Circuit overturned district court decisions of patent invalidity for drug products in this study was 8 percent.

In most instances when the 30-month

[1] For ease of discussion purposes, the term "generic applicant" means those applicants who have filed an ANDA containing a paragraph IV certification. *See* Appendix A for a glossary of frequently used terms.

stay has expired without a decision of a district court and the FDA approved the generic applicant's ANDA, the generic applicant did not enter the market until it secured a district court decision of patent invalidity or non-infringement.

How Frequently Have Brand-Name Companies Sued the First Generic Applicant?

The study sought to determine the frequency with which brand-name companies have initiated patent infringement lawsuits against generic applicants within the required 45-day period, thus triggering the 30-month stay provision. The data revealed 75 drug products, out of a total of 104 NDAs (72 percent), in which the brand-name company sued the *first* generic applicant. For all but 5 of the 104, the first generic applicant for one dosage strength of the drug product (*e.g.*, 10, 20, and 40 mg tablets) was the first applicant for all strengths of the drug product. In light of this fact, unless otherwise noted, all of the drug products with multiple strengths (with the same 5 exceptions) involved one NDA, and therefore were counted as one brand-name drug product with one first generic applicant. The 5 exceptions are presented in footnotes 4, 7, and 8 to ensure completeness. Table 2-1 summarizes this result.

Table 2-1 Patent Litigation Frequency

Litigation Between Brand-name Company and Generic Applicant	Number of NDAs
Brand-Name Company Sued the First Generic Applicant	75
Brand-Name Company Did Not Sue the First Generic Applicant	29[2]
Total	**104**

For the 75 drug products where patent litigation was brought, the median net sales in the year the first generic applicant filed its ANDA were $190 million per year. By contrast, the majority of the 29 NDAs for which no suit was filed had net sales of less than $100 million in the year the generic applicant filed its application.[3]

For 15 of the 29 drug products where the brand-name company did not sue the first generic applicant, the generic applicant began commercial marketing soon after FDA approval and prior to patent expiration. In 6 cases, the FDA has not approved the generic applicant's ANDA as of June 1, 2002, and the patents have not yet expired. In 6 cases the FDA has approved the ANDA, but commercial marketing has not yet begun. And in the remaining 2 cases, the

[2] For 1 of the 29 drug products, 2 different generic applicants were the first to file for each of the 3 different strengths of this drug product. In each strength, the brand-name company did not sue the generic applicant. As noted above, this brand-name drug product is only counted once in the total of 29.

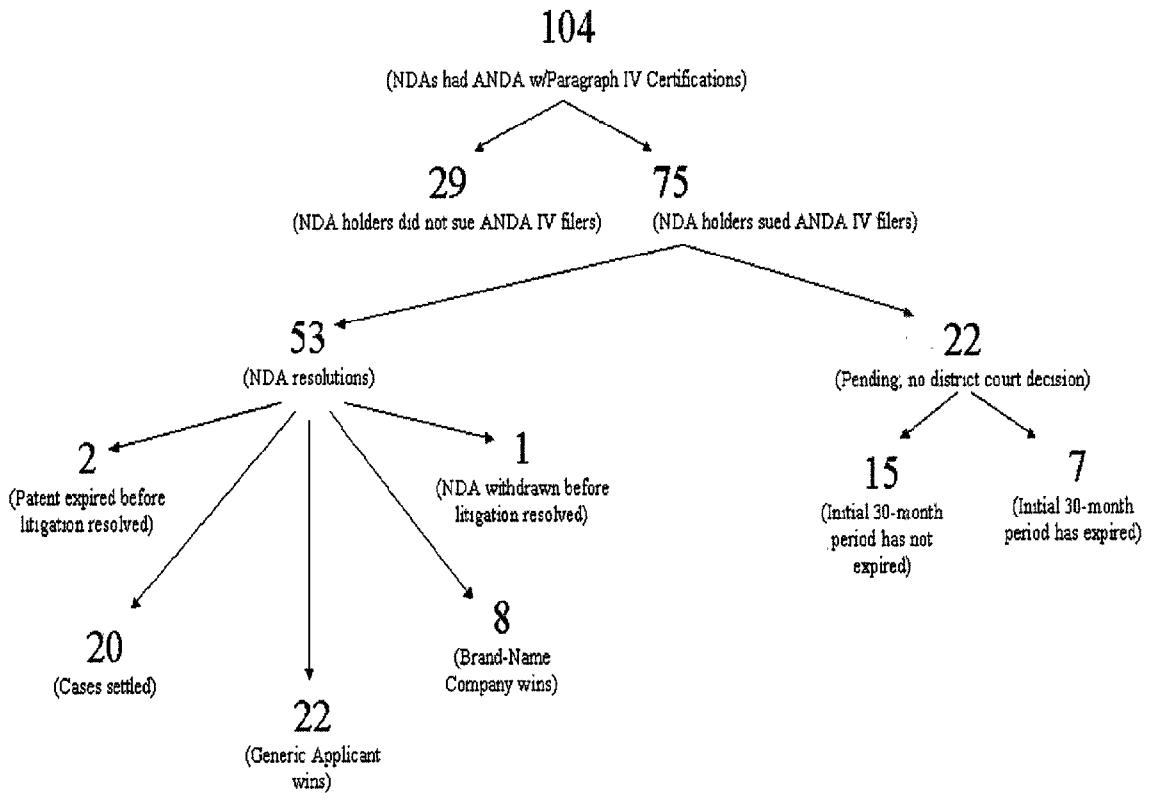
[3] For 2 of the 29 drug products in which no suit was filed, the brand-name company's patents would have expired during the first several months of the 30-month stay. Because patent expiration terminates the 30-month stay, it may not have made sense in those cases to initiate patent infringement litigation, which takes, on average, 25 months to resolve.

patents expired before FDA approved the generic applicant's ANDA.

What Were the Results of Patent Infringement Litigation with the First Generic Applicant?

The brand-name company sued the first generic applicant for patent infringement involving 75 NDAs. Figure 2-1 shows a graphical depiction of the resolution (*i.e.*, a decision of a court, a final settlement, or miscellaneous resolutions) of each case as of June 1, 2002. For 4 drug products, different generic applicants were the first to file on different dosage strengths of the drug product, thus contributing to multiple suits on the same drug product (and the same patent) with different generic applicants. For clarity, the results of more than one suit involving the same drug product are not included in the totals reported, but are described in footnotes 4, 7, and 8. Only results from the first applicant for a drug product are included in the totals discussed below.

Figure 2-1 Summary of Brand Company and 1st ANDA IV Filer Activity



Pending Patent Infringement Litigation

As of June 1, 2002, for 22 of the 75 drug products,[4] the district court hearing the lawsuit has not yet ruled on the merits of the patent infringement allegations.[5] For 7 of these 22 drug products, the 30-month stay has expired. For 3 of these 7 drug products, the brand-name company also sued for infringement of a patent that was listed in the Orange Book *after* the first generic applicant had filed its ANDA.[6] In these cases, it has been possible for a brand-name company to obtain more than one 30-month stay. The first 30-month stay has expired in these 3 cases, but the second (or even later) one has not. In none of these cases has the generic applicant entered the market.

Resolution of Patent Infringement Suits

There has been a court decision for 53 drug products (75 in total less 22 pending). The resolution of each is classified in Table 2-2 and also is described in Figure 2-1. Settlements were used in 38 percent of the instances (20 drug products out of 53 settled).[7] A court decision resolved the patent infringement claims for 30 drug products. Generic applicants prevailed 73 percent of the time (22 out of 30),[8] and brand-name companies prevailed 27 percent of the time (8 out of 30). In 3 miscellaneous instances, either the patents expired before the 30-month stay expired, or the brand-name company withdrew the NDA due to safety reasons.

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[4] In addition to these 22 cases, there are 2 more pending cases on a dosage strength of a drug product for which the patent litigation on another strength has been resolved. The resolution of these cases is discussed in the following section.

[5] In one pending case, the FDA determined that the brand-name company failed to submit the required information for a particular patent in a timely manner. Therefore, the generic applicant was not required to submit a patent certification to address that patent, the 30-month stay was dissolved, and the FDA subsequently approved the ANDA. Commercial patent litigation was still pending as of June 1, 2002, however, and the generic applicant has not yet entered the market.

[6] As discussed further in Chapter 4, if a brand-name company lists in the Orange Book later-issued patents (*i.e.*, patents obtained from the U.S. Patent and Trademark Office after obtaining NDA approval) after receiving notification from a generic applicant, the generic applicant must re-certify that its ANDA does not infringe the later-issued patent. If the brand-name company initiates a patent infringement suit within 45 days of notice of the generic applicant's re-certification, then FDA approval of the ANDA is stayed automatically for an *additional* 30 months from the notice date or upon final determination of non-infringement or patent invalidity by a court in the patent litigation.

[7] For one of these 20 drug products, a different generic applicant was first for each of the product's 3 strengths; the brand-name company settled with 2 of these applicants, and the litigation involving the other strength is pending. This drug product is counted only once as "settled." *See supra* n. 4. For another of these 20 drug products, a different generic applicant was first for each of the product's 2 strengths; the brand-name company entered a settlement with one generic applicant, and the first applicant for the other strength prevailed on non-infringement at the Federal Circuit. This drug product is counted only as "settled."

[8] For one of these 22 drug products, a different generic applicant was first for each of the product's 2 strengths; the first generic applicant prevailed on non-infringement at the Federal Circuit on one strength, while the other case is pending. This drug product is counted only once as "generic prevails." *See supra* n. 4. For another of these 22 products, a different generic applicant was first for each of the product's 3 strengths; the first generic applicant for each strength prevailed in each patent suit, which were on the same patent. This drug product is counted only once as "generic prevails."

Table 2-2 Results of Lawsuits with the First Generic Applicant

Resolution of Patent Litigation with First Generic Applicant	Number of NDAs
Settlement Between Brand-Name Company and Generic Applicant	20
Generic Applicant Prevails in Patent Infringement Suit	22
Brand-Name Company Prevails in Patent Infringement Suit	8
Miscellaneous	3
Total Number of Cases Resolved	**53**

Patent Settlements with the First Generic Applicant

As shown in Table 2-2, the brand-name company and the first generic applicant settled patent infringement litigation involving 20 drug products. Most of the settlements can be classified into 3 types. Nine of these settlements contained a provision by which the brand-name company, as one part of the settlement, paid the generic applicant (settlements involving "brand payments"). Seven of the 20 settlements involved the brand-name company licensing the generic applicant to use the patents for the brand-name drug product prior to patent expiration. Two of the settlements allowed the generic applicant to market the brand-name drug product as a generic product, under the brand-name company's NDA, not the generic applicant's own ANDA. The remaining 2 settlements do not fit into any of these 3 categories. The provisions of each of these settlement agreements are discussed more fully in Chapter 3.

Generic Applicant Prevails

Table 2-3 shows that the generic applicant prevailed in litigation over 22 drug products.[9] In 18 instances, a court held that the brand-name company's patents were either invalid or not infringed. Of these 18 court decisions, 13 were appellate and 5 were district court (4 of which the brand-name companies have appealed as of June 1, 2002, but the decisions are pending). In 9 of these instances, the court held that the generic applicant's ANDA did not infringe the brand-name company's product; in the remaining 9 instances, a court held that the underlying patent was invalid for reasons such as being anticipated by prior art or double patenting.

For 2 of the 18 drug products, the parties implemented interim settlements that included brand payments to the generic applicant. For both of these drug products, the generic applicant began marketing after the interim settlement was terminated and the Federal Circuit had affirmed the district court's ruling of patent invalidity.[10]

For 3 of the 4 remaining drug

[9] This total does not include the resolution of follow-on lawsuits on 2 drug products that are counted as "settled." In the first instance, after the parties settled, the brand-name company submitted a late-issued patent for listing in the Orange Book, and a second round of litigation ensued in which the generic applicant prevailed. In the second instance, the parties settled the initial lawsuit, but the generic applicant later re-filed an ANDA for a reformulated version of the product. The brand-name company dismissed this second case with prejudice after determining that the reformulated version did not infringe its patents.

[10] One of these drug products (Hytrin tablets) was discussed in *Abbott Laboratories*, No. C-3945 (May 22, 2000) (consent order), *available at* <http://www.ftc.gov/os/2000/03/abbott.do.htm>.

products (of the 22), the brand-name company dismissed the litigation after receiving samples of the generic applicant's proposed product. In 2 of these cases, the FDA approved the generic drug soon thereafter, and generic entry occurred after the case was dismissed.[11] In the other case, the FDA had not approved the generic drug product as of June 1, 2002. For the last of the 4 drug products, the brand-name company dismissed the litigation without prejudice. Entry was delayed in light of an interim settlement on a later-listed patent for which the brand-name company failed to sue the first generic applicant within the requisite 45 days.[12]

The patents covering the 22 brand-name drug products in which the generic applicant prevailed involved formulation or method of use patents. In 3 instances (out of 6 where a drug substance patent was at issue), a drug substance patent was found invalid or not infringed.

Brand-Name Company Prevails

For 8 drug products, the brand-name company prevailed in the patent infringement litigation. For 7 drug products, a court held that the generic applicant's ANDA infringed the brand-name company's patents. Two of these decisions were appellate decisions; the other 5 were district court decisions, of which only one has been appealed by the generic applicant. As of June 1, 2002, this appeal is pending. By contrast, brand-name companies appealed nearly 90 percent of the cases in which they obtained an adverse district court opinion. In the last of the 8 cases, the generic applicant abandoned its ANDA after it was sued, and the court did not issue a final judgment.

The patent claims in 3 of these patent lawsuits involved drug substance claims, and the other 5 involved method of use and/or formulation claims.

How Frequently Have Brand-Name Companies Sued the Second Generic Applicant?

If the brand-name company sued the first generic applicant, it also sued the second generic applicant, if there was one, in nearly 85 percent of the cases. There were 43 such instances. Of the suits that have been resolved as of June 1, 2002, in no instance did different district courts reach different results in resolving infringement issues over the same brand-name drug product.

The brand-name company generally sued all generic applicants if the drug product had annual sales larger than $500 million in the year the first generic applicant filed its ANDA. Twenty such drug products are included in the study.

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[11] For the details of one of these case, *see* Hoechst Marion Roussel, Inc., No. 9293 (May 8, 2001) (consent order), *available at* <http://www.ftc.gov/os/2001/05/hoechstdo.pdf>.

[12] This drug products (Hytrin capsules) was discussed in *Abbott Laboratories*, No. C-3945 (May 22, 2000) (consent order), *available at* <http://www.ftc.gov/os/2000/03/abbott.do.htm>.

What Are the Results of Litigation with the Second Generic Applicant if the Brand-Name Company Settles with the First Generic Applicant?

Table 2-3 shows the results of litigation with the second generic applicant in those instances in which the first generic applicant settled its patent infringement litigation. Out of a total of 20 drug products with first generic settlements (*see* Figure 2-1), 9 drug products involved litigation with the second generic applicant.[13] In 1 case, litigation is still pending. Table 2-3 shows the resolution of the 8 decided cases.

Table 2-3 Resolution of Patent Litigation with Second Generic Applicant if the First Generic Applicant Settled its Litigation

Resolution of Subsequent Litigation	Number of NDAs
Settlement with Second Generic Applicant	4
Second Generic Applicant Wins Patent Infringement Suit	3
Brand-Name Company Wins Patent Infringement Suit	1
Total	**8**

In these 8 cases, the parties settled in 4, while in 3 the generic applicant prevailed (2 non-infringement decisions and 1 invalidity decision). In 1 case, the brand-name company won a decision of infringement.

For Those Patent Litigations that Resulted in a Court Decision, How Often Did Generic Applicants Prevail for All of the Drug Products in the Study?

For many drug products, the brand-name company sued several generic applicants over the same patents. Thus, in determining how frequently generic applicants or brand-name companies prevailed in patent litigation on a drug product basis, it would be misleading simply to count the number of decisions in either party's favor, because several of the decisions may be related to the same patent. Table 2-4 shows the results of the resolution of the patent suits without counting any similar outcomes involving the same drug product. For example, if both the first and second generic applicant obtained court decisions of non-infringement, the drug product is included only once as a generic win. If the case against the first generic applicant settled or is pending, but the case against the second applicant was resolved, the resolution of the second case is included. In no instance were the outcomes of the suits against the first and second generic applicant different.

There were court decisions on 40 different drug products. Table 2-4 presents the resolution of the patent litigation derived from five sources: (1) litigation with the first generic applicant (Table 2-2), (2) litigation with the second generic applicant if the first

[13] Eleven drug products either did not have a second generic applicant, or the brand-name company did not sue the second applicant.

generic applicant settled (Table 2-3), (3) litigation with the second generic applicant was resolved, but either the first generic applicant was not sued or the case is pending (3 drug products), (4) litigation with a third generic applicant when the first two generic applicants had settled, and (5) follow-on litigation with the first generic applicants on two drug products described in footnote 9.

Generic applicants prevailed for 29 out of 40 drug products (or 73 percent). Decisions involving 14 drug products held that the generic applicant did not infringe the patent, decisions involving 11 drug products held the relevant patent(s) invalid, and in 4 cases, the brand-name company abandoned the litigation with the first generic applicant before a decision of a court.

The brand-name company prevailed against the generic applicant in litigation involving 11 drug products. In one of these 11 cases, the generic applicant abandoned the litigation and admitted infringement before the court issued a decision.

Table 2-4 Patent Litigation Results per Drug Product

Result of Litigation	Number of NDAs
Generic Applicant Wins	29
Brand-Name Company Wins	11
Total	**40**

Results of Litigation and Patent Invalidity Rates

Out of 40 drug products in Table 2-4, 11 drug products had at least one patent listed in the Orange Book that was determined to be invalid. Thus, the minimum invalidity rate of patents that the parties chose to litigate to conclusion is 28 percent (11 invalid findings / 40 total). This rate assumes that the patents underlying the non-infringement decisions and cases when the brand-name company abandoned the litigation are valid, even though the courts in these cases may not have addressed the validity question. Thus, the invalidity rate may be higher than 28 percent, although we do not have data to determine it.

The recent empirical literature on the outcome of patent litigation provides a point of comparison with these findings, and suggests that this invalidity rate, although it may be understated as noted above, is not out of line with that of patents generally. Moore compares the outcomes of patent cases decided by judges with the outcomes of patent cases in which the finder-of-fact is a jury.[14] In her data set of 1209 patent trial decisions from 1983 through 1999, she finds that patents are invalidated in 36 percent of cases with a judge as the adjudicator and in 29 percent of cases with a jury.[15]

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[14] Kimberly A. Moore, *Judges, Juries & Patent Cases: An Empirical Peek Inside the Black Box*, 98 Mich. L. Rev. 365 (2000).

[15] *Id.* at 391. *See, also*, John R. Allison & Mark A. Lemley, *Empirical Evidence on the Validity of Litigated Patents*, 26 AIPLA L.Q. 185 (1998). Allison and Lemley study the outcomes of patent validity cases from 1989 to 1996. They focus on those cases in which there exist final written decisions at either the district court or the Federal Circuit levels. In their study, a district court decision is "final" if a later decision by the Federal Circuit does not supersede it. In their data set of 299 patents in 239 different cases, they find that 46 percent of the final decisions hold the relevant patent invalid. In contrast to this figure which covers all patent validity decisions, they find that pharmaceutical patents are found invalid in 27 percent of cases. Allison and Lemley do not consider decisions that focus only on infringement.

How Frequently Did the Federal Circuit Reverse a District Court Decision of Non-Infringement or Patent Invalidity?

Of the 29 NDAs where the generic applicant prevailed, as noted in Table 2-4, in 14 instances, the brand-name company appealed a district court decision that the patent at issue was either invalid or not infringed in a patent suit against either the first or second generic applicant.[16] In 13 of these decisions, the U.S. Court of Appeals for the Federal Circuit affirmed district court decisions of patent invalidity or non-infringement – 8 affirmed decisions of non-infringement,[17] and 5 affirmed decisions of patent invalidity. In the remaining case, two patents were at issue. The district court had determined both patents to be valid, but the Federal Circuit reversed as to one of the patents, and affirmed the validity decision for the other. Thus, the rate at which the Federal Circuit reversed decisions of invalidity and non-infringement for drug products included in this study was 8 percent.[18]

Table 2-4 shows that the brand-name company prevailed in litigation for 11 drug products. Of the 4 cases in which the generic applicant appealed the district court's decision of infringement, the Federal Circuit affirmed all 4 of these district court decisions of infringement.

In Which District Courts Did Brand-Name Companies Initiate Patent Infringement Litigation?

In 62 percent of the cases involving litigation with the first and second generic applicants, brand-name companies initiated patent litigation in just five federal judicial districts. These were the District of New Jersey, the Southern District of New York, the Southern District of Indiana, the Northern District of Illinois, and the Southern District of Florida. Thus, these courts have more experience with ANDA patent infringement litigation than most other federal district courts.[19]

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[16] To ensure no double counting, if the suits against the first and second generic applicant were consolidated into 1 district court opinion, and that decision was appealed, the appellate decision is counted only once. This also does not include one case where the district court's decision on summary judgment was vacated and remanded. Moreover, of the 29 drug products in which the generic applicant prevailed, some of the appeals are pending, or the district court decision was not appealed.

[17] In one of these decisions, the district court held the patent invalid and not infringed. The Federal Circuit upheld the non-infringement holding, but reversed on the invalidity holding. This has not been counted in the rate at which the Federal Circuit reversed decisions of invalidity and non-infringement for drug products included in this study because the non-infringement decision was affirmed and generic entry occurred prior to patent expiration.

[18] This rate does not include Federal Circuit overrules of summary judgement or collateral estoppel decisions.

[19] For those drug products in which both the first and second generic applicant were sued, approximately 50 percent of the suits were pursued in different district courts.

When Did Generic Applicants Enter the Market?

If a generic applicant was sued for patent infringement, it generally did not enter the market until there was a district court holding that the brand-name company's patent was invalid or not-infringed. In no instance has a generic applicant (either the first or second) entered the market and then a court later has found that the patent was infringed, making the generic applicant subject to damages.

In 22 cases (out of 75, Table 2-1) involving litigation between the brand-name company and the first generic applicant, as of June 1, 2002, the first 30-month stay had expired before the district court decision. In 8 of those cases, the FDA approved the generic applicant's ANDA prior to a district court ruling on the merits of the patent infringement suit.[20] In the first 2 cases, the district court case was ongoing as of June 1, 2002, and the generic applicant had not entered, although it had FDA approval to do so. In the next 2 cases, the generic applicant entered after obtaining a district court decision, but prior to the Federal Circuit's decision.[21] In the fifth case, the generic applicant waited until the Federal Circuit affirmed the district court's ruling. In the sixth case, the generic applicant reformulated its product and the brand-name company dismissed the litigation before a ruling on the merits. The generic applicant entered the market soon thereafter.

In the seventh case in which the FDA approved the generic applicant after the 30-month stay had expired but before a district court decision, there were two generic applicants for different dosage strengths (30 mg and 60 mg) of the same drug product (Drug Product A). The discussion of generic entry that follows only relates to the 60 mg product. The brand-name company sued each generic applicant over the same patent in different district courts. The first generic applicant on the 30 mg product obtained a district court decision of non-infringement and the Federal Circuit affirmed this decision. The 60 mg generic applicant entered once the Federal Circuit affirmed the district court's decision of non-infringement on the 30 mg product. This occurred, however, before the district court reached a decision on the litigation involving the 60 mg generic applicant's litigation.

In the eighth case involving a drug product that was covered by the same patent that covered Drug Product A (described above), the generic applicant also entered prior to a district court decision. Like the 60 mg generic applicant, the first applicant for this drug product also entered after the 30 mg decision of non-infringement of Drug Product A was affirmed by the Federal Circuit.

In separate instances involving the drug products Taxol and BuSpar, which are not included in the 22 described above, the generic applicants began commercial marketing without waiting for a district

[20] In the other 14 cases (22 less 8), either the district court had not ruled as of June 1, 2002 and the FDA has not yet approved the ANDA, or the district court ruled and the FDA acted accordingly, depending upon the outcome of the litigation.

[21] In addition to these 2 instances, generic applicants for 3 other drug products entered after a district court case, but prior to the Federal Circuit's ruling. In these cases, however, the 30 month stay had not expired before the district court ruled.

court decision in their favor on the patent the brand-name companies had listed in the Orange Book after the generic applicants had filed their ANDAs.[22] In both cases the district court eventually held the patent to be invalid or not infringed.

[22] *See* Chapter 4 for a full discussion of multiple 30-month stays. Both suits on the later-issued patents raised questions whether the patents should be listed in the Orange Book.

Chapter 3 Settlements Related to Paragraph IV Certifications

Introduction

Certain patent settlement agreements between brand-name companies and potential generic competitors have received antitrust scrutiny in recent years. Parties have debated whether these settlements increased or harmed consumer welfare.

Patent settlements can resolve disputes in whole, or in part, and in a timely manner. Public policy favors the use of settlements to reduce the use of limited judicial resources. Moreover, settlements may provide for generic entry that might otherwise be delayed by patent disputes, and can reduce uncertainty by clarifying intellectual property rights among the parties. Thus, patent settlements can be procompetitive. This potential is not always fulfilled, however. As noted earlier, the FTC has alleged that certain settlements between brand-name and generic companies were anticompetitive.

This chapter describes the contours of agreements that settled patent litigation between brand-name companies and generic applicants concerning patents listed in the Orange Book for the drug products this study covers.[1] The chapter discusses trends concerning the settlements produced in the study, and describes similarities and differences among such settlements. It also describes how these settlements compare to the ones that the Commission alleged to be anticompetitive in its enforcement actions. This chapter does not reach any conclusions about the competitive effects of the settlements produced.

Twenty final[2] and 4 interim[3] agreements that settled litigation between the brand-name company and the first generic applicant were produced in response to the FTC's special orders. In 9 of the final settlement agreements, the brand-name company agreed to pay the generic applicant (a "brand payment"). In 7 of the 20 final settlements, the brand-name company granted a license to the generic applicant to use the patents that cover the brand-name drug product prior to patent expiration so that the generic applicant could market under its ANDA. Two of the final settlements allowed the generic applicant to distribute the brand-name drug product as a generic product, marketed under the brand-name company's NDA, not the generic applicant's own ANDA. The remaining 2 final settlements do not fit into any of these 3 categories of settlement types.

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[1] Brand-name and generic companies produced a range of other types of agreements relating to the drug products included in the study. These agreements are not discussed in this report.

[2] One of these agreements is subject to litigation currently pending at the FTC. *See Schering-Plough Corp., et al.*, Docket No. 9297, Initial Decision (Jul. 2, 2002), *available at* <http://www.ftc.gov/os/2002/07/scheringinitialdecisionp1.pdf>.

[3] For 3 out of the 4, see *Abbott Laboratories*, No. C-3945 (May 22, 2000) (consent order), *available at* <http://www.ftc.gov/os/2000/03/abbott.do.htm> (this consent order related to 2 drug products: Hytrin tablets and Hytrin capsules). *Hoechst Marion Roussel, Inc.*, No. 9293 (May 8, 2001) (consent order), *available at* <http://www.ftc.gov/os/2001/05/hoechstdo.pdf>.

Fourteen of the final settlements with the first generic applicants, at the time they were executed, had the potential to delay the triggering of the first generic applicant's 180-day exclusivity for some period of time, and thus to delay FDA approval of any subsequent eligible applicants.[4] This potential to delay the triggering of the 180-day exclusivity existed because the settlement contained a waiting period before which the generic applicant could enter the market. All of the waiting periods expired at some time either before the patent(s) expired or at patent expiration. Ten brand-name companies and 10 generic companies used agreements with respect to 14 drug products. *See* Chapter 5 for a further discussion of 180-day exclusivity.

Most of the final settlements with brand payments involved drug products with higher sales than the drug products that the brand-name companies chose to license or supply to generic applicants. Final settlements with brand payments have been used by 7 brand-name companies (of which two companies had 2 such agreements) and 8 generic companies (one of which was a party to 2 agreements).

In addition to the final settlements with the first generic applicant, in 7 instances, brand-name companies entered final patent settlements with the second generic applicant. In 6 of the 7, the brand-name company also had settled with the first generic applicant.

Finally, in 6 instances (out of the 53 resolved cases noted in Chapter 2), the first and second generic applicants entered into agreements with each other that related to generic market entry. Most involved either relinquishing the 180-day exclusivity or determining which generic company had rights to the 180-day exclusivity in light of agreements between the first generic applicant and the brand-name company.

Scope of Information Requested and Received

The FTC's special orders required each brand-name company to submit all agreements between itself and any person relating to an ANDA containing a paragraph IV certification involving any drug product, when the brand-name company holds the rights to the NDA corresponding to the ANDA that is the subject of the agreement. Examples of such agreements include, but are not limited to: (a) patent litigation settlements; (b) agreements related to the filing (or non-filing) of an ANDA by any applicant (or potential applicant) involving any drug product; (c) licensing agreements between the company and persons that have filed an ANDA involving any drug product; and (d) agreements related to any acquisition, divestiture, joint venture, alliance, license, or merger by the company of any business involving the research, development, manufacture, or sale of any drug product that is the subject of an ANDA. The companies were also requested to produce all studies, surveys, analyses, and reports prepared by or for any officer(s) or director(s) of the company (or, in the case of unincorporated entities, individuals exercising similar functions) that evaluate or

[4] Whether the FDA actually was prevented from approving subsequent eligible generic applicants depends on specific facts, including whether there were subsequent generic applicant(s) and the result(s) of any patent litigation with those applicants.

analyze the reasons for making such agreements. Generic companies received similar requests.

Brand-name and generic companies produced a variety of other agreements relating to the drug products subject to the study. Examples of these agreements include brand-name and generic companies obtaining third-party arrangements for the supply of raw materials, manufacturing, repackaging, distribution, marketing, development, and license of formulation technologies relating to the drug products. These agreements are not analyzed in this chapter.

Overview of Patent Settlements

As discussed in Chapter 2, litigants reached agreements that finally settled patent suits involving 20 out of 53 drug products for which a brand-name company sued the first generic applicant who had filed an ANDA containing a paragraph IV certification (*see* Figure 2-1).

For 9 drug products, the brand-name company and the generic applicant settled the patent infringement litigation through a license or supply agreement.[5] Six of these agreements occurred in 2000 and 2001. For 9 other drug products, one component of the settlement agreement was a payment from the brand-name company to the generic applicant. The existence of brand payment provisions distinguished these agreements from those involving a license or supply arrangement, which did not contain a brand payment.[6] The remaining 2 of the 20 settlements did not fit into either of these categories. Table 3-1 categories these 20 final settlements.

Settlements Involving Patent Licenses or Supply Arrangements

In light of the confidential nature of many of the provisions of these settlements, the following discussion has been written to ensure anonymity. Each lettered drug product corresponds to a distinct brand-name drug product.

[5] Two different generic applicants were the first to file on different strengths of the same drug product. The brand-name company settled the litigation with both applicants (one settlement was a license agreement and the other was a supply agreement). Because the different strengths are covered by only one NDA, the drug product is counted only once as a "supply agreement" to ensure consistency in counting drug products with agreements.

[6] Two district court decisions have examined the use of brand payment provisions in the settlement agreements involving Cardizem CD and Hytrin. Both courts have found the agreements to be *per se* restraints of trade under Section 1 of the Sherman Antitrust Act. *In re Cardizem CD Antitrust Litigation*, 105 F.Supp.2d 618, 684 (E.D. Mich. 2000) and 105 F.Supp.2d 618, 622 (E.D. Mich. 2000); *In re Terazosin Hydrochloride Antitrust Litigation*, 164 F.Supp.2d 1340, 1342 (S.D. Fl. 2000). Both of these district court decisions are currently on appeal.

Table 3-1 Overview of Final Settlements with the First Generic Applicant

Type of Agreement	Number of Drug Products	Net Sales	Number of Brand-Name Companies	Number of Generic Applicants
License Agreements	7	Less than $100 million = 3 Between $100 and $250 million = 4; Between $250 and $500 million = 0; Greater than $500 million = 1	6 (two had 2 agreements)	7 (one had 2 agreements)
Supply Agreements	2	Between $250 and 500 million = 1; Greater than $500 million = 1	2	2
Agreements with Brand Payments	9	Less than $100 million = 3 Between $100 and $250 million = 2; Between $250 and $500 million = 2; Greater than $500 million = 2	7 (two had 2 agreements)	8 (one had 2 agreements)
Other	2	Less than $100 million = 1 Between $100 and $250 million = 1	2	2
Total	**20**	**N/A**	**11 (3 had 2 agreements each, 2 had 3 agreements each, and 1 had 4 agreements)**	**14 (3 had 2 agreements each, and 2 had 3 agreements)**

Settlements Involving Patent Licenses

As discussed in Table 3-2, for 8 drug products,[7] the generic applicant obtained a non-exclusive, royalty-bearing license (except for drug product F, which was an exclusive license, and drug product H, which was royalty-free) to use the brand-name company's patents for the particular brand-name product prior to the patent expiration. In 4 instances (B, C, D, and G), generic entry proceeded immediately after executing the settlement and obtaining FDA approval. In the other 4 instances (A, E, F, and H), the parties agreed to a waiting period before the generic applicant could enter.

[7] Although 8 drug products involved licenses with the first generic applicant, the generic applicant for drug product G was first for only one strength of the product. At the time the brand-name company entered into this license, it had already entered a supply agreement, *see* discussion in the following section, with the first generic applicant for another strength of the drug product. *See* supra n. 5. For purposes of Table 3-2, this license agreement is discussed separately.

Table 3-2 Settlement Agreements Involving Patent Licenses

Drug Product	Time Between Agreement Date and Patent Expiration	Effective Date of the License	Brand-Name Products' Annual Net Sales in the Year Prior to the Agreement	Royalties Paid by the Generic Company to the Brand-Name Company for the License Agreement
A	15 years, 2 months	7 months after date of agreement.	Less than $100 million	1.5% of sales for 5 years.
B	13 years, 10 months	Immediately	Between $100 and $250 million	$1 million at signing. $500,000 when the FDA approves the generic product; $1.5 million if generic company sells its product prior to another entity having sold a generic version of the product; and an additional payments of $500,000 if the generic company is the sole company selling a generic version of the product at certain future dates.
C	15 years, 8 months	Immediately	Less than $100 million	A license fee of $3 million plus a royalty of 3.0% of net sales for first 6 years of sales; $1 million when the suit is dismissed; and $1 million at the first and second anniversaries of the shipment of the generic product.
D	5 years, 2 months	Immediately	Between $100 and $250 million	$2.5 million upon dismissal of litigation.
E	2 years, 6 months	15 months after date of agreement.	Between $100 and $250 million	The generic company's royalty payment is 20% of generic company's first $15 million in net sales, 40% of net sales between $15 and $30 million; and 60% of net sales greater than $30 million.
F	3 years, 6 months	17 months after date of agreement.	Between $100 and $250 million	A royalty payment of 7.5% of the generic company's net sales for months 21 through 15 prior to expiration of patents, 5% royalty of net sales for months 14 through 8, and 2.5% of net sales for months 7 through end of patent term.
G	10 years, 5 months	Immediately	Less than $100 million	No royalty payment unless generic company changes its formulation, then it must pay a 5% royalty.
H	1 year, 11 months	14 months after date of agreement.	Between $500 and $750 million	Royalty-free license.

In 4 instances (A, E, F, and H), there was only one generic applicant for the drug product. The brand-name company did not sue the second generic applicant for 3 drug products (B, C, and D) as of June 1, 2002. The brand-name company sued the second generic applicant for drug product G, and this litigation settled.

Table 3-2 describes the attributes of

these 8 patent license agreements and the royalty provisions in each. The licenses were for formulation or method of use patents. In each case, except for drug product D, the generic applicant affirmed the validity and enforceability of the patent(s) at issue. None of the license agreements prohibited the generic applicant from developing non-infringing generic versions of the brand-name drug product, nor did they involve licenses for other products other than the one subject to the ANDA litigation.

Among the license agreements described in Table 3-2, the four agreements with waiting periods (A, E, F, and H) related to brand-name drug products in which there was not yet a second generic applicant for the drug product as of January 1, 2001.

Settlements Involving Supply Agreements

As part of two settlements, the brand-name company entered into a supply agreement that allowed the generic applicant to market the brand-name company's product as a generic product. These agreements differ from the licenses described above because the generic applicant distributes the brand-name company's drug and does not sell product pursuant to its ANDA.

- In one of the supply agreements, generic marketing did not begin until *a subsequent* generic applicant was ready to ship its product to customers. Annual net sales for this drug product in the year prior to the agreement date were over $500 million. The district court had not yet ruled in the brand-name company's patent infringement suit against subsequent generic applicants when the supply agreement with the first generic applicant was executed. Under the agreement, if the patent litigation with these subsequent applicants resulted in the patent being declared invalid or not infringed, then the brand-name company's obligation to supply the first generic applicant would be triggered.[8] The patents at issue were formulation patents, and the time difference between the agreement date and patent expiration was 14 years and one month.

- In the other supply agreement, the generic applicant agreed to pay a substantial royalty to distribute exclusively a generic version of the brand-name product manufactured by the brand-name company.[9] Alternatively, the generic company could choose a patent license agreement (similar to those discussed above) in exchange for a small royalty on net sales. The agreement is dated 10 years, 9 months before the formulation/method of use patent was due to expire.

Miscellaneous Agreements with the First Generic Applicant

Two additional agreements did not appear to raise issues related specifically to Hatch-Waxman. For example, one of the agreements settled litigation over when the

[8] The supply agreement sets forth the transfer price at which the generic company is obligated to purchase all of its requirements. The generic applicant is required to pay a 50% royalty of the net profits from all sales of the generic product.

[9] The supply agreement was for not only the strength of the drug product for which the generic company was the first ANDA IV filer, but also for two additional strengths of the same drug product for which it had not filed an ANDA with a paragraph IV certification.

brand-name company's patent should expire. These agreements are not discussed in this report.

Final Settlements Involving Brand Payments

Nine out of 20 final settlements between brand-name companies and generic applicants involved brand payments from the brand-name company to the generic applicant. The first such agreement included in the study was executed in March 1993.

The Basic Model

Eight of the 9 agreements with brand payments followed the same basic model. Each prohibited the generic applicant from purchasing, manufacturing, using, selling, distributing, and shipping to third parties any form of the generic's drug product until the expiration of the patents (or in 2 cases, until the end of waiting period specified in the agreement, which occurred prior to patent expiration).

Four of these settlements also prohibited the generic applicant from marketing *any* other form of the brand-name company's drug product, which was the subject of the ANDA, prior to patent expiration or the waiting period established in the agreement. These four settlements involved formulation or method of use patents.

Two of the settlements included licenses for drug products other than one subject to the ANDA litigation.[10]

These 8 settlements each had the effect of precluding FDA approval of the generic applicant's ANDA until patent expiration or, in 2 cases, until the date specified in the agreement. Each also had the further effect of precluding the FDA, for the duration of the agreement, from approving a later-filed ANDA with a paragraph IV certification for the same brand-name drug product, unless a second (or later) generic applicant obtained a court decision of non-infringement or invalidity. None of these 8 agreements contained a provision that prohibited the generic applicant from relinquishing the 180-day exclusivity.

As described in Table 3-3, the range of brand payments was $1.75 million to $132.5 million, and the time between the date of agreement and patent expiration ranged between 4 months and 10 years.

[10] For a discussion of one of these agreements, see *Schering-Plough Corp.*, *supra* n. 2.

Table 3-3 Settlement Agreement with Brand Payments: Basic Model

Drug Product	Total Brand Payment from Brand-name Company to Generic Applicant	Time Between Agreement Date and Patent Expiration	Brand-Name Company's Annual Net Sales in Year of Agreement
I	$132.5 million (in part to settle additional patent litigation)	1 year, 9 months	Greater than $1 billion
J	$72.5 million paid in four installments of increasing amounts	4 years, 1 month	Between $250 and $500 million
K	$66.4 million in a lump sum (includes payments to ANDA filer and its raw material manufacturer)	9 years, 5 months	Less than $100 million (year after agreement)
L	$60 million (includes fees for licenses to other products)	4 years, 3 months*	Between $100 and $250 million (year after agreement)
M	$49.1 million, plus optional annual payments for 6 years of at least $50 million in lieu of a supply agreement	6 years, 11 months	Between $750 million and $1 billion
N	$22 million paid in 2 installments (plus $2.5 million per month beyond the 4th month if certain events occur)	4 months	Between $250 and $500 million
O	An 8.5 percent royalty fee of the brand-name company's sales of the product during the first and second year of the 2.5 year period (based on sales of the first year, the payment was approximately $5 million), a 7.5 percent royalty fee for the remaining 6 months of the 2.5 year period.	2 years, 6 months*	Less than $100 million
P	$1.75 million divided in three equal installments.	10 years	Less than $100 million

* Time between agreement date and generic entry allowed under the agreement. In each case generic entry was permitted prior to patent expiration pursuant to a license.

Additional Conditions: These 8 final agreements included additional conditions. For example, in most of the agreements, the generic applicant agreed not to cause, aid, assist others in the purchase, manufacture, use, sale of a generic version of the drug product prior to patent expiration or the date the patent is held invalid by a court of competent jurisdiction and the decision becomes final. Another frequent provision was that the generic applicant not aid or assist any third party in the preparation, filing, or processing of an application for a generic version of the drug product, including the sharing of any information obtained through the litigation.

Timing of Settlements: The agreements were entered at various times in relation to whether a court had ruled on the underlying patent infringement lawsuit. A court had not yet ruled on the merits of the patent infringement suit for 4 drug products. For the other 4 drug products, a district court had ruled on the merits of the brand-name company's infringement claims as follows: (1) the district court held the patent invalid on summary judgment, but the Federal

Circuit reversed and remanded for trial on certain factual issues; (2) the district court held the patent invalid, but the parties settled and the lower court's decision was then vacated; (3) the district court denied the brand-name company's summary judgment motion of infringement, thus indicating triable issues of fact remained; and (4) the brand-name company obtained a temporary restraining order prohibiting the generic applicant's sale of the drug product.

Optional Licenses: The brand-name company for one drug product had the option of granting the generic company a non-exclusive, royalty-free license for the underlying patent rather than making the brand payments to the generic applicant. If the license had been granted, the generic applicant would have been able to seek approval of its ANDA and brand payments would have stopped. The brand-name company did not exercise this option.

Optional Supply Agreements: Three of the final settlements in Table 3-3 involved optional supply agreements under which the generic applicant would distribute the brand-name product as a generic. For 2 of these drug products, the supply agreements were implemented. For the other product, the supply agreement was not implemented. These 3 supply agreements are described below.

The supply agreement involving one drug product specified that the brand-name company would supply brand-name product to foreign affiliates of the generic applicant for marketing outside the United States during the 6-month period prior to patent expiration.

Under the supply agreement involving another drug product, the brand-name company appointed the generic applicant as the non-exclusive distributor for the sale of the product under a private label at a cost to the generic applicant equal to 75% of the brand-name company's wholesale druggist price. The generic applicant used this supply agreement to market the brand-name company's product as a generic product.

The brand-name company of the third drug product entered into an agreement, not implemented, to supply the generic applicant with the drug to sell as the generic version; the agreement prohibited the generic applicant from manufacturing the product drug itself. This agreement specified the generic's resale price at a limited discount (15% to 30%, based on certain contingencies) off the brand-name drug product's price. The brand-name company was to receive substantial royalties from the generic company's sales of the product (40% to 33.3%, based on when the royalty was paid).

Alternatively, this brand-name company could decide to make quarterly payments to the generic applicant instead of fulfilling the supply agreement. The payment schedule, which continued until expiration of the patent, provided for total annual payments of at least $50 million. The agreement guaranteed the generic company the right to enter the market with a generic version of the product (under the NDA) either 6 months prior to patent expiration, or immediately upon the patent being declared invalid or unenforceable. Because the supply agreement was not implemented, the brand-name company

made the brand payments to the generic applicant.

Miscellaneous Final Agreement with Brand Payments

A ninth final agreement involved brand payments, but did not fit into the basic model described above. In this case, the parties agreed to terminate the 30-month stay and allow the generic applicant's ANDA to be approved soon thereafter. Prior to executing the settlement agreement, the two companies had been involved in commercial patent infringement litigation over the brand-name drug product (and another related drug product) that the generic company had initiated. The parties settled that litigation, entering into an agreement with cross-royalty provisions. One of the cross-royalty provisions provided the generic company with a 1 percent royalty on net sales of the brand-name drug product. Thus, the brand payment was in the form of a royalty on the brand-name drug company's drug product.

Final Agreements with the First Generic Applicant that Could "Park" the Applicant's 180-Day Exclusivity

Fourteen of the 20 settlements obtained through the study, at the time they were executed, had the potential to "park" the first generic applicant's 180-day exclusivity for some period of time, and thus to prevent FDA approval of any subsequent eligible applicants. Whether the FDA actually was prevented from approving subsequent eligible generic applicants depends on specific facts, including whether there were subsequent generic applicant(s) and the result(s) of any patent litigation with those applicants.

These agreements include the 4 license agreements with waiting periods (drug products A, E, F, and H in Table 3-2), the 2 supply agreements, and settlements with brand payments (drug products I through P in Table 3-3) that had the effect of precluding FDA approval of the generic applicant's ANDA. Ten brand-name companies and 10 generic companies used agreements with respect to the 14 drug products. Chapter 5 discusses how these settlements could be used to delay FDA approval of any subsequent eligible generic applicants.

Interim Agreements

In addition to the 20 final settlements, 4 interim settlements with the first generic applicant were produced. The interim settlements did not resolve the underlying patent litigation, but were contingent upon the outcome of the litigation. The FTC has taken law enforcement actions relating to 3 of these drug products.[11] The FTC's actions relating to 2 of those agreements, involving Hytrin tablets and capsules, are described in Box 3-1. No settlements similar to the interim settlements challenged by the Commission were executed after April, 1999 (shortly after the FTC's investigations in this area became public) and the end of the period covered by this study.

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[11] *See supra*, n. 3. The FTC's action regarding Hytrin involved two drug products (Hytrin capsules and Hytrin tablets).

Box 3-1 Summary of the Commission's Action in the Abbott/Geneva Matter

In May 2000, the Commission issued a complaint and consent order against Abbott Laboratories and Geneva Pharmaceuticals, Inc. The complaint charged that Abbott paid Geneva approximately $4.5 million per month to keep Geneva's generic version of Abbott's Hytrin, in both tablets and capsules, off the U.S. market, potentially costing consumers hundreds of millions of dollars a year. Hytrin is used to treat hypertension and benign prostatic hyperplasia (BPH or enlarged prostate) - chronic conditions that affect millions of Americans each year. BPH alone afflicts at least 50% of men over 60. In 1998, Abbott's sales of Hytrin amounted to $542 million (over 8 million prescriptions) in the United States. Abbott projected that Geneva's entry with a generic version of Hytrin would eliminate over $185 million in Hytrin sales in just six months.

According to the complaint, Geneva agreed not to enter the market with any generic version of Hytrin, even if it were non-infringing, until the earlier of: (1) the final resolution of the patent infringement litigation involving Geneva's generic version of Hytrin tablets, including review through the U.S. Supreme Court; or (2) entry of another generic Hytrin product. Geneva also agreed not to transfer, assign, or relinquish its 180-day exclusivity right. These provisions ensured that no other company's generic version of Hytrin could obtain FDA approval and enter the market during the term of the agreement, because Geneva's agreement not to launch its product meant the 180-day exclusivity period would not begin to run.

Under the Commission's consent order, Abbott and Geneva are barred from entering into agreements pursuant to which a first-filing generic company agrees with a manufacturer of a branded drug that the generic company will not (1) give up or transfer its exclusivity or (2) bring a non-infringing drug to market. In addition, agreements to which Abbott or Geneva is a party that involve payments to a generic company to stay off the market must be approved by the court when undertaken during the pendency of patent litigation (with prior notice to the Commission), and the companies are required to give the Commission 30 days' notice before entering into such agreements in other settings. Moreover, Geneva was required to waive its right to a 180-day exclusivity period for its generic version of Hytrin tablets, so other generic tablets

The fourth interim agreement involved a brand-name drug that had net sales of over $1 billion per year in the year before the settlement was executed. The settlement was entered at approximately the same time the 30-month stay had expired. To ensure that the generic drug applicant did not begin commercial marketing until the district court ruled on the patent infringement claims, the brand-name company agreed that, if the patent was found invalid, the brand-name company would pay the generic applicant based on the generic applicant's lost profits from the date of the expiration of the 30-month through appeals. Since the date of this agreement, generic entry has occurred because of a court decision.

Agreements Between Brand-Name Companies and the Second Generic Applicant

Brand-name companies settled patent litigation with the second generic applicant for 7 drug products, out of a total of 43 suits against the second generic applicant (*see* Chapter 2) – or at a rate of 16 percent. This settlement rate is substantially lower than the settlement rate between brand-name companies and the first generic applicant of 38 percent (20 of 53 total lawsuits against the first generic applicant settled). In 6 of the 7 instances, the brand-company had also entered into a patent settlement with the first generic applicant.

One of the 7 settlements involved brand payments. The agreement specified that the brand-name company would make brand payments up to $15 million, and that entry by the second generic could not occur until 5 years and 6 months after the date of the agreement (or 2 years and 9 months before patent expiration).

Four of the 7 agreements involved patent licenses that allowed the second generic applicant to enter the market prior to patent expiration using the generic version of the brand-name drug product approved through its ANDA. In 2 of these instances, the second generic applicant was allowed to market its generic product immediately after executing the agreement, obtaining FDA approval, and paying the brand-name company a royalty.

In 1 of the 4 instances, the license agreement prohibited the generic applicant from introducing its product into the market until the brand-name company or another licensee marketed a generic version of the brand-name company's generic product. The brand-name company also entered a license agreement with the third generic applicant for the drug product, specifying that it could come on the market 4 years and 2 months prior to patent expiration.

In the remaining license agreement, the parties agreed to cross-license related products in settlement of not only the patent infringement litigation in response to the ANDA that had been filed, but also related infringement litigation involving another drug product.[12]

Agreements Between First and Second Generic Applicants

For 6 out of 68 drug products in which there was more than one generic applicant, the first and second generic applicants entered into agreements related to generic market entry. In 4 of these agreements, one of the main provisions specified which generic applicant had or retained rights to the 180 day exclusivity.[13] The other two agreements did not focus on the 180-day exclusivity provision.

Agreements Focusing on 180-Day Exclusivity: In 1 agreement, the first generic applicant relinquished its rights to 180-day exclusivity for a $3.5 million license and royalty payment based on the second generic applicant's sales for a period of 7 years. In another agreement, the first and second generic applicants entered into a supply arrangement under which the first generic applicant relinquished its rights to 180-day exclusivity so that the second generic applicant's ANDA could be approved, and the first applicant could market the second applicant's product. This step was necessary because the first generic applicant's ANDA was not ready to be approved at the time of the agreement.

Two other agreements clarified

[12] The other 2 of the 7 settlements with the second generic applicant did not appear to raise issues related specifically to Hatch-Waxman.

[13] For a fuller discussion of the 180-day exclusivity, *see* Chapter 5, n. 18 and accompanying text.

which generic applicant had rights to the 180-day exclusivity in light of a settlement agreement between the first generic applicant and the brand-name company. In one case, the first generic applicant changed its patent certification from a paragraph IV to a paragraph III, and the agreement settled a dispute between the first and second generic applicant regarding whether the first generic applicant retained its 180-day exclusivity in those circumstances. In the other case, the agreement related to a drug product that had been the subject of one of the court cases that invalidated certain of the FDA's rules governing the 180-day exclusivity.[14]

Remaining Agreements: The other 2 agreements involve more detailed relationships between the first and second generic applicants. In one instance, the brand-name company had licensed its patents to an over-the-counter product to the first generic applicant, with a right to sublicense the patents. The first generic applicant granted the sublicense to the second generic applicant. In the second agreement, the first and second generic applicants allegedly entered into a supply and distribution agreement that unreasonably restrained their incentives to compete against each other.[15]

[14] *Granutec Inc. v. Shalala*, 139 F.3d 889(4th Cir. 1998).

[15] *See* FTC, In the Matter of Biovail Corp. and Elan Corp., File No. 011 0132, Agreement Containing Consent Order, *available at* <http://www.ftc.gov/os/2002/06/biovailelanagreement.pdf >.

Chapter 4 Orange Book Patent Listing Practices and Use of Multiple 30-Month Stays

Introduction

The 30-month stay provision of the Hatch-Waxman Amendments protects brand-name companies beyond their existing intellectual property rights. A 30-month stay of FDA approval of a potential generic competitor is invoked if a brand-name company receives notice of a generic applicant's paragraph IV certification and files suit for patent infringement within 45 days of that notice. Filing of the lawsuit stays the FDA's approval of the ANDA until the earliest of: (1) the date the patents expire; (2) a final determination of non-infringement or patent invalidity by a court in the patent litigation; or (3) the expiration of 30 months from the receipt of notice of the paragraph IV certification. The 30-month stay affords both the brand-name company and the generic applicant the opportunity to resolve patent disputes prior to commercial marketing, and in tandem with FDA review of the ANDA for approval.

The 30-month stay has received increased attention, because it can have a significant impact on market entry by generic drugs. One 30-month period to resolve disputes over patents listed in the Orange Book prior to the ANDA's filing date appears unlikely to delay generic entry, however, because it historically has approximated the time necessary for FDA review and approval of the ANDA and the duration of a patent lawsuit. FDA approval of generic applicants that filed paragraph IV certifications and were not sued took, on average, 25 months and 15 days from the filing date. On average, the time between the complaint and a district court decision in litigation between a brand-name company and first or second generic applicants was 25 months and 13 days. The average time between the complaint and an appellate decision was 37 months and 20 days.

Prior to 1998, litigation between a brand-name company and a first or second generic applicant generated, at most, one 30-month stay per drug product per ANDA, except for two drug products. For 8 out of the 9 "blockbuster" drug products (*i.e.*, drug products that are among the top 20 drug products, ranked publicly by annual gross sales, during one of the years included in the study) as to which the brand-name company filed suit against the first generic applicant prior to 1998, the brand-name company alleged infringement of 1 or 2 patents. In the remaining case, the brand-name company alleged infringement of 3 patents.

Since 1998, however, two new phenomena appear to be emerging. First, for drug products with substantial annual net sales, brand-name companies are suing generic applicants over more patents. Since 1998, for only 3 of the 8 "blockbuster" drug products as to which the brand-name company filed suit against the first generic applicant, the brand-name company alleged infringement of 1 or 2 patents. In the remaining 5 instances, the brand-name company alleged infringement of 3 or more

patents. With additional patents to be litigated, the average time to obtain a court decision has increased. As of June 1, 2002, for 6 of the 7 cases that have been pending for more than 30 months without a decision from a district court, the brand-name company has alleged infringement of 3 or more patents.

Second, by the timely listing of additional patents in the Orange Book *after* a generic applicant has filed its ANDA (later-issued patents), brand-name companies can obtain additional 30-month stays of FDA approval of the generic applicant's ANDA. Although the generic applicant had already certified to the patents previously listed in the Orange Book for a particular drug product, it must re-certify to the newly listed patent(s) and notify the brand-name company of its re-certification. If the brand-name company sues for patent infringement on the new certification within 45 days of notification, a new 30-month stay will begin to run. The FDA is prohibited from approving the ANDA until the new 30-month stay expires.

In 8 instances, brand-name companies have listed later-issued patents in the Orange Book after an ANDA has been filed for the drug product. For the 8 drug products, the additional delay of FDA approval (beyond the first 30 months) ranged from 4 to 40 months. In all of the 4 cases so far with a court decision on the validity or infringement of a later-issued patent, the patent has been found either invalid or not infringed by the ANDA.

Moreover, most of the later-issued patents in the Orange Book raise questions about whether the FDA's patent listing requirements have been met. For example, many of the later-issued patents do not appear to claim the approved drug product or an approved use of the drug. Recent court opinions hold that Hatch-Waxman does not provide a right of action through which generic applicants may challenge a patent listing in the Orange Book. Thus, to terminate a second 30-month stay, a generic applicant's only recourse is to obtain a decision of a court on patent infringement or invalidity.

This chapter sets forth the legal and regulatory background of the 30-month stay provision, including a discussion of the patent listing requirements. It then reviews the patent-related information requested from brand-name company and generic companies. For each NDA that was within the scope of the study, brand-name companies were required to identify all patents that the company has listed in the Orange Book and the date of listing (regardless of whether currently listed in the Orange Book).[1] This information provides the basis for an examination of the patents that led to the granting of multiple 30-month stays. Generic companies were required to provide information on instances in which they alleged that a patent had been improperly or untimely listed in the Orange Book. This information was used to identify any trends in the patent listings.

[1] Many brand-name companies noted that they could only provide information about when they had submitted the patent to the FDA for Orange Book listing rather than the date on which the patent was actually listed.

Legal and Regulatory Background of the 30-Month Stay Provision

As part of the FDA process to obtain approval of a new drug product under Hatch-Waxman, brand-name companies must submit information on any patent claiming the approved drug and for which a claim of patent infringement could reasonably be asserted. The FDA then lists the approved drug and its related patents in the Orange Book. Box 4-1 describes how patents are obtained and how the pharmaceutical industry uses them. A generic applicant, as part of the ANDA process, must provide a certification to the FDA regarding its generic product and any patents listed in the Orange Book that claim the brand-name drug. When a generic applicant makes a paragraph IV certification, it claims that the patents listed in the Orange Book either are invalid or will not be infringed by the manufacture, use, or sale of the generic drug product for which the ANDA is submitted. Frequently, a generic applicant will make multiple certifications in its ANDA, depending upon the number of patents listed in the Orange Book. For example, a generic applicant may make a paragraph III certification (indicating that it will not begin commercial marketing until that patent expires) for a brand-name drug product's drug substance patent, but also make paragraph IV certification(s) with respect to listed method of use and/or formulation patents.

The Hatch-Waxman Amendments further provide that each generic applicant making a paragraph IV certification must notify each patent owner and the brand-name company for the listed drug. If the patent owner and/or brand-name company do not initiate a patent infringement suit within 45 days after receiving notice of a paragraph IV certification, then the FDA's review and generic approval process may proceed according to the FDA's schedule. If, however, a patent infringement suit is filed within the 45-day window, the FDA's approval of the ANDA is automatically stayed until the earliest of: (1) the date the patents expire; (2) a final determination of non-infringement or patent invalidity by a

Box 4-1 Patents and Patentability

A patent is the grant of a right to exclude others from "making, using, offering for sale, or selling" an invention. U.S. patent laws are enacted pursuant to Article I, Section 8 of the U.S. Constitution, which states that Congress shall have the power "[t]o promote the Progress of Science and useful Arts, by securing for limited times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."

There are three basic types of patents: utility, plant, and design patents. Utility patents generally have a term of 20 years from the date on which the application for the patent was filed. Utility patents are divided into three basic categories: chemical, electrical and mechanical. Pharmaceutical patents are a subset of chemical patents and are issued over four different categories: drug substance, method of use, formulation, and process. Drug substance patents cover the compound or active ingredient in the drug product, such as fluoxetine hydrochloride, which is the active ingredient in Prozac. Method of use patents cover the use of the product to treat certain health problems, such as depression or asthma. Formulation patents cover the physical composition or delivery mechanism of the drug product, such as an extended release tablet or capsule. Process patents generally cover the procedure used to make the active ingredient.

To be patentable, an invention must be new and useful, as well as non-obvious. The Patent Office determines novelty by searching prior patents and publications. The patent must also contain a written description to "enable any person skilled in the art to which it pertains . . . to make and use" the invention. Non-obviousness is determined in light of the prior art and involves asking whether a person skilled in the art would consider the invention to be "obvious."

court in the patent litigation; or (3) the expiration of thirty months from the receipt of notice of the Paragraph IV certification.

The initial 30-month stay is not dependent upon the number of patents for which a paragraph IV certification is made. Whether a generic applicant makes an initial paragraph IV certification with respect to one patent, or to multiple patents, only one 30-month stay will be invoked.

The 30-month stay provision provides the brand-name company an additional exclusionary right beyond those granted by the patent system. Even absent the 30-month stay, a brand-name company may file suit against an accused infringer, such as an ANDA applicant, and prevent the accused infringer from marketing its product by obtaining a preliminary injunction.[2] To obtain a preliminary injunction, a patentee must establish four factors: (1) a reasonable likelihood of success on the merits; (2) irreparable harm if the injunction were not granted; (3) the balance of the hardships, and (4) the impact of the injunction on the public interest.[3]

Patent Listing Statute and Regulations

The Hatch-Waxman Amendments describe the patent information that brand-name companies must file with any new drug application (NDA). Once the FDA approves the drug, it then lists the patents in the Orange Book. Specifically, the listing statute requires that an NDA filer "shall file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the [new drug] application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug."[4]

The FDA has adopted regulations governing the types of patents that can be listed in the Orange Book.[5] The listing regulation is separated into 6 subsections below for ease of reading. Specifically, the brand-name company must list in the Orange Book each patent which:

[1] claims the drug or a method of using the drug that is the subject of the new drug application or amendment or

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[2] *See, e.g., Purdue Pharma L.P., v. Boehringer Ingelheim GMBH*, 237 F.3d 1359, 1363 (Fed. Cir. 2001) (affirming district court's grant of a preliminary injunction blocking marketing of a generic drug product).

[3] Relatively little case law exists to indicate the ease or difficulty for the brand-name company to obtain a preliminary injunction against an ANDA applicant. A few cases do suggest circumstances in which a preliminary injunction may be granted. When a patentee establishes a likelihood of success on the merits, it is entitled to a rebuttable presumption of irreparable harm. For example, when the brand-name company is able to show evidence of price erosion and its expected loss of market share caused by introduction of a competing drug product, or of a generic applicant's likely inability to pay the brand-name company's lost profit damages, a preliminary injunction may be granted. *See, e.g., Purdue Pharma L.P., v. Boehringer Ingelheim GMBH*, 2000 U.S. Dist. LEXIS 6563 (S.D.N.Y. 2000), *aff'd* 237 F.3d 1359, 1363 (Fed. Cir. 2001); *Glaxo Group, Ltd v. Ranbaxy Pharms., Inc.*, 262 F.3d 1333, 1338 (Fed. Cir. 2001) (discussing district court's decision to grant preliminary injunction because generic manufacturer could not pay NDA holder's potential damages); *see* Chisum on Patents, § 20.04(e)(iv) (Matthew Bender).

[4] 21 U.S.C. § 355(b)(1).

[5] 21 C.F.R. § 314.53(b) (the "listing regulation").

supplement to it and

[2] with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use or sale of the drug product.

This portion of the listing regulation, requiring that a listed patent satisfy two independent prongs, is nearly identical to the governing statute, 21 U.S.C. § 355(b)(1), except that the regulation substitutes the term "drug product" for the term "drug" in the second prong. The FDA interprets the term "drug" in the statute's first prong to mean "drug product." A district court has affirmed this interpretation.[6] Thus, it is the drug product,[7] approved through the NDA, that controls the listing analysis of the two prongs ("claims the drug" and "a claim of patent infringement").

The remainder of the listing regulation elaborates on the meaning of the two independent prongs:

[3] For purposes of this part, such patents consist of drug substance (ingredient) patents, drug product (formulation and composition) patents, and method of use patents.

[4] Process patents are not covered by this section and information on process patents may not be submitted to FDA.

[5] For patents that claim a drug substance or drug product, the applicant shall submit information only on those patents that claim a drug product that is the subject of a pending or approved application, or that claim a drug substance that is a component of such a product.

[6] For patents that claim a method of use, the applicant shall submit information only on those patents that claim indications or other conditions of use of a pending or approved application.[8]

Timing of Listing Later-Issued Patents

Brand-name companies may list later-issued patents (*i.e.*, patents obtained from the U.S. Patent and Trademark Office after obtaining NDA approval) so long as they do so within 30 days of being granted the patent.[9] Two scenarios are possible, depending on whether a later-issued patent is listed *prior to* or *after* the generic applicant files its ANDA. If the later-issued patent is listed *prior* to a generic applicant's filing of an ANDA, then the generic applicant will certify regarding that patent along with all the other listed patents. A brand-name company's suit on those patents within 45 days will generate only one 30-month stay, despite the fact that multiple patents are at issue in the litigation.

If, however, the later-issued patent is listed *after* a generic applicant has filed its

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[6] *Pfizer, Inc. v. FDA*, 753 F. Supp. 171 (D. Md. 1990).

[7] The FDA's regulations define "drug product" as "a finished dosage form, for example, a tablet, capsule, solution, etc., that contains an active drug ingredient generally, but not necessarily, in association with inactive ingredients." 21 C.F.R. § 210.3(4).

[8] *Id.*

[9] 21 U.S.C. § 355(c)(2). Of course, a brand-name company can list a patent more than 30-days after issuance; however, pending generic applicants do not have to re-certify to that patent.

ANDA with a paragraph IV certification, then the generic applicant must re-certify that its ANDA does not infringe the later-issued patent. If the brand-name company sues within 45 days of the generic applicant's *re-certification*, then a *second* 30-month stay will issue. Thus, a brand-name company can obtain an additional 30-month stay of FDA approval if it lists patents in the Orange Book *after* notice of an ANDA containing a paragraph IV certification, and then sues for patent infringement upon notice of the generic applicant's re-certification. It is not necessary for the multiple 30-month stays to run consecutively; it is possible for gaps to exist between the multiple 30-month stays. For example, the first stay may have expired without a decision of a court or FDA approval of the ANDA, but a later-issued patent triggers an additional 30-month stay.

Lack of Review of Patents in the Orange Book

The FDA has stated that it lacks the resources and the expertise to review patents submitted with NDAs. The agency does not ensure that a submitted patent claims the approved drug before listing it in the Orange Book.[10] Moreover, the FDA has declined to enact any administrative procedures for resolving listing disputes. If a party disputes the accuracy of a listed patent, it may notify the FDA. The FDA then will request the brand-name company to confirm the correctness of the listed patent information. Unless the brand-name company voluntarily withdraws or amends its listed information, the FDA will not change the patent information in the Orange Book. If the information remains unchanged, generic applicants must certify to the disputed patent.[11] Two courts have upheld this policy.[12]

Several generic applicants have attempted to obtain court orders requiring the FDA or brand-name companies to delist certain patents from the Orange Book. When a patent is delisted, the 30-month stay will not run and, hence, the FDA is free to approve the ANDA, if other regulatory requirements are met. However, two recent court decisions have held that there is no private right of action under Hatch-Waxman.[13]

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[10] 59 Fed. Reg. 50338, 50343 (Oct. 3, 1994) ("FDA does not have the expertise to review patent information. The agency believes that its resources would be better utilized in reviewing applications rather than reviewing patent claims."); Abbreviated New Drug Application Regulations, 54 Fed. Reg. 28872, 28910 (1989) ("In deciding whether a claim of patent infringement could reasonably be asserted . . . the agency will defer to the information submitted by the NDA applicant.").

[11] 21 C.F.R. § 314.53(f).

[12] *See aaiPharma v. Thompson*, 2002 WL 1473429 (4th Cir. Jul. 10, 2002); *Watson Pharmaceuticals v. Henney*, Civil Action No. 00-3516 (D. Md. Jan. 17, 2001).

[13] *Andrx Pharm, Inc. v. Biovail Corp.*, 276 F.3d 1368 (Fed. Cir. 2002); *Mylan Pharm, Inc. v. Thompson*, 268 F.3d 1323 (Fed. Cir. 2001). Nor do the patent laws permit an assertion of improper listing as a defense to patent infringement. *Mylan*, 268 F.3d at 1330-32. The Federal Circuit, however, has suggested that a generic applicant might sue the FDA under the Administrative Procedures Act to compel it to delist a patent and to approve an ANDA subject to a 30-month stay that flows from an improperly listed patent. *Andrx*, 276 F.3d at 1378-79. This suggestion contradicts the FDA's court-approved policy of not reviewing patents submitted with NDAs.

Box 4-2 discusses the BuSpar matter in which these holdings were made.

Box 4-2 Private Parties Have No Right to Seek the Delisting of a Patent in the Orange Book

The issue of whether a generic applicant could seek to delist a patent from the Orange Book was recently addressed in a court decision regarding BuSpar. Bristol-Myers Squibb ("BMS") had listed one patent in the Orange Book relating to buspirone (Patent No. 4,182,763 (the '763 patent)) when it had sought approval of its NDA. This patent was to expire on November 21, 2000.

Prior to expiration of this patent, Mylan Pharmaceuticals, among others, submitted an ANDA with a paragraph III certification, because it sought approval to market buspirone only after BMS's final patent covering BuSpar expired at 12:00 am on November 22, 2000. Only 12 hours before that time, however, the Patent Office issued Patent No. 6,150,365 (the '365 patent) to BMS; BMS immediately submitted the '365 patent to the FDA for listing in the Orange Book. This listing prevented FDA from granting final approval to any pending ANDA, including Mylan's.

Mylan sued BMS in the District Court for the District of Columbia, seeking an order requiring BMS to remove the patent from the Orange Book. The district court allowed the suit and agreed with Mylan that the '365 patent did not claim the drug product. Rather, the court held that the '365 patent claimed the buspirone metabolite, not buspirone itself, because BMS surrendered coverage of buspirone itself in order to convince the patent examiner to allow the patent. *Mylan v. Thompson*, 139 F.Supp. 1, 24-25 (D.D.C. 2001). The district court ordered BMS to delist the patent, which it did on March 28, 2001. This decision allowed generic buspirone to enter the market immediately. At this point, the '365 patent had delayed generic entry for about four months.

BMS appealed, however, and the Court of Appeals for the Federal Circuit reversed, holding that generic applicants have no private right of action to challenge an NDA holder's Orange Book listing as improper. Furthermore, the court ruled that Mylan's delisting suit was not a recognized patent infringement defense, but rather an attempt to assert a private right of action under Hatch-Waxman. *Mylan Pharmaceuticals, Inc. v. Thompson*, 268 F.3d 1323 (Fed. Cir. 2001).

Following this decision, BMS chose not to relist the patent, although BMS continued to sue the generic applicants for patent infringement. *In re Buspirone Patent Litigation*, 185 F.Supp. 2d 363 (S.D.N.Y. 2002). As a result, generic buspirone remained on the market. Had BMS relisted the patent, however, the FDA could have revoked its approval of generic buspirone, thereby extending the effect of the '365 patent beyond the four month delay it initially created.

Immunity From the Antitrust Laws for Listing Patents in the Orange Book

The Commission recently has addressed whether the act of submitting a patent for listing in the Orange Book is immune from the antitrust laws, because it is a form of petitioning the government protected under the *Noerr Pennington* doctrine.[14] As discussed in Box 4-3, the District Court for the Southern District of New York agreed with the Commission's argument that the act of listing patents in the Orange Book is not immune from the antitrust laws.

[14] *In re Buspirone Patent Litigation/In re Buspirone Antitrust Litigation*, Memorandum of Law of Amicus Curiae the Federal Trade Commission in Opposition to Defendant's Motion to Dismiss *available at* <http://www.ftc.gov/os/2002/01/busparbrief.pdf>. The Commission first raised concerns about the potential anticompetitive impact of improper Orange Book listings in *American Bioscience, Inc. v. Bristol-Myers Squibb Co., et al.*, Dkt. No. CV-00-08577 (C.D. Cal. Sept. 7, 2000). *See* Federal Trade Commission Brief as *amicus curiae available at* <http://www.ftc.gov/os/2000/09/amicusbrief.pdf>. In that case, the parties sought court approval of a settlement containing a specific factual finding that Bristol-Myers was required to list American Bioscience's patent for Bristol-Myers's branded drug Taxol in the Orange Book. The Commission was concerned that the court's approval of the settlement would amount to a judicial finding that the patent met the statutory requirements for listing in the Orange Book and would prejudice parties who may later challenge the listing.

Box 4-3 Noerr-Pennington and Orange Book Listings

The *Noerr* doctrine – first articulated as an interpretation of the Sherman Act in *Eastern R.R. Presidents Conf. v. Noerr Motor Freight, Inc.*, 365 U.S. 127 (1961) and *United Mine Workers of America v. Pennington*, 381 U.S. 657 (1965) – provides antitrust immunity for individuals "petitioning" government. Although the *Noerr* doctrine is an important limitation on the antitrust laws that protects the right of individuals to communicate with government entities, some courts have interpreted the doctrine broadly in ways that are inconsistent with Supreme Court precedent. The *Noerr* doctrine was never intended to protect what Robert Bork has characterized as "[p]redation through the misuse of government processes." Robert H. Bork, The Antitrust Paradox: A Policy at War with Itself 364 (Free Press 1993) (1978).

In January 2002, several plaintiffs alleged that, through fraudulent patent filings with the FDA, BMS violated Section 2 of the Sherman Act by causing the FDA to list a patent in the Orange Book to block generic competition with its BuSpar product. In response, BMS moved to dismiss, claiming *Noerr-Pennington* immunity. On February 14, 2002, the court denied BMS's motion to dismiss. *In re Buspirone Patent Litigation/In re Buspirone Antitrust Litigation*, 185 F.Supp.2d 363 (S.D.N.Y. 2002).

The court's decision rejected BMS's claim of *Noerr-Pennington* immunity on three independent and alternative grounds. The first, and perhaps most important, of these grounds was that Orange Book filings simply do not constitute protected "petitioning." The court reasoned that an Orange Book filing is analogous to a tariff filing. In both cases, "the government does not perform an independent review of the validity of the statements, does not make or issue an intervening judgment, and instead acts in direct reliance on the private party's representations." 185 F.Supp.2d at 370. The court also stated that an Orange Book filing is not incidental to petitioning, holding that BMS could have listed its patent in the Orange Book "without subsequently bringing infringement suits . . . [and] could have brought these suits without relying on its Orange Book listing." *Id.* at 372.

The court further concluded that, even if Orange Book filings were to constitute "petitioning," application of two specific exceptions to the *Noerr* doctrine – the *Walker Process* and "sham" exceptions – would preclude a finding of antitrust immunity. Under *Walker Process*, a patent holder may be subject to antitrust liability for attempting to enforce a patent procured through fraudulent misrepresentations to the Patent and Trademark Office ("PTO"). *Walker Process Equipment, Inc. v. Food Machinery & Chemical Corp.*, 382 U.S. 172 (1965). The *Buspirone* court concluded that the Orange Book listing and patent prosecution processes were sufficiently analogous to warrant extension of the *Noerr* exception beyond the PTO context, and that plaintiffs' allegations satisfied *Walker Process*. 185 F.Supp.2d at 372-75.

Under the "sham" exception, the opponent of *Noerr* immunity must demonstrate that defendant's petitioning conduct – in this case, BMS's patent filing with the FDA – was "objectively baseless." *Professional Real Estate Investors, Inc. v. Columbia Pictures Industries, Inc.*, 508 U.S. 49, 60 (1993). After an examination of the prosecution history of BMS's patent, as well as the specification and claims, the *Buspirone* court concluded that the filing was, indeed, "objectively baseless." The court further observed that BMS's argument to the contrary "ignores the law and tries to justify taking property that belongs to the public."

In light of the *Buspirone* decision, and the underlying force of the court's reasoning, the *Noerr-Pennington* doctrine may not prove as large an obstacle to using the antitrust laws to remedy improper Orange Book filings as some may have anticipated. It is worth noting, and indeed emphasizing, that *Buspirone* does not mean that all improper Orange Book filings will give rise to antitrust liability. Any antitrust liability must necessarily be predicated on a clear showing of a violation of substantive antitrust law. But, under *Buspirone*, Orange Book filings are not *immune* from those laws or exempt from their scrutiny.

Definition of a "Court" Decision to Terminate the 30-Month Stay

Once a 30-month stay begins, FDA regulations govern what constitutes a decision of a "court" for purposes of terminating the 30-month stay. These regulations recently have changed. Originally, the FDA interpreted a decision of a "court" to mean "the court that enters final judgment from which no appeal can be or has been taken."[15] The FDA also used this definition of a decision of a "court" when it assessed whether the 180-day exclusivity had been triggered.[16]

In *TorPharm v. Shalala*,[17] the

[15] 21 CFR 314.107(e)(1) (1999).

[16] *See* Chapter 5 for further discussion of the 180-day exclusivity.

[17] TorPharm, Inc. v. Shalala, No. 97-1925, 1997 U.S. Dist. LEXIS 21983 (D.D.C. Sep. 15, 1997), *appeal withdrawn and remanded*, 1998 U.S. App. LEXIS 4681 (D.C. Cir. Feb. 5, 1998); *vacated* No. 97-1925 (D.D.C.

District Court for the District of Columbia found the FDA's interpretation of "court" to be inconsistent with the statute's plain meaning; the FDA was directed to approve an ANDA upon a decision of a *district court* finding a patent invalid, unenforceable, or not infringed.

To comply with this decision, the FDA has provided a "Guidance for Industry" that redefines "court" to be a district court. This definition applies, however, only to ANDAs containing paragraph IV certifications that were filed with the FDA after March 2000. If a generic applicant filed its ANDA with the paragraph IV certification prior to March 2000, the definition of a court will remain "the court that enters final judgment from which no appeal can be or has been taken."[18]

Duration of Patent Infringement Litigation

Table 4-1 shows the average time it took to obtain a decision of a district court and, then, an appellate court in ANDA patent infringement cases involving the drug products included within the scope of the study. On average, the time between complaint and district court decisions in litigation with the first generic applicant was 25 months and 21 days. The time between complaint and an appellate decision was 38 months and 27 days. For ANDA infringement litigation with the second generic applicant, the time frames were slightly shorter as shown in Table 4-1. Table 4-1[19] also shows the average for litigation involving both first and second generic applicants.

Table 4-1 Length of Patent Cases

Average Time Period	First Generic Applicant	Second Generic Applicant	Weighted Average
Between Complaint and District Court Decision	25 months, 21 days (31 cases)	24 months, 29 days (22 cases)	25 months, 13 days (53 cases)
Between Complaint and Appellate Decision	38 months, 27 days (14 cases)	36 months, 4 days (12 cases)	37 months, 20 days (26 cases)

Several observations can be made from the data. First, patent infringement litigation over blockbuster drugs increasingly has involved more patents. Prior to 1998, for 8 out of the 9 blockbuster drug products as to which the brand-name company filed suit against the first generic applicant, the brand-name company alleged infringement of 1 or 2 patents. In the remaining case, the brand-name company alleged infringement of 3 patents. Since 1998, for only 3 out of the 8 blockbuster drug products as to which the brand-name company filed suit against the first generic applicant, the brand-name company alleged

Apr. 9, 1998).

[18] FDA, Guidance for Industry, Court Decisions, ANDA Approvals, and 180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act (Mar 2000). This guidance document also discusses the definition of a court to trigger the 180-day exclusivity, *see* Chapter 5.

[19] Table 4-1 contains cases that resulted in a court opinion, including cases involving the same drug product, but a different dosage strength or generic applicant (if different generic applicants were first for different dosage strengths). It does not include stipulated dismissals or consent entered by the court pursuant to a patent settlement agreement.

infringement of 1 or 2 patents. In the remaining 5 instances, the brand-name company alleged infringement of 3 or more patents. For example, the brand-name company for blockbuster drug products such as Prilosec, Claritin, and Paxil sued the first generic applicant for patent infringement on six, three, and six patents, respectively. One drug product, Lupron, has 12 listed patents for which the brand-name company has alleged infringement.

Second, cases involving multiple patents appear to extend beyond the average time it took to resolve the patent infringement cases identified in Table 4-1. The data suggest that cases involving multiple patents take longer to resolve than those involving fewer patents. As of June 1, 2002, for 6 out of the 7 cases that have been pending for more than 30 months without a decision from a district court (*see* Figure 2-1), the brand-name company has alleged infringement of 3 or more patents.

Third, district courts have issued decisions about non-infringement in a shorter period of time than decisions of patent invalidity. The average time between the filing of the complaint against either the first or second generic applicant and a decision of non-infringement was 19 months, 23 days. By contrast, the average time to obtain a district court decision of patent invalidity was 33 months, 5 days.

Multiple 30-Month Stays on Later-Issued Patents For Drug Products in the Study

The data revealed 8 drug products (out of 104 in the study) for which the brand-name company listed a patent in the Orange Book *after* the first generic applicant had filed its ANDA.[20] In these cases, the brand-name company obtained one or more additional 30-month stays for the drug product. Table 4-2 shows that the majority of the second 30-month stays have issued since 1999.[21] In contrast to the discussion in Chapter 3 concerning settlement agreements, the discussion here is not anonymous because the Orange Book listings and patent information is readily available in the public domain.

Table 4-2 Usage of Later-Issued Patents

Year in Which 2nd Stay Issued	Number of Drug Products	Drug Product(s)
1996	2	Hytrin (tablets); Platinol*
1997/98	0	
1999	1	Paxil
2000	4	Taxol; BuSpar; Neurontin (capsules); Neurontin (tablets)
2001 (thru 6/25/01)	1	Tiazac
Total	**8**	

* The earlier-filed ANDAs contained paragraph III certifications, but the later-issued patent was listed in the Orange Book shortly before the underlying patents were to expire.

[20] This total does not include instances in which the brand-name company initiated suit on a different strength of the same drug product.

[21] There may be additional drug products that have obtained a second 30-month stay that are not included within this study because the first ANDA with a paragraph IV certification was filed after January 1, 2001. *See* Chapter 1 for the scope of the study.

Table 4-3 describes the total time per drug product during which the FDA was prohibited from approving a generic applicant's ANDA because of one or more 30-month stays generated by a later-listed patent. In most cases, the brand-name company companies only obtained one additional 30-month stay, typically based on a formulation or method of use patent. Appendix G describes the relationship of these additional patents to the brand-name company's approved drug product. Appendix H describes issues about the listing of these patents in the Orange Book.

Table 4-3 Multiple 30-Month Stays Caused by Patents Later-Issued Patents

Drug Product/ Active Ingredient	Patent Claims in Original Lawsuit	Patent Claims in Subsequent Suit(s)	Total Number of Stays	Timing of Subsequent Stay(s)	Total Length of Stays	Net Sales in Year the Second Stay was Issued
Platinol (Cisplatin)	N/A, Paragraph III Certification	Formulation	1	Beginning 2 months prior to the last patent claiming the drug expired	30 months	Between $100 and $250 million
Hytrin – tablets (Terazosin)	Drug substance	Drug Substance	3	Beginning 43 months after the first stay began	70 months*	Between $500 and $750 million
Paxil (Paroxetine Hydrochloride)	Drug Substance, Formulation, Method of use	Drug Substance, Formulation, Method of Use	5	Beginning 17 months into the first stay	65 months	Over $1 billion
Taxol (Paclitaxel)	Method of Use	Formulation	2	Beginning after 1st 30-month stay had expired	Potentially 60 months**	Between $750 million and $1 billion
BuSpar (Buspirone)	Method of Use, Paragraph III Certification	Method of Use	2	Beginning the day the last patent claiming the drug expired	Potentially 30 months**	Between $500 and $750 million
Neurontin – capsules (Gabapentin)	Drug Substance, Method of Use	Formulation	2	Beginning 23 months into first stay	53 months	Between $250 and $500 million
Neurontin – tablets (Gabapentin)	Drug Substance, Method of Use	Formulation	2	Beginning 7 months into first stay	37 months	Between $250 and $500 million
Tiazac (Diltiazem)	Formulation	Formulation	2	Beginning 30 months after first stay began	Potentially 60 months**	Between $100 and $250 million

* The time from the beginning of the first stay until the end of the final stay lasted approximately 70 months, but the stays were not overlapping. *See* Appendix G for a further discussion of Hytrin.

** The actual total length of the stays were shorter because of the court actions in each of the cases, *see* discussion in Boxes 4-2, 4-3, and Appendix G.

In four instances (Hytrin (tablets), BuSpar, Paxil, and Tiazac), the brand-name company applied for the patents more than one year after the FDA had approved the drug product covered by the NDA, suggesting that the patents cannot cover the approved drug product and be valid, due to the "on sale bar" of patent law. The later-issued patents for Hytrin, Platinol, Taxol, and BuSpar were determined to be invalid patents or not infringed. The suit involving the later-issued patent listed for Tiazac was dismissed pursuant to the Commission's recent enforcement action described in Box 4-4. The infringement litigation involving the later-issued paents for the remaining drug products (Paxil, and Neurontin (tablets and capsules)) is still pending.

For Neurontin and Platinol, the second stay was generated by a patent that had been pending for an extended period in the Patent Office. In the case of Neurontin, the '482 patent had been pending for ten years. In the case of Platinol, U.S. Patent No. 5,562,925 had been pending for 26 years before it issued.

Box 4-4 The FTC's Enforcement Action Involving Tiazac

Tiazac is a drug for treatment of high blood pressure and chronic chest pain; it had annual sales in 2000 of almost $200 million. Andrx filed the first ANDA for a generic version of Tiazac in June 1998 with a Paragraph IV certification regarding the only patent then claiming Tiazac, the '791 patent. Biovail filed a patent infringement lawsuit within 45-days of its notification, alleging that Andrx's generic Tiazac product would infringe the '791 patent. This lawsuit triggered a 30-month stay of final regulatory approval of Andrx's ANDA, which was to expire on February 26, 2001.

On March 6, 2000, the U.S. District Court presiding over the patent infringement suit found that Andrx's product did not infringe the '791 patent. *Biovail Corp. Int'l v. Andrx Pharm. Inc.*, 2000 WL 33354427 (S.D. Fla. Mar 6, 2000). Biovail appealed this decision to the U.S. Court of Appeals for the Federal Circuit. On February 13, 2001, the Federal Circuit affirmed the district court's ruling that Andrx's product did not infringe Biovail's '791 patent, thus ending the first 30-month stay.

Before the Federal Circuit issued its decision, however, Biovail, on January 8, 2001, listed a second patent in the Orange Book as claiming Tiazac. Biovail acquired this patent, U.S. Patent No. 6,162,463 ("the '463 patent"), from DOV Pharmaceuticals, Inc. through an exclusive licensing arrangement that also included plans to develop new diltiazem products jointly using the '463 patent. Because of this listing, Andrx was required to submit a second Paragraph IV certification asserting non-infringement of the '463 patent. After receiving Andrx's certification, Biovail filed another infringement suit, triggering a second 30-month stay, and further delaying the potential entry of Andrx's generic Tiazac product until at least June 2003 or until the '463 was declared invalid or not infringed.

The FTC's complaint alleged that Biovail was aware that the '463 patent did not claim the formulation of Tiazac that it had been marketing. Accordingly, Biovail did not need the '463 patent in order to make or sell its existing FDA-approved formulation of Tiazac, and it could have continued to do so without infringing the '463 patent. Moreover, in prosecuting the patent before the U.S. Patent and Trademark Office, DOV was required to distinguish the '463 patent from the prior art - including Biovail's Tiazac - before the patent examiner approved the patent. This fact suggests that the '463 patent could not simultaneously be valid and properly listed in the Orange Book for Tiazac.

The Commission alleged that Biovail misleadingly represented to the FDA that the new patent claimed existing-and-approved, rather than revised-and-unapproved, Tiazac, to avoid de-listing from the Orange Book and termination of the stay against Andrx. The Commission alleged that Biovail's patent acquisition, wrongful Orange Book listing, and misleading conduct before the FDA were acts in unlawful maintenance of its Tiazac monopoly, in violation of Section 5 of the FTC Act, and that the acquisition also violated Section 7 of the Clayton Act.

The proposed consent order would require Biovail to divest the illegally acquired patent to its original owner, except as to new product developments outside the Tiazac market; to dismiss its infringement case against Andrx, which would end the stay, thereby allowing entry of generic Tiazac to the benefit of consumers; and to refrain from any action that would trigger another 30-month stay on generic Tiazac entry. Further, the order prohibits Biovail from unlawfully listing patents in the Orange Book and requires Biovail to give the Commission prior notice of acquisitions of patents that it will list in the Orange Book for Biovail's FDA-approved products.

The patent listings involving GlaxoSmithKline's (GSK)[22] drug product Paxil illustrate the impact that multiple 30-month stays can have on the timing of FDA approval, and thus the beginning of generic competition. Four additional 30-month stays have prevented FDA approval of generic competition against Paxil for approximately 65 months.[23] GSK manufactures and distributes Paxil, which the FDA has approved for the treatment of depression, obsessive compulsive disorder, panic disorder, and social anxiety disorder.[24]

The FDA approved Paxil in December 1992. Patent No. 4,007,196 (the '196 patent) covering the active ingredient paroxetine hydrochloride had expired prior to this date and, therefore, was not listed in the Orange Book. However, GSK listed Patent No. 4,721,723 (the '723 patent) which claims paroxetine hydrochloride hemihydrate. (A hemihydrate is a form of the active ingredient that has one water molecule for every two paroxetine molecules incorporated into its crystalline structure.)

Apotex Corporation filed an ANDA for generic Paxil on March 31, 1998. With the ANDA, Apotex submitted a paragraph IV certification for the '723 patent, the only patent listed in the Orange Book at that time. GSK's infringement suit generated the first 30-month stay, which expired in approximately November 2000. Since March 1998, however, GSK has listed nine additional patents in the Orange Book and brought infringement suits against Apotex on four of them. The four infringement suits generated four additional 30-month stays that created an automatic stay on FDA approval of generic Paxil totaling over 5 years. Figure 4-1 depicts graphically the stay on FDA approval of Apotex's ANDA.

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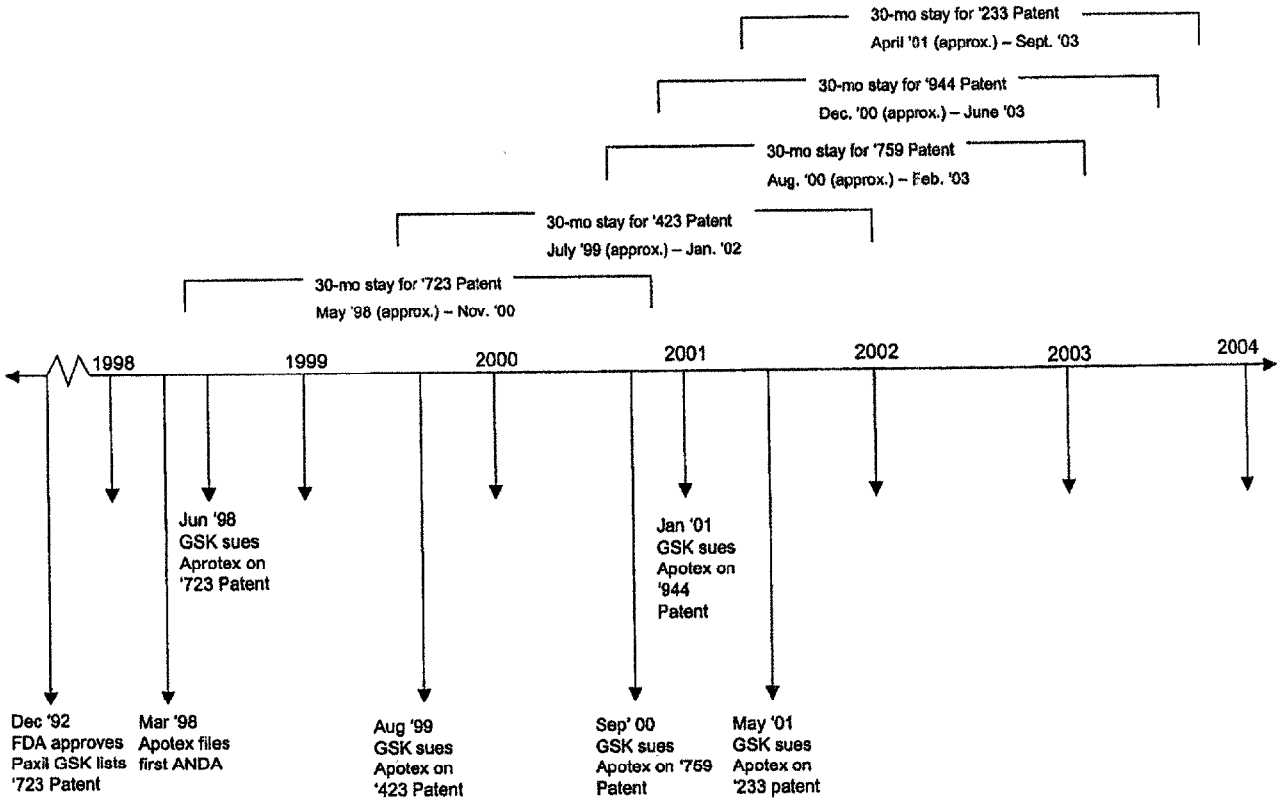
[22] Before the merger of Glaxo Wellcome and SmithKline Beecham, Paxil was manufactured and distributed by SmithKline Beecham, which was also the original NDA holder. For simplicity, however, we will refer throughout to GSK.

[23] Apotex Corporation, Novartis (Geneva), Mylan, Alphapharm, IVAX, and Pentech have all filed ANDAs for generic Paxil. GSK sued each of them for infringing at least some of the patents discussed. For simplicity in demonstrating the effect of the more recently listed patents and the 30-month stays they generated, we will focus on the suits GSK brought against Apotex.

[24] *Physician's Desk Reference*, 55th ed. (2001) at 3114.

Figure 4-1 30-Month Stays Obtained for Paxil



Analysis of Later-Issued Patents in the Orange Book

To gain some insight into patent listing issues, the FTC staff reviewed the patents listed for drug products as to which the responding generic companies indicated that they had challenged a listing in some way.[25] The analysis indicates that three categories of patents listed in the Orange Book raise significant listability issues – *i.e.*, issues concerning whether the listed patents fall within the statutorily defined class.

Four points bear emphasizing as defining the class of listable patents according to the listing statute and regulation. First, a brand-name company may list only those patents that claim the approved drug product or a method of using the drug product described in its NDA. The key relationship governing whether a patent is properly listed in the Orange Book is the relationship between the patent and the brand-name drug product. *The relationship between the patent and any bioequivalent generic drug is irrelevant to the listing question.* As the discussion of litigation outcomes in Chapter 2 demonstrates, it is entirely possible, and in fact common, for a patent to claim the brand-name drug (and hence be listed in the Orange Book), but not

[25] *See* Appendix E, Question 4 for generic companies. These drug products encompass the eight products listed in Table 4-3 as subject to multiple 30-month stays.

to be infringed by a bioequivalent generic product. Conversely, it is possible for a bioequivalent generic product to infringe a patent that does not claim the brand-name drug (and hence should not be listed in the Orange Book).[26]

Second, the Hatch-Waxman Amendments and listing regulations grant brand-name companies the 30-month stay *only* for those patents that claim its approved drug product or an approved use of that product. *The Amendments do not grant the protection of the 30-month stay to every patent that a bioequivalent generic product may infringe.* This does not mean, however, that a brand-name product is left vulnerable to infringing generic products. A brand-name company may obtain and enforce patents covering bioequivalent "design-around" formulations of its product. In fact, the brand-name company may bring its infringement suit at the time the generic files its ANDA, even when the patent is not listed in the Orange Book.[27] Moreover, just like any patent holder, brand-name company companies may prevent initial marketing of a generic product by demonstrating entitlement to a preliminary injunction in patent infringement litigation. Thus, Orange Book listings control only whether a brand-name company may obtain an automatic 30-month stay, not whether and when it may obtain and assert patent protection.

Third, even after a patent satisfies the first prong of the statute ("claims the drug"), to be properly listed it must still satisfy the independent second prong, requiring that a "claim of patent infringement could reasonably be asserted" against the NDA holder's approved drug product.[28] The analysis depends on whether the branded and approved drug product, rather than the generic product, infringes the patent, absent a license. Whether a patentee can "reasonably" assert a claim of patent infringement is not limited to infringement but also includes the validity and enforceability of the patent.

Fourth, the listing regulation requires

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[26] This is especially true for formulation patents, which cover composition of a drug product, rather than its active ingredient. A generic drug company may formulate its drug product differently than the brand-name product, but still produce a bioequivalent product. The generic's different formulation may not infringe the brand's patent covering its own formulation. *See, e.g., Biovail Corp. v. Andrx Pharma., Inc.*, 239 F.3d 1297 (Fed. Cir. 2001) (Andrx's formulation did not infringe listed patent). On the other hand, a generic company's own formulation may be sufficiently different to merit its own patent protection. *See* U.S. Patent No. 5,567,441 (patent on diltizem formulation assigned to Andrx).

[27] 35 U.S.C. § 271(e)(2) makes it an act of infringement to submit an ANDA for a drug "claimed in a patent." This statute allows infringement litigation based on the filing of an ANDA in spite of § 271(e)(1)'s safe harbor provision protecting activities related to obtaining FDA approval from infringement allegations. As one district court has recognized, nothing in the statute limits suits under § 271(e)(2) to those based on patents listed in the Orange Book. *In re Buspirone Antitrust Litigation*, 185 F. Supp. 2d 363, 372 (S.D.N.Y. 2002) (patentee could have brought its infringement suit without relying on its Orange Book listing); *see also Mylan Pharma., Inc. v. Thompson*, 268 F.3d 1323, 1331-32 (Fed. Cir. 2001) (rejecting argument that Mylan's challenge to Orange Book listing could be viewed as a defense to Bristol's assertion of patent infringement under 35 U.S.C. § 271(e)(2) suggesting that an infringement suit under § 271(e)(2) does not require that the asserted patent be listed in the Orange Book). In spite of this fact, one recent district court decision suggested that an Orange Book listing and a paragraph IV certification is a necessary predicate to a patent suit under § 271(e)(2). *Allergan Inc. v. Alcon Labs, Inc.*, 200 F.Supp.2d 1219 (C.D. Cal. 2002). To ensure that litigation can proceed upon the filing of an ANDA, without such an Orange Book listing and a paragraph IV certification, this decision should be overruled.

[28] 21 C.F.R. § 314.53(b).

that the patent "claim" the approved drug product.[29] The Court of Appeals for the Federal Circuit has explained that the term "claim" under the Hatch-Waxman Amendments has the standard meaning as understood in patent law.[30] A patent "claims" a product only when the written section of the issued patent labeled the "claims" define it. As the Federal Circuit stated, "the plain meaning of 'claims' is not the same as the plain meaning of infringement."[31] Even though a drug product or its use may infringe a patent under the doctrine of equivalents,[32] or indirectly through theories of contributory infringement or inducement to infringe, that patent does not "claim" the product.[33] Consequently, a brand-name company may not list a patent in the Orange Book when its approved drug product infringes the patent only indirectly or under the doctrine of equivalents, and not directly and literally.

One general concern overlays all four points. One function of the Orange Book is to provide notice to ANDA applicants of relevant patents. There is, however, a trade-off between using the Orange Book to provide notice of all relevant patents and implementing a methodology that grants the protection of the 30-month stay to a defined class of patents, as does the current statutory methodology. One consequence of restricting the patents listed in the Orange Book is that the Orange Book would then not provide notice of every patent that an ANDA filer might infringe. For example, beyond those patents that do not claim the brand-name company's drug product, the Orange Book also provides no notice of process patents. The importance of the notice function of the Orange Book is unclear, however. Many companies may not need an Orange Book listing to provide notice, given the sophistication of their patent searching techniques and the common practice of monitoring newly listed patents on a regular basis.[34]

The analysis identified three broad categories of patents that raise questions about whether they fall within the class the Hatch-Waxman Amendments defines as listable in the Orange Book. These categories, which are more fully explained in Appendix H, are:

1. Patents that may not be

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[29] *Id.*

[30] *Hoechst-Roussel Pharms., Inc. v. Lehman*, 109 F.3d 756 (Fed. Cir. 1997) (interpreting the term "claims" in the Patent Term Restoration portion of the Hatch-Waxman Amendments at 35 U.S.C. § 156(a)). A district court has held that this interpretation of "claims" applies to the listing statute. *Mylan Pharma., Inc. v. Thompson*, 139 F. Supp. 2d 1, 19-21 (D.D.C. 2001), *rev'd on other grounds*, 268 F.3d 1323 (Fed. Cir. 2001).

[31] *Hoechst-Roussel Pharms., Inc.*, 109 F.3d at 759.

[32] If an accused device does not literally infringe a patent claim because it lacks some element of that claim, it may infringe under the doctrine of equivalents if it contains some element that is insubstantially different from the claim element which it lacks. *Warner-Jenkinson Co., Inc. v. Hilton Davis Chemical Co.*, 520 U.S. 17, 35-36 (1997).

[33] *Hoechst-Roussel Pharms., Inc.*, 109 F.3d at 759 ("The relationship between infringement and the claims becomes even more tenuous under the doctrine of equivalents, where a product is deemed to infringe the patentee's right to exclude even though the product does not fall within the scope of the patent's claims.").

[34] *See, e.g.*, Testimony of Michael Kirschner, Immunex Corp., FTC Public Hearings: Competition and Intellectual Property Law and Policy in the Knowledge-Based Economy (Feb. 26, 2002) *available at* <http://www.ftc.gov/opp/intellect/020226trans.pdf>.

considered to claim the drug formulation or method of use approved through the NDA. For example:

a. *Metabolite patents* that claim the chemical compound into which a patient's body converts the approved drug product;

b. *Drug intermediate patents* that claim a chemical compound used during production of the active ingredient, but not appearing in the final drug product; and

c. *Polymorph patents* that claim a crystalline form of the active ingredient that differs from the approved crystalline form;

2. Product-by-process patents that claim a drug product produced by a specified process; and

3. Patents that constitute double-patenting because they claim subject matter that is obvious in view of the claims of another patent invented by the same person.

Several points emerge from the analysis in Appendices G and H comparing these patents to the class of patents defined as listable by the statute. The large majority of patents creating an additional 30-month stay raise some kind of listing issue. It is important to note that this patent analysis applies not only to late-issued patents, but also potentially to patents listed prior to the filing of ANDA. The patents generating the first or sole 30-month stay have, on occasion, raised similar listability issues.

Determining whether these patents are appropriately listed sometimes involves an analysis of chemistry, patent law, and FDA law. Many of the listing issues concern the FDA's listing regulations, however, rather than interpretations of patent scope. For instance, the question of whether metabolite, drug intermediate, polymorph, and product-by-process patents may be listed appears to depend on interpretations of the listing regulations. As Appendix H details, the identification of individual patents as falling into one of those categories is usually relatively straight-forward.

To the degree there is uncertainty about the scope of the listing regulations, they could be clarified by regulation or guidance. The FDA's clarification of these issues is important to antitrust challenges to improper Orange Book listings. The question of whether a patent claims some unapproved aspect (and hence should not be listed) may depend more on an interpretation of the NDA's scope of approval than an interpretation of the patent. A mechanism by which the FDA could comment on the scope of an NDA would be helpful in resolving some listing disputes, as occurred in the Tiazac situation described in Box 4-4. An antitrust suit involving complex elements beyond the propriety of the listing is the only current mechanism to challenge an Orange Book listing.

To clarify some of these issues (but not all), the FTC staff has submitted a Citizen Petition to the FDA that seeks guidance concerning the criteria that a patent

must meet before it can be listed in the Orange Book.[35] The requested guidance could eliminate uncertainty surrounding the appropriateness of listing some types of patents, in particular polymorph patents, in the Orange Book, but it will leave other issues unaddressed. The FTC staff Citizen Petition is pending.

[35] Appendix F contains a copy of the FTC Staff Citizen Petition, *available at* <http://www.fda.gov/ohrms/docket/dailys/01/May01/052901/cpa.pdf>.

Chapter 5 180-Day Marketing Exclusivity Under the Hatch-Waxman Amendments

Introduction

The Hatch-Waxman Amendments provide 180 days of marketing exclusivity to the first generic application that seeks entry prior to expiration of the patents listed for the relevant brand-name drug product. The exclusivity allows this first generic applicant to sell the only generic substitute for a brand-name drug product for 180 days after either i) first commercial marketing by the first generic applicant, or ii) a decision of a court holding the relevant patents to be invalid or not infringed.[1] The grant of 180-day exclusivity to the first generic applicant creates an incentive for a generic company to challenge a brand-name company's drug product patents. One court has explained that 180-day exclusivity rewards the first generic applicant for the expense and effort involved with challenging a listed patent.[2]

If the 180-day exclusivity for the first generic applicant does not run, then the FDA may not approve any subsequent eligible generic applicants. Thus, if the first generic applicant agrees not to trigger the 180-day exclusivity, the possibility exists that no generic applicant may enter the market. The Commission's interest in 180-day exclusivity has focused on the agreements between brand-name and generic companies that have affected whether and when first generic applicants have triggered the running of 180-day exclusivity. The Commission's antitrust law enforcement actions have alleged that certain brand-name and generic companies have entered into agreements that, among other things, have had the effect of delaying entry by the first generic that otherwise would trigger the running of the 180-day exclusivity, thereby creating a bottleneck for any subsequent eligible generic entry.[3]

The regulatory landscape implementing the 180-day exclusivity provision has shifted over the last several years, and this may have affected the frequency with which generic applicants obtain 180-day exclusivity. Before 1992 (a time period not included in the FTC's study), the FDA granted 180-day exclusivity to 3 generic applicants. From 1992 until 1998, the FDA granted 180-day exclusivity to no generic applicants. Since 1998, when the FDA changed its regulations in response to a court ruling,[4] and more ANDAs containing paragraph IV certifications have been filed, the FDA has granted 180-day exclusivity to the first generic applicant for 31 drug products.

For the drug products within the

[1] 21 U.S.C. § 505(j)(5)(B)(iv).

[2] *Mova v. Shalala*, 140 F. 3d 1060, 1074 (D.C. Cir. 1998).

[3] *See Abbott Laboratories*, No. C-3945 (May 22, 2000) (consent order), *available at* <http://www.ftc.gov/os/2000/03/abbott.do.htm> (this consent order related to 2 drug products: Hytrin tablets and Hytrin capsules).

[4] *See Mova, supra* n. 2.

scope of this study, the generic applicant's commercial marketing has triggered the 180-day exclusivity in 19 of 31 instances. The data show that when the brand-name company did not sue the first generic applicant for patent infringement (29 drug products, see Table 2-1), the first generic applicant began commercial marketing soon after receiving FDA approval.

The data show that 14 of the 20 final settlements obtained through the study (discussed in Chapter 3) had the potential, at the time they were executed, to "park" the first generic applicant's 180-day exclusivity for some period of time, thus preventing FDA approval of any eligible subsequent applicants. In addition to the 20 final settlement agreements, there were 4 interim settlement agreements pursuant to which the patent litigation continued, but the parties agreed upon certain conditions in the meantime. The Commission, as noted above, has challenged interim settlements for 3 drug products.

This chapter describes the 180-day provision in the Hatch-Waxman Amendments and details how FDA's rules governing 180-day exclusivity have evolved. The chapter examines how the 180-day exclusivity has been triggered, and it also reviews the agreements that were obtained through the study that affect the triggering of the 180-day exclusivity.

The Shifting Regulatory Landscape Implementing the 180-Day Exclusivity Period

FDA rules implementing the 180-day exclusivity have changed over the last several years. This section describes the FDA's initial approach to implementing the 180-day exclusivity through the "successful defense" requirement and the current rules that no longer require a successful defense. The section then discusses the FDA's regulations governing what constitutes a decision of a "court" and "commercial marketing" sufficient to trigger the first generic applicant's 180-day exclusivity. Finally, it discusses recent developments surrounding the awarding of "shared" exclusivity to multiple generic applicants.

Successful Defense Requirement

In October 1994, the FDA issued final regulations governing how it would award the 180-day exclusivity period to generic applicants.[5] FDA regulations required that, to obtain the 180-day exclusivity, the first generic applicant had to *defend successfully* against a patent claim of the brand-name company.[6] The FDA asserted that only those generic applicants that had devoted considerable time and money to defend successfully the patent infringement lawsuit were entitled to be the first and only generic company on the market for 180 days. The FDA reasoned that a first generic applicant that a brand-

[5] *See* 59 Fed. Reg. 50338 *et seq.* (Oct. 3, 1994). Prior to this time, the FDA used an approach similar to that outlined in these regulations.

[6] *See id.*

name company had not sued might have an incentive to delay marketing. This delay would prolong the period of no generic competition, because other generic products may not be approved until the first generic product begins commercial marketing.[7]

These regulations were challenged in *Mova v. Shalala*, a case involving the brand-name drug product Glynase.[8] Mova Pharmaceuticals was the first generic applicant for Glynase. Pharmacia & Upjohn, the brand-name company, sued Mova for patent infringement within the requisite 45-day period, thus initiating the 30-month stay on FDA approval of Mova's application. Pharmacia did not sue the second generic applicant, Mylan Pharmaceuticals, for the same drug product within 45 days of being notified; thus, the 30-month stay was not triggered. FDA was about to approve Mylan's ANDA prior to the expiration of Mova's 30-month-stay, but before the district court had ruled on the merits of patent infringement case against Mova, the first generic applicant. Mova therefore sued the FDA to delay the effective date of the approval of Mylan's application until Mova had won its patent infringement suit or begun commercial marketing of its generic product.

The district court granted a preliminary injunction against the FDA on January 23, 1997, requiring the FDA to delay approval of Mylan until after Mova's 180 days of exclusivity took effect. This ruling rejected FDA's "successful defense" requirement as inconsistent with the plain language of the Hatch-Waxman Amendments.[9] The Court of Appeals for the District of Columbia Circuit affirmed the District Court's ruling in its April 1998 decision.[10]

The FDA revoked the "successful defense" requirement and now makes exclusivity decisions on a case-by-case basis applying the literal words of the statute.[11] The FDA also has proposed new regulations to address issues that these court decisions have raised.[12] This rulemaking proceeding has been pending since August 1999.

Definition of the "Court" As Used in the 180-Day Marketing Exclusivity Provision

The FDA originally interpreted the definition of a court that would trigger 180-day exclusivity to be "the court that enters final judgment from which no appeal can be or has been taken."[13] In *Mylan*

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[7] *See* 54 Fed. Reg. 28872 (Jul. 10, 1989).

[8] 955 F. Supp. 128 (D.D.C. 1997), *aff'd*, 140 F. 3d 1060 (D.C. Cir. 1998).

[9] *See Mova*, 140 F.3d at 1069.

[10] The Court of Appeals also referenced *Granutec Inc. v. Shalala*, 139 F.3d 889, 1998 WL 153410 (4th Cir. 1998); 46 USPQ2d 1398 (4th Cir. 1998) (unpublished opinion), in dicta, "We note that the Fourth Circuit recently came to the same conclusion in an unpublished opinion." Mova, 140 F.3d at 1069.

[11] The FDA also subsequently published guidance for industry entitled "180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act" (June 1998), describing its approach to 180-day exclusivity in light of *Mova* and *Granutec*.

[12] 64 Fed. Reg. 42873 (Aug. 6, 1999).

[13] 21 CFR 314.107(e)(1) (1999).

Pharmaceuticals, Inc. v. Shalala,[14] the District Court for the District of Columbia found FDA's interpretation of "court" to be incorrect; the court instead held that "court" means "district court." The FDA amended its rules to implement the *Mylan* decision by defining the "court" decision that triggers the running of the 180-day marketing exclusivity period as the decision of a district court. This definition applies, however, only to ANDAs containing paragraph IV certifications filed with the FDA after March 2000. Thus, if a generic applicant filed its ANDA with the paragraph IV certification prior to March 2000, the definition of a court will remain "the court that enters final judgment from which no appeal can be or has been taken."[15]

Triggers for the 180-Day Exclusivity Period

Prior to the *Mova* court of appeals decision on April 14, 1998, the FDA had granted the 180-day exclusivity to 3 generic applicants for drug products covered by 3 NDAs.[16] In each case, a court had decided that the patent was invalid or not infringed such that the generic applicant had "successfully defended" the patent litigation suit. Each of these grants of the 180-day exclusivity occurred prior to 1991 and involved drugs not included in the scope of the study.

Since *Mova*, the FDA has granted the 180-day exclusivity to the first generic applicant for 31 drug products.[17] Table 5-1 categorizes these grants of exclusivity by the triggering mechanism (either by commercial marketing or the decision of a court) as of June 1, 2002.

Table 5-1: Marketing Exclusivity Triggering Event Since 1998[18]

Triggering Event	Number of ANDAs
Commercial Marketing	19
Court Decision of Patent Invalidity or Non-Infringement	12
Total	**31**

[14] *Mylan Pharmaceuticals, Inc. v. Shalala*, 81 F.Supp.2d 30 (D.D.C. 2000).

[15] FDA, Guidance for Industry, Court Decisions, ANDA Approvals, and 180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act (Mar 2000). This guidance document also discusses the definition of a court for purposes of when the 30-month stay expires, *see* Chapter 4.

[16] This information was provided by the FDA to the FTC staff.

[17] For 8 drug products, the FDA has provided two or more generic applicants the 180-day exclusivity for drug products covered by the same NDA, because different generic applicants had the first ANDA for a particular strength of the drug product (*e.g.*, 30mg, 60 mg, and 90 mg tablets). To ensure no overcounting, the totals referred to in this section (and throughout the report unless otherwise noted) relate only to the number of NDAs for which 180-day exclusivity has been granted. For each drug product where this occurred, the same 180-day exclusivity was activated by the same trigger (*i.e.*, commercial marketing or a court decision).

[18] For 2 drug products not included in Table 5-1 but within the scope of this study, the first generic applicant relinquished its eligibility for the 180-day exclusivity, thus eliminating any delay for subsequent generic applicants to market their generic products. In addition, for 3 other drug products not included in Table 5-1, but within the scope of the study, the FDA has indicated that certain generic applicants are eligible for 180-day exclusivity, but the period has not yet started to run, because neither trigger has been activated.

Trigger: Commercial Marketing

For 19 of the 31 drug products in Table 5-1, the first generic applicant's commercial marketing triggered the running of the 180-day exclusivity period.

In 5 of the 19 instances, commercial marketing occurred when the FDA did not consider a *district court* decision sufficient to trigger the 180-day exclusivity. In these 5 instances, the generic applicants had prevailed at the district court and the 30-month stay period had expired, so that the FDA approved the generic applicant's ANDA. Rather than waiting for an appellate decision, the generic applicants began commercial marketing. In each of these instances, the generic applicant ultimately prevailed in the appellate court, but commercial marketing, not a court decision, triggered the 180-day exclusivity.

For another 5 of the 19 drug products in Table 5-1, the first generic applicant was not sued. Thus, the only available trigger for the 180-day exclusivity period was the first generic applicant's commercial marketing.[19] In each of these instances, the first generic applicant began commercial marketing soon after receiving FDA approval. For 3 of these 5 drug products, the second generic applicant was approved at the end of the 180-day exclusivity period, and there was not a second generic applicant for the other 2 drug products.

In 8 of the 19 instances, the brand-name company and the generic applicant settled the patent litigation and the generic applicant's commercial marketing triggered the 180-day exclusivity. These 8 settlements can be grouped into 4 categories:

- For 3 drug products, the generic applicant entered an interim settlement with the brand-name company. Following termination of the settlement and FDA approval, the generic applicant was granted 180-day exclusivity.[20]

- For 2 drug products, the generic applicant obtained a license to use the patents that were subject to the paragraph IV certification prior to the patent's expiration. The generic applicant then obtained FDA approval and began marketing the generic product that was the subject of its ANDA

[19] There was one other drug product for which the first applicant was not sued, but its 180-day exclusivity was triggered by a court decision favorable to the second generic applicant. In this case, the FDA had not approved the first applicant's ANDA, but the second generic applicant appeared to be ready to market – except that it had to wait for the running of the first applicant's 180-day period. That the 180-day exclusivity had not run for the first generic applicant, because its ANDA had not yet been approved, delayed FDA approval of the second generic applicant's ANDA. To remedy this problem, the second generic applicant sought a court decision of non-infringement to activate the "court decision" trigger. The district court hearing this declaratory judgment action dismissed the case for lack of case or controversy, because the brand-name company indicated that it would not sue the generic applicant for infringement. The second generic applicant argued that this constituted a "court decision" sufficient to trigger the 180-day period. The Court of Appeals for the District of Columbia agreed and ruled that a district court's earlier dismissal of the second generic applicant case for lack of case or controversy activated the court decision trigger and, thus, started the running of the first generic applicant's 180-day exclusivity. *See Teva Pharmaceuticals, USA, Inc. v. FDA*, 182 F.3d 1003 (D.C. Cir. 1999). There is some uncertainty regarding whether this reasoning would apply to trigger the 180-day exclusivity in the future.

[20] *See Abbott Labs.*, *supra* n 3.

(*see* drug products A and C in Table 3-2).[21]

- For 2 drug products, the settlement involved a supply agreement allowing the generic applicant to market the brand-name company's product as a generic prior to patent expiration (*see* drug product K in Table 3-3,[22] and the description of the second supply agreement in the text of Chapter 3).[23]

- For 1 drug product, the settlement specified a date on which entry of the generic product could occur, which was prior to patent expiration (*see* drug product L in Table 3-3).[24]

In the last of the 19 instances in which commercial marketing triggered the 180-day exclusivity, commercial marketing began after the brand-name company dismissed the patent suit upon determining the ANDA did not infringe the brand-name product.

Trigger: Court Decision

For 12 out of the 31 drug products, the FDA granted 180-day exclusivity to a generic applicant following a court decision of patent invalidity or non-infringement. Other than the 2 drug products involved in the challenge to the FDA's successful defense requirement,[25] in most instances the court that activated the court decision trigger was an appellate court decision. More recently, in 2 of the 12 cases, a district court decision has triggered the running of the 180-day exclusivity. In one case, the FDA approved the ANDA after 21 days of the 180-day period had already run, and in the other case, FDA approval came 120 days into the 180-day period, thus shortening the effective life of the 180-day period.

Effect of 180-Day Exclusivity on FDA Approval of Subsequent Eligible Generic Applicants

As noted in the introduction, in addition to encouraging entry by the first generic applicant, the 180-day exclusivity can delay when the FDA approves any subsequent eligible generic application that also contains a paragraph IV certification. If the 180-day exclusivity for the first generic applicant does not run, then the FDA may not approve any subsequent eligible generic applicants. Once the 180-day exclusivity

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[21] The generic applicant that was party to the remaining license agreements in Table 3-2 did not receive the 180-day exclusivity for one of 2 reasons: (1) the agreement was executed at a time when the FDA required the first applicant to defend successfully the patent infringement suit; having failed to do so, they were ineligible for 180-day exclusivity, or (2) the license has not yet taken effect, because of a waiting period in the agreement, such that commercial marketing has not yet occurred.

[22] *See* Letter to Deborah A. Jaskot, Teva Pharmaceuticals USA, FDA Docket No. 00P-1446/CP1 (Feb. 6, 2001).

[23] Although the 180-day exclusivity has run in these 2 instances, there is some uncertainty as to whether commercial marketing by the first generic applicant of the brand-name company's product will always activate the commercial marketing trigger.

[24] In most cases, the generic applicant that was the party to the remaining settlements in Table 3-3 (settlements with brand payments), did not obtain the 180-day exclusivity because entry did not occur until patent expiration, thus the generic applicant was ineligible for the 180-day exclusivity.

[25] *See Mova* and *Granutec, supra n. 8-10* and accompanying text.

runs, the FDA may approve any additional generic ANDAs that have been filed and meet regulatory requirements.

As discussed in Chapter 3, 14 of the 20 of the settlement agreements obtained through the study, at the time they were executed, had the potential to "park" the first generic applicant's 180-day exclusivity for some period of time, thus preventing FDA approval of any subsequent eligible applicants.[26] These agreements include the 4 license agreements with a waiting period before the license took effect (drug products A, E, F, and H in Table 3-2), the 2 supply agreements described in the text of Chapter 3, and settlements with brand payments (drug products I through P in Table 3-3). Ten brand-name companies and 10 generic companies used agreements with respect to14 drug products.

In addition to the 20 final settlement agreements, there were 4 interim settlement agreements pursuant to which the patent litigation continued, but the parties agreed upon certain conditions until the patent litigation was resolved. The Commission has challenged interim settlements for 3 drug products. In those agreements, the Commission alleged that the brand-name drug company paid the first generic applicant not to enter the market, thereby retaining its (unused) 180-day marketing exclusivity and precluding the FDA from approving any eligible subsequent generic applicants.[27]

Between April 1999 (shortly after FTC investigations in this area became public) and the end of the period covered by this study, brand-name companies and first generic applicants have not entered agreements similar to the interim agreements challenged by the FTC.

[26] Whether FDA was actually prevented from approving subsequent eligible generic applicants depends on a number of factors, including whether there were subsequent generic applicant(s) and the result of any patent litigation with those applicants.

[27] *See supra.* n. 3.

Chapter 6 FDA Citizen Petitions and Generic Drug Applications

Introduction

This chapter reviews FDA regulations concerning the use of citizen petitions. It also examines the citizen petitions that brand-name companies have filed about drug products in this study, and discusses their effect on the development of generic drug competition for these drug products.

The FDA has generally resolved the issues raised by the citizen petitions that brand-name companies file about drug products in this study in a timely manner, and in most instances prior to a district court ruling on the merits of the patent infringement litigation. Thus, for drug products in the study, citizen petitions that have been answered by the FDA have not delayed generic competition.

No general conclusions about the use of citizen petitions can be drawn from this study, however, because it did not examine citizen petitions filed in connection with ANDAs that contained paragraph I, II, or III certifications. Citizen petitions may have a greater potential to delay generic competition in those circumstances, in which no 30-month stay would be applicable.

FDA Regulations Governing Citizen Petitions

The FDA has several informal and formal mechanisms by which it can be contacted on a particular issue (including via letter, fax, email or meeting). A formal procedure, which has been used by both brand-name and generic pharmaceutical companies, is the filing of a citizen petition.[1] The FDA can be petitioned on any matter or issue which is within the Agency's jurisdiction.

The petition can request that the Commissioner issue, amend, or revoke a regulation or order, or take or refrain from taking any other form of administrative action. The Commissioner must furnish a response to a petitioner within 180 days of receipt of the petition.[2] The FDA's reply must approve, deny, or provide a tentative response. If the FDA provides a tentative response, it must indicate why the agency has been unable to reach a decision on the petition and may indicate when a final response may be furnished.[3] Unlike ordinary correspondence, the FDA treats the response to a citizen petition as the official position of the agency.[4]

Individuals and companies often use the formal citizen petition process to raise issues regarding the safety and efficacy of pharmaceuticals. Brand-name companies, for example, have petitioned the FDA on issues relating to bioequivalence for particular generic drugs.

The FTC staff has commented to the

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[1] 21 C.F.R. § 10.30.

[2] *Id.* at 10.30(e)(2).

[3] *Id.*

[4] *Id.* at § 10.45(d).

FDA on the potential for such petitions, on occasion, to mask anticompetitive strategies. The FTC staff has suggested changes to the FDA's proposed rules governing citizen petitions that might reduce the potential for regulatory abuse.[5] The FTC staff comment explained there is a potential for anticompetitive abuse of nearly any regulatory process.[6] To delay competition may be a lucrative strategy for an incumbent, especially in an industry in which entry is regulated, such as pharmaceuticals. Improper petitioning may be appealing in part because it can be used against any size firm, regardless of relative resources of the parties. The cost of filing an improper citizen petition may be trivial compared to the value of securing a delay in a rival's entry into a lucrative market.[7]

The Noerr-Pennington doctrine often protects participation in the regulatory process from antitrust scrutiny.[8] As discussed in Chapter 4, in its simplest terms, the Noerr-Pennington doctrine shields private parties from antitrust liability when they engage in concerted but genuine efforts to influence governmental action, even though the conduct is undertaken with an anticompetitive intent and purpose. If regulatory intervention (or a series of interventions) is used, however, to impede competition, antitrust concerns may be raised if not shielded by Noerr-Pennington.[9]

One of the recommendations in the FTC Staff Comment on Citizen Petitions was that the FDA consider requiring notification of whether the citizen petitioner has received, or will receive, consideration for filing the citizen petition and identification of the party furnishing the consideration. This information may be important in evaluating the competitive effect of the petition.

The Use of Citizen Petitions About Drug Products for Which an ANDA Containing a Paragraph IV Certification Was Filed

Each brand-name company was required to state, for each drug product included in the study for which the company has been notified that an ANDA containing a paragraph IV certification has been filed with the FDA, whether the company has filed, or contributed to the filing of, in whole or in part (*e.g.*, provided funds, legal or regulatory assistance to support the filing), a citizen petition with FDA concerning an ANDA related to that drug product and to identify the FDA docket number assigned to such citizen petition.

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[5] Comment of the Staff of the Bureau of Competition and the Office of Policy Planning of the Federal Trade Commission, Citizen Petitions; Actions That Can be Requested by Petition; Denials, Withdrawals, and Referrals for Other Administrative Action, FDA Docket No. 99N-2497 (Mar. 2, 2000) (FTC Staff Comment on Citizen Petitions).

[6] Robert H. Bork, *The Antitrust Paradox* 347 (1978) ("The modern profusion of [. . .] governmental authorities offers almost limitless possibilities for abuse.").

[7] *Id.* at 348.

[8] *Eastern Railroad Presidents Conference v. Noerr Motor Freight, Inc.*, 365 U.S. 127 (1961); *United Mine Workers v. Pennington*, 381 U.S. 657 (1965).

[9] *Professional Real Estate Investors, Inc. v. Columbia Pictures Indus. Inc.*, 508 U.S. 49 (1993); *see also* Bork, *see* n. 5, at 354.

Of the 104 drug products included in this study, brand-name companies filed citizen petitions relating to generic versions of 12 drug products. The data showed that for 1 drug product, the brand-name company filed 3 citizen petitions against different generic applicants; each petition sought different relief. For 2 other drug products, the brand-name company filed 2 citizen petitions, each seeking different relief. Thus, brand-name companies filed a total of 16 separate citizen petitions relating to the 104 drug products included in the study.

In each case, the brand-name company was the author of the petition and there was no effort on behalf of the company to withhold its identity from the FDA.

For 11 of the 12 drug products covered by citizen petitions, the brand-name company that had filed the citizen petition also had either settled the patent infringement litigation with an agreement that contained a brand payment (*see* Chapter 3), filed a late-issued patent to obtain a second 30-month stay (*see* Chapter 4), or has patent litigation pending in which the brand company has claimed the ANDA infringes more than one patent (*see* Chapter 4).

Table 6-1 breaks down the type of request that was included in each petition.

Table 6-1 Brand-Name Company Use of Citizen Petitions

Relief Requested by the Brand-name Company in the Citizen Petition	Number of Citizen Petitions
Additional bioequivalence studies or safety studies	7
Additional patent certifications	3
FDA to classify the NDA as a different dosage form	2
Other	4

Almost 50 percent of the citizen petitions requested that the FDA require additional bioequivalence studies before approving the generic applicant's ANDA. Of these 7 petitions regarding bioequivalence, the FDA denied 3 of these petitions, granted 1, granted and denied 1 in part, and 2 petitions were pending as of June 1, 2002. In each case in which the petition was denied, the brand-name company also had initiated patent infringement litigation against the generic applicant.

In the 5 cases in which the FDA ruled on the merits of the bioequivalence issues raised by the petition, it did so prior to a district court ruling on the merits of the infringement litigation and prior to the expiration of the 30-month stay. Thus, the filing of the citizen petition in these cases did not affect the generic product's entry. For the other 2 bioequivalence petitions, the FDA has not yet approved the generic applicant's ANDA.

In the second category of citizen petitions described in Table 6-1, brand-name companies requested the FDA refrain from approving a generic version of the drug product unless the generic company certified

to a new patent that was listed after the generic applicant had filed its ANDA. The FDA denied one of the petitions, and in the other two, the petitions were withdrawn because of a merger or because the generic applicant made the requisite patent certification. In each case, the citizen petition did not affect when the FDA approved (if it did) the generic applicants' ANDAs.

In the third category of citizen petitions described in Table 6-1, brand-name companies requested FDA redefine dosage forms with varying release mechanisms as distinct dosage forms. If the FDA were to grant this category of petitions, the generic applicant also would have been required to file a suitability petition that sought an FDA ruling that the two dosage forms were bioequivalent. In other words, it would have been procedurally more difficult for the generic applicant to have its ANDA approved in a timely manner.

The FDA denied both of these petitions. In each case, the brand-name company had sued the generic applicant for patent infringement, and the citizen petition was resolved by the FDA within the 30-month stay period. Thus, the petition had no effect on the timing of generic drug approval.

The last 4 citizen petitions dealt with issues unique to the underlying drug product. In one case, the petition was withdrawn, in another the FDA responded to the petition in an informal manner that satisfied the parties involved, in the third instance, the petition was denied, and in the fourth case, the petition was pending as of June 1, 2002. In the first 3 cases, the resolution of the citizen petition did not effect market entry by the generic applicant.

Conclusions

The citizen petitions related to drug products in the study that have been resolved did not affect the timing of generic entry. The FDA has addressed the issues raised by those citizen petitions in a timely manner and prior to the expiration of the 30-month stay related to the underlying patent infringement litigation.

No general conclusions about the use of citizen petitions, however, can be drawn from this study, however, because it only examined citizen petitions filed in connection with ANDAs that contained paragraph IV certifications.

Appendix A:
Glossary of Terms

"ANDA" means Abbreviated New Drug Application.

"Drug product" means the finished dosage form of a drug approved through an NDA or ANDA.

"Generic applicant" means those companies that have filed an ANDA containing a paragraph IV certification.

"Brand-name company" is synonymous with the NDA holder.

"180-day exclusivity" is the grant of 180 days of exclusive marketing to the first generic applicant that files an ANDA containing a paragraph IV certification after either i) first commercial marketing by the first generic applicant, or ii) a decision of a court holding the relevant patents to be invalid or not infringed.

"NDA" means New Drug Application. Pursuant to the Federal Food, Drug, and Cosmetic Act, a brand-name company seeking to market a new drug product must first obtain FDA approval by filing an NDA.

"Orange Book" means the FDA's publication entitled "Approved Drug Products with Therapeutic Equivalence," in which the patents claiming a drug product approved through an NDA are listed.

"Paragraph I certification" means a certification that a generic applicant seeks FDA approval of its ANDA for a relevant NDA for which no patent information has been filed in the Orange Book.

"Paragraph II certification" means a certification that a generic applicant seeks FDA approval of its ANDA for a relevant NDA for which a patent filed in the Orange Book has expired.

"Paragraph III certification" means a certification that a generic applicant seeks FDA approval of its ANDA as of the date a patent listed in the Orange Book for a relevant NDA expires.

"Paragraph IV certification" means a certification that a patent listed in the Orange Book is invalid or will not be infringed by the generic drug for which the ANDA applicant seeks approval.

"Settlements" means agreements settling patent litigation between brand-name companies and a generic applicant that has filed an ANDA containing a paragraph IV certification.

"30-month stay" prohibits the FDA from approving an ANDA with a paragraph IV certification for 30 months if the relevant brand-name company brings a patent infringement suit within 45 days of notice of the generic applicant's paragraph IV certification. The 30-month stay is terminated by (1) the expiration of the patents; (2) a final determination of non-infringement or patent invalidity by a court in the patent litigation; or (3) the expiration of thirty months from the receipt of notice of the Paragraph IV certification.

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VIA FEDERAL EXPRESS

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane
Room 1061 (HFA-305)
Rockville, MD 20852

Re: Submission of Citizen Petition by IVAX Pharmaceuticals, Inc.

Dear Sir or Madam:

Please accept the attached citizen petition (in four copies) submitted on behalf of IVAX Pharmaceuticals, Inc., pursuant to 21 C.F.R. § 10.35.

Sincerely,

David G. Adams