January 2004

Hatch-Waxman 2003 - Patented v. Generic Drugs: Regulatory, Legislative and Judicial Developments

Richard J. Smith

Follow this and additional works at: http://digitalcommons.law.scu.edu/chtlj

Part of the Law Commons

Recommended Citation
Available at: http://digitalcommons.law.scu.edu/chtlj/vol20/iss3/4

This Article is brought to you for free and open access by the Journals at Santa Clara Law Digital Commons. It has been accepted for inclusion in Santa Clara High Technology Law Journal by an authorized administrator of Santa Clara Law Digital Commons. For more information, please contact sculawlibrarian@gmail.com.
HATCH-WAXMAN 2003—PATENTED V. GENERIC DRUGS: REGULATORY, LEGISLATIVE AND JUDICIAL DEVELOPMENTS†

Richard J. Smith‡

TABLE OF CONTENTS

I. INTRODUCTION .................................................................................. 697
   A. Overview of Hatch-Waxman ......................................................... 697
      1. Pre-Hatch-Waxman ................................................................. 697
      2. Hatch-Waxman Amendments .................................................. 698
      3. Summary of FDA Approval Process ....................................... 698
   B. FTC Recommendations .............................................................. 700

II. REGULATORY DEVELOPMENTS ..................................................... 702
   A. FDA Regulations ........................................................................ 702
      1. One 30-Month Stay Per ANDA .............................................. 703
      2. Patent Listing Regulations ....................................................... 703
         a. Polymorphs ....................................................................... 704
         b. Method-of-Use Patents ......................................................... 704
   B. FTC Enforcement ......................................................................... 705
      1. Bristol-Myers Squibb .............................................................. 705
      2. Schering-Plough ................................................................... 706

III. LEGISLATIVE DEVELOPMENTS .................................................... 707
   A. Limits to 30-Month Stay .............................................................. 707
   B. Agreements By Generic Applicants .......................................... 708
   C. Declaratory Judgment Actions .................................................. 708
   D. Orange Book Listing Remedies .................................................. 709

† This paper is an updated version of a paper presented at the Institute for Law and Technology, 41st Annual Program on Intellectual Property Law, Dallas, Texas (Nov. 6, 2003).
‡ Richard J. Smith is a Partner in the Palo Alto office of Finnegan Henderson Farabow Garrett & Dunner LLP, specializing in Intellectual Property litigation. The views expressed in this paper are those of the author and not necessarily those of Finnegan Henderson or any of its clients.
IV. JUDICIAL DEVELOPMENTS.......................................................... 710
A. § 271(e)(1) Safe Harbor......................................................... 710
B. § 271(e)(2) and Method-of-Use Patents......................... 712
C. Battle of the Generics—TorPharm and Purepac .... 716
D. Antitrust Issues—In re Cardizem and Valley Drug 718
V. CONCLUSION.............................................................................. 720
I. INTRODUCTION

Enacted twenty years ago, the Hatch-Waxman Amendments\(^1\) sought to balance the two competing policy interests of (1) inducing pioneering research and development of new drugs, and (2) enabling competitors to bring low-cost generic copies of those drugs to market.\(^2\) The increasing costs of drug development and public concerns over consumer drug prices have resulted in a renewed focus on the desired balance between these competing policy objectives.

A. Overview of Hatch-Waxman

1. Pre-Hatch-Waxman

The regulatory framework of the drug approval process before the Hatch-Waxman Amendments created a number of obstacles, both for brand-name and generic pharmaceuticals. Notwithstanding the substantial time and expense of drug discovery and development, brand-name pharmaceutical companies often had the effective terms of their patents shortened due to issuance of the patents before FDA approval of the corresponding drugs and the time required for the FDA to ensure the safety and efficacy of the brand-name drug.\(^3\) Generic pharmaceutical companies also faced hurdles, such as the requirement to perform their own safety and efficacy studies.\(^4\) In addition, a generic company could not begin the required FDA approval process until after patents on the relevant brand-name product had expired, since to begin earlier would typically have infringed the patents of the brand-name company.\(^5\) As a result, by 1984 there were approximately 150 brand-name drugs whose patents had expired but for which there was no generic equivalent.\(^6\)

---

3. See Unimed, Inc. v. Quigg, 888 F.2d 826, 829 (Fed. Cir. 1989) (noting that the intent of the Hatch-Waxman Amendments was to "ameliorate the loss incurred when patent terms tick away while the patented product is awaiting regulatory approval").
2. Hatch-Waxman Amendments

The Hatch-Waxman Amendments provided brand-name pharmaceutical companies with the opportunity to extend the term of a patent in certain circumstances, thereby restoring patent protection as compensation for the time used to obtain FDA approval. Generic drug companies were also provided substantial relief from the approval time delays in two ways. First, generic companies were allowed to rely on the innovators’ safety and efficacy data and merely demonstrate that their generic drug was “bioequivalent” to the relevant brand-name product. Second, the patent statute was amended to clarify that it was not an act of infringement to make, use, or sell a patented invention “solely for uses reasonably related to the development and submission of information” to the FDA.

3. Summary of FDA Approval Process

A pharmaceutical company seeking to manufacture a new drug must file a New Drug Application (“NDA”) for consideration by the FDA. Preparing an NDA is a time-intensive and costly process since it must contain, among other things, detailed clinical studies of the drug’s safety and efficacy, as well as a list of patents that claim the drug. If the FDA approves the NDA, it publishes a listing of the drug and patents on the drug's approved aspects in Approved Drug Products with Therapeutic Equivalence Evaluations, referred to as the “Orange Book.”


8. 21 U.S.C. § 355(j)(2)(A)(iv) (2000). In general, 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 pioneer drug when administered at the same dosage. Id. § 355(j)(8)(B).


10. The framework governing the approval of pioneering and generic drugs has been outlined in several recent opinions of the Federal Circuit. See, e.g., Apotex, Inc. v. Thompson, 347 F.3d 1335 (Fed. Cir. 2003); Allergan, Inc. v. Alcon Labs., Inc., 324 F.3d 1322 (Fed. Cir. 2003); Andrx Pharms., Inc. v. Biovail Corp., 276 F.3d 1368 (Fed. Cir. 2002); and Mylan Pharms., Inc. v. Thompson, 268 F.3d 1323 (Fed. Cir. 2001). See also Eli Lilly & Co. v. Medtronic, Inc., 496 U.S. 661 (1990).


12. Id. § 355 (b)(1). The statute provides for listing only if: (1) the patent “claims the drug . . . or . . . a method of using such drug” and (2) the patent is one “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.” Id.

13. Id. § 355(b)(1), (j)(7)(A)(iii).
A company seeking approval of a generic drug may file an Abbreviated New Drug Application ("ANDA"). In addition to containing sufficient information to demonstrate that the generic drug is "bioequivalent" to the relevant brand-name product, the ANDA process also requires a certification regarding each patent listed in the Orange Book that relates to the relevant NDA product for which the applicant is seeking to make a generic version. In particular, the ANDA applicant must certify that: (I) no such patent information has been submitted to the FDA; (II) the patent has expired; (III) the patent is set to expire on a certain date; or (IV) such patent is invalid or will not be infringed by the manufacture, use, or sale of the new generic drug for which the ANDA is submitted.

When an ANDA applicant makes a paragraph IV certification, two additional provisions of the Hatch-Waxman Amendments are implicated. The first is the automatic "30-month stay" protection afforded brand-name companies. When an ANDA contains a paragraph IV certification, the ANDA applicant must give notice to the patentee and NDA holder, providing a detailed basis for its belief that the patent is invalid or will not be infringed. The patentee is then given 45 days to sue the ANDA applicant for infringement. If the patentee does not file suit, the ANDA application may be approved, provided other regulatory requirements (such as bioequivalence) are satisfied. If the patentee files suit within the 45-day period, the FDA may not approve the ANDA until the expiration of the 30-month period beginning on the date of receipt of notice. However, if before the expiration of such period the district court decides that the patent is invalid or not infringed, the approval will be

14. *Id.* § 355(j). Certain other drug applications, known as 505(b)(2) applications, include provisions similar to those implicated by the filing of an ANDA.


16. 21 U.S.C. § 355(j)(2)(A)(vii). These are commonly referred to as paragraph I, II, III and IV certifications. If one of the listed patents is a method-of-use patent which does not claim a use for which the applicant is seeking approval, the applicant must make a statement to that effect (a "section viii statement"). *Id.* § 355(j)(2)(A)(viii).

17. *Id.* § 355(j)(5)(B)(iii).

18. *Id.* § 355(j)(2)(B). The FDA regulations state that the notice should include a detailed statement of the factual and legal basis for the applicant's opinion that the patent is not valid, unenforceable, or will not be infringed. 21 C.F.R. §§ 314.52(c)(6), 314.95(c)(6) (West, WESTLAW through Mar. 12, 2004).


20. See *id.* § 355(j)(4).

21. *Id.* § 355(j)(5)(B)(iii). The statute further provides for "such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action." *Id.*
made effective on the date of the judgment, settlement order or consent decree reflecting the court’s decision. If the district court decides the patent has been infringed and the judgment of the district court is appealed, the approval shall be effective on the date the appellate court decides the patent is invalid or not infringed, or the date of a settlement order or consent decree signed by the appellate court stating that the patent is invalid or not infringed. If the court decides that the patent has been infringed, and the judgment is not appealed or is affirmed, the approval is effective on the date the district court orders pursuant to 35 U.S.C. § 271(e)(4)(A).

The second provision implicated by a paragraph IV certification 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 market exclusivity, during which the FDA may not approve subsequent ANDAs for the same drug product. This exclusivity period increases the economic incentives for a generic company to be the first to file an ANDA containing a paragraph IV certification, as well as an incentive for generic companies to litigate patents that may be invalid or not infringed.

B. FTC Recommendations

In July 2002, the Federal Trade Commission published the final results of its industry-wide study focused on certain aspects of generic drug competition under the Hatch-Waxman Amendments. The automatic 30-month stay and 180-day period of exclusivity implicated by a generic ANDA applicant making a paragraph IV certification were at the heart of the FTC Report. The FTC Report concluded with two recommendations:

22. Id.
23. Id.
24. Id. This section provides that “the court shall order the effective date of any approval . . . to be a date which is not earlier than the date of the expiration of the patent which has been infringed.” 35 U.S.C. § 271(e)(4)(A) (2000).
26. Id. The 180-day exclusivity period is triggered by the first commercial marketing of the generic product. Id. Sometimes ANDA applicants share the 180-day period. See, e.g., Apotex, Inc. v. Thompson, 347 F.3d 1335, 1341 (Fed. Cir. 2003).
29. See id. at 6–8, 39–63.
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.\(^\text{30}\)

The FTC cited several reasons for this recommendation. It noted that one 30-month period historically has approximated the time needed for FDA review and approval of the generic’s ANDA.\(^\text{31}\) Further, the data uncovered by the FTC indicated that court decisions in ANDA-related patent litigation typically are not reached much earlier than 30 months from notice of the generic’s ANDA.\(^\text{32}\) Against these findings, the FTC noted that the history of multiple 30-month stays caused by the filing of later-issued patents appeared “problematic.”\(^\text{33}\) The FTC further noted that multiple 30-month stays prevented FDA approval of the generic applicants’ ANDAs for 4 to 40 months beyond the initial 30-month period.\(^\text{34}\)

Regarding this recommendation, the FTC also surmised that permitting only one 30-month stay per drug product per ANDA should eliminate most of the potential for improper Orange Book listings to generate unwarranted 30-month stays.\(^\text{35}\) The FTC made some suggestions in this regard, including clarification of the FDA listing requirements and permitting a generic applicant to raise listability issues as a counterclaim in the context of patent infringement litigation initiated by the brand-name company.\(^\text{36}\)

Recommendation 2: Pass legislation to require brand-name companies and first generic applicants to provide copies of certain agreements to the Federal Trade Commission.\(^\text{37}\)

In making this recommendation, the FTC noted that generic applicants prevailed in nearly 75% of the patent litigation ultimately resolved by a court decision.\(^\text{38}\) Further, the data indicated that, upon receiving FDA approval, first generic applicants that were not sued began commercial marketing in a timely manner, thereby triggering

\(\text{30. FTC REPORT, supra note 28, at ii, 39.}\)
\(\text{31. Id. at iv.}\)
\(\text{32. Id.}\)
\(\text{33. Id. The FTC noted that of the eight drug products involving later-issued patents identified in the FTC Report, all four that had been adjudicated resulted in the later-issued patent being found invalid or not infringed. Id. at iii–iv, 40.}\)
\(\text{34. FTC REPORT, supra note 28, at iii, 40.}\)
\(\text{35. Id. at v.}\)
\(\text{36. Id. See also infra Parts II.A, III.D.}\)
\(\text{37. FTC REPORT, supra note 28, at vi, 40}\)
\(\text{38. Id. at viii.}\)
the running of the 180 days and allowing FDA approval of any subsequent eligible generic applicant once the 180-day exclusivity period had run. The FTC noted, however, that antitrust issues 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. The FTC stated that 14 of the 20 final settlement agreements obtained through its study had this potential as of the time they were executed. Thus, the FTC concluded that notification of such agreements to the FTC and the U.S. Department of Justice was warranted.

II. REGULATORY DEVELOPMENTS

A. FDA Regulations

In response to concerns raised in the FTC Report and elsewhere, the FDA amended its regulations (21 C.F.R. pt. 314) effective August 18, 2003. The new regulations permit only one 30-month stay per ANDA and clarify the patent submission and listing requirements for new drug applications. In particular, the final rule:

- Allows a full opportunity for only one 30-month stay per ANDA or 505(b)(2) application;
- Prohibits the submission of patents claiming packaging, intermediates, or metabolites;
- Requires the submission of certain patents claiming a different polymorphic form of the active ingredient described in the NDA;
- Adds a requirement that for submission of polymorph patents the NDA holder must have test data demonstrating that a drug product containing the

39. Id. at viii, 34.
40. Id. at viii.
41. Id. at viii. See also infra Part III.B.
42. Id. at viii. See infra Part III.B.
43. Applications for FDA Approval to Market a New Drug: Patent Submission and Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug Is Invalid or Will Not Be Infringed, 68 Fed. Reg. 36,676 (Jun. 18, 2003) (to be codified at 21 C.F.R. pt. 314) [hereinafter FDA Approval Applications]. The compliance date for submission of information on polymorph patents is Dec. 18, 2003. Id. Drug substances that are the same active ingredient, but in different physical forms, are often called “polymorphs.” Id. at 36,678.
44. Id. at 36,677–78.
polymorph will perform the same as the drug product described in the NDA;

- Makes changes to the patent information required to be submitted and provides declaration forms for submitting that information to the FDA, both with the NDA and after NDA approval; and

- Does not require claim-by-claim listing on the declaration form except for method-of-use patents claiming approved methods of use.\(^\text{45}\)

1. One 30-Month Stay Per ANDA

Acknowledging a "change in position," the FDA amended its regulations on the notice required by an applicant filing a paragraph IV certification by eliminating that requirement when the application already contains a paragraph IV certification.\(^\text{46}\) The amendment was construed by the FDA as allowing "a full opportunity for only one 30-month stay per ANDA or 505(b)(2) application."\(^\text{47}\)

In amending its regulations, the FDA stated that "[m]ultiple 30-month stays increase the delay in approval of generic drugs and result in increased costs to consumers."\(^\text{48}\) The FDA explained in some detail that "the act is ambiguous on this issue of multiple 30-month stays" and that "the statutory language may plausibly be read in different ways."\(^\text{49}\) It nevertheless concluded that its "pre-existing regulations permitting multiple 30-month stays have led to protracted delays in generic drug approvals and, therefore, need to be changed."\(^\text{50}\)

2. Patent Listing Regulations

The new regulations seek to clarify the types of patents for which information must be submitted and for which information must not be submitted.\(^\text{51}\) Patents for which information must be submitted include drug substance (active ingredient) patents, drug product

\(^{45}\) Id. at 36,677.

\(^{46}\) Id. at 36,693. The Medicare Act of 2003, discussed infra Part III, essentially reversed this regulation by requiring notice "regardless of whether the applicant has already given notice." Medicare Act of 2003, supra note 11, § 1101(a)(1).

\(^{47}\) FDA Approval Applications, supra note 43, at 36,677.

\(^{48}\) Id. at 36,690.

\(^{49}\) Id. at 36,693.

\(^{50}\) Id. at 36,694.

\(^{51}\) 21 C.F.R. § 314.53(b) (West, WESTLAW through Mar. 12, 2004).
(formulation and composition) patents, and method-of-use patents. Information on process patents, and patents claiming packaging, metabolites, and intermediates, must not be submitted to the FDA. The new regulations raise particular issues about polymorphs and method-of-use patents.

a. Polymorphs

For patents that claim a polymorph that is the same as the active ingredient described in the approved or pending application, the new regulations require the applicant to certify in the declaration forms that it has certain test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the new drug application. The regulations further specify the nature of the test data required to support the statement in the declaration. The FDA noted that the test-data certification requirement replaces the test data required of ANDA applicants to demonstrate that the drug product containing the polymorph described in the ANDA will perform the same as the drug product described in the NDA.

b. Method-of-Use Patents

For patents that claim a method of use, the new regulations require the applicant to submit information only on those patents that claim indications or other conditions of use described in the pending or approved application. Further, the applicant must separately identify each pending or approved method of use and related patent claim. For approved applications, the applicant must identify with specificity the section of the approved labeling that corresponds to the method of use claimed by the patent submitted.

The FDA cited the recent Federal Circuit opinions in Warner-Lambert and Allergan, both discussed below, as being consistent with its position that method-of-use patents that do not claim an FDA

---

52. Id. § 314.53(b)(1).
53. Id.
54. Id.
55. Id. § 314.53(b)(2).
57. 21 C.F.R. § 314.53(b)(1).
58. Id.
59. Id.
approved use must not be submitted for listing in the Orange Book.\textsuperscript{60} The FDA's requirement that an applicant separately identify each pending or approved method of use and related patent claim is tied to the "section viii statement" whereby an ANDA or 505(b)(2) applicant may avoid certifying to a patent by stating that it is not seeking approval for the use claimed in the listed patent.\textsuperscript{61} The FDA believed it was necessary that NDA holders submit more specific information on the approved methods of use protected by a submitted patent to effectively implement the certification and section viii statement provisions.\textsuperscript{62}

\textbf{B. FTC Enforcement}

The FTC has continued to exercise its enforcement authority in matters related to competition in the pharmaceutical industry.\textsuperscript{63}

1. Bristol-Myers Squibb

On April 14, 2003, the FTC issued its Decision and Order against Bristol-Myers Squibb ("BMS") regarding anticancer drugs Taxol and Platinol and the antianxiety agent BuSpar.\textsuperscript{64} The Complaint giving rise to the Consent Order alleged a course of conduct by BMS that included paying a would-be competitor $72.5 million to abandon its challenge to a BMS patent and stay off the market until the patent expired, abusing FDA regulations to block generic entry, making false statements to the FDA in listing patents in the Orange Book, engaging in inequitable conduct before the PTO, and filing baseless patent infringement suits.\textsuperscript{65}

\textsuperscript{60} Applications for FDA Approval to Market a New Drug: Patent Submission and Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug Is Invalid or Will Not Be Infringed, 68 Fed. Reg. at 36,681–82. Warner-Lambert and Allergan are discussed infra Part IV.B.

\textsuperscript{61} Id.

\textsuperscript{62} Id. at 36,682–83.


The FTC identified BuSpar, Taxol, and Platinol, and their respective generic bioequivalent versions, as three distinct antitrust markets in which BMS had monopoly power. Further, a significant focus of the FTC's Complaint was on the alleged improper listing of patents in the Orange Book. The FTC asserted that "the Orange Book listing scheme is susceptible to opportunistic behavior" and affirmatively pled in its complaint that BMS's conduct was not immune from antitrust liability under the Noerr-Pennington doctrine.

The Consent Order includes a specific prohibition against the listing of U.S. Patent No. 6,150,365 (issued November 21, 2000) in the Orange Book, as well as a general prohibition against Orange Book listings that are contrary to the statutes and regulations governing the listings. Also included in the Consent Order are certain prohibitions against triggering the 30-month stay of FDA approval of a generic applicant. Finally, the Consent Order prohibits certain agreements with ANDA filers, including certain agreements prohibiting the ANDA filer from researching, developing, manufacturing, marketing and selling certain products, certain agreements restricting relinquishment of the right to the 180-day exclusivity period, and certain agreements in patent infringement disputes prohibiting the sale of certain products by the ANDA filer.

2. Schering-Plough

On December 8, 2003, the FTC issued its Final Order against Schering-Plough Corporation ("Schering") and Upsher-Smith Laboratories, Inc. ("Upsher") involving the settlement of patent

66. Complaint, supra note 65, ¶¶ 64, 104, 123.
67. Complaint, supra note 65, ¶¶ 50, 90, 94, 137, 142, 149.
68. FTC ANALYSIS, supra note 65, at 8.
71. Consent Order, F.T.C. No. C-4076, ¶ VI.
72. Id. ¶ VII.
73. Id. ¶ XIII.
74. Id. ¶ XIV.
75. Id. ¶ XV.

The Final Order provides for prospective relief only. It provides certain prohibitions on final and interim settlement agreements in the context of Hatch-Waxman patent infringement litigation. It further provides for notification to the FTC prior to consummation of certain agreements.

III. LEGISLATIVE DEVELOPMENTS

On December 8, 2003, President Bush signed the Medicare Act of 2003 into law. Among other amendments, the legislation addresses limits to the 30-month stay provisions, certain agreements entered into by generic applicants, declaratory judgment actions by generic applicants, and Orange Book listing remedies.

A. Limits to 30-Month Stay

The Medicare Act of 2003 amended the provisions of the FDCA relating to the 30-month stay by stating that the action triggering such stay is one brought for infringement of the patent that is the subject of the paragraph IV certification and "for which information was


77. THOMAS B. LEARY, OPINION OF THE COMMISSION ON IN THE MATTER OF SCHERING-PLOUGH CORPORATION, ET AL. 2 [hereinafter OPINION OF THE COMMISSION], available at http://www.ftc.gov/os/adjpro/d9297/031218commissionopinion.pdf. Although AHP was initially named as a Respondent, it agreed to a settlement and a Final Consent Order was approved Apr. 2002. Id. at 5.

78. Id. at 86.

79. Id. at 12–13, 87. The Commission's Opinion discusses In re Cardizem and Valley Drug, both discussed infra Part IV.D.

80. OPINION OF THE COMMISSION, supra note 77, at 87; Final Order, supra note 76.

81. Final Order, supra note 76, ¶¶ II, IV.

82. Id. ¶ V.


84. Id.
submitted to the Secretary under subsection (b)(1) or (c)(2) before the
date on which the application (excluding an amendment or
supplement to the application), which the Secretary later determines
to be substantially complete, was submitted. Such language
essentially limits the 30-month stay to infringement suits based on
patents listed before the date of submission of the generic drug
application.

B. Agreements By Generic Applicants

As noted above, the FTC Report identified potential antitrust
concerns arising from agreements between brand-name and generic
companies. The Medicare Act of 2003 addresses these concerns by
providing for forfeiture of the 180-day exclusivity if an applicant
submitting a paragraph IV certification has entered into an agreement
with another applicant, or the holder of the NDA or patent owner, in
violation of the antitrust laws. In addition, the legislation sets
certain filing requirements for (1) agreements between generic drug
applicants and brand-name drug companies regarding (a) the
manufacture, marketing, or sale of the brand-name or generic drug, or
(b) the 180-day exclusivity period, and (2) agreements between
generic drug applicants regarding the 180-day exclusivity period.
Each party must file the agreement and certain related agreements
with the Assistant Attorney General and the FTC not later than ten
business days after the date of execution.

C. Declaratory Judgment Actions

The Medicare Act of 2003 includes provisions amending the
FDCA and Title 35 to allow a generic applicant to file a declaratory

86. These amendments apply with respect to patent information submitted under
subsection (b)(1) or (c)(2) of section 505 of FDCA on or after August 18, 2003, the effective
date of the FDA regulations discussed supra Part II.A.
87. FTC REPORT, supra note 28, at viii.
88. Medicare Act of 2003, supra note 11, § 1102(a). The legislation contemplates a
decision resulting from a complaint filed by the FTC or the Attorney General. The term
"antitrust laws" includes section 1 of the Clayton Act (15 U.S.C. § 12) and section 5 of the
Federal Trade Commission Act (15 U.S.C. § 45) to the extent that that section applies to unfair
methods of competition. Id.
89. Id. § 1112.
90. Id. §§ 1112-13. Violation includes liability for a civil penalty of up to $11,000 for
each day an entity fails to comply, recoverable in a civil action brought by the United States or
the FTC. Id. § 1115.
judgment of patent invalidity or noninfringement if the patent owner or NDA holder does not bring a patent infringement suit on or before the date that is 45 days after receipt of notice from the generic applicant.91 Section 271(e) of the Patent Act has also been amended to clarify that the federal courts shall have subject matter jurisdiction in such declaratory judgment actions "to the extent consistent with the Constitution."92 This language was included to assuage concerns raised during deliberation of the legislation. The Department of Justice had argued that a federal court's jurisdiction emanates from Article III of the Constitution and that Congress cannot expand the courts' power to hear cases beyond what the Constitution provides.93 Jon W. Dudas, Deputy Director of the USPTO, had also raised a concern that the proposed statutorily-created right to a declaratory judgment action could result in unnecessary harassment of patent owners through litigation and patent uncertainty as a result of such litigation.94

D. Orange Book Listing Remedies

The Medicare Act of 2003 amends the FDCA to permit an applicant to assert a counterclaim requiring the holder of the NDA to correct or delete the patent information on the ground that the patent does not claim either the drug for which the application was approved or an approved method of using the drug.95 The provision only permits a counterclaim to a patent infringement action, not an independent cause of action, and does not permit the recovery of damages from a successful counterclaim.96

91. Medicare Act of 2003, supra note 11, § 1101(a)(2)(C). If the notice relates to noninfringement, it must be accompanied by a document providing an offer of confidential access to the application for the purpose of determining whether an infringement action should be brought. Id. Similar amendments are included in 21 U.S.C. § 355(c)(3). Id. § 1101(b)(2)(D).
92. Id. § 1101(d); see also the newly created 35 U.S.C. § 271(e)(5).
94. See id., at 7 (statement of Jon W. Dudas, Deputy Under Secretary of Commerce for Intellectual Property and Deputy Director of the United States Patent and Trademark Office).
96. Id.
IV. JUDICIAL DEVELOPMENTS

A. § 271(e)(1) Safe Harbor

In *Integra LifeSciences I, Ltd. v. Merck KGaA*, the Federal Circuit considered the scope of the "safe harbor" against patent infringement defined by 35 U.S.C. § 271(e)(1). Section 271(e)(1) recites in pertinent part:

It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention ... solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.

The Federal Circuit affirmed the district court's determination that 35 U.S.C. § 271(e)(1) did not immunize Merck KGaA against liability for patent infringement. However, the Federal Circuit reversed and remanded the jury's damage award to Integra of $15,000,000 as a reasonable royalty.

Integra owns several U.S. patents related to a short tri-peptide segment having the amino acid sequence arginine-glycine-aspartic acid (the "RGD peptide"). The RGD peptide promotes cell adhesion and, in theory, plays a role in wound healing, biocompatibility of prosthetic devices, and the growth of blood vessels.

Merck entered into an agreement with Scripps to fund the "necessary experiments to satisfy the biological bases and regulatory (FDA) requirements for the implementation of clinical trials." The agreement contemplated conducting clinical trials with a drug candidate within three years. According to the agreement, Scripps scientists conducted experiments directed at evaluating several drug candidates, explaining the mechanism by which they work, determining which could be safely tested in humans, and determining

---

99. *Integra*, 331 F.3d at 862, 868.
100. *Id.* at 872.
101. *Id.* at 862.
102. *Id.* at 862–63.
103. *Id.* at 863.
104. *Id.*
the mode of administering the candidate drugs that would produce the optimum therapeutic effect.\textsuperscript{105} This research resulted in the identification of a lead candidate for clinical development.\textsuperscript{106}

After license negotiations failed, Integra sued Merck, Scripps, and the scientist in charge of the research that identified the leading drug candidate, asserting that the research infringed its patents.\textsuperscript{107} The defendants answered that the research was protected by the safe harbor afforded by 35 U.S.C. § 271(e)(1) and that Integra's patents were invalid.\textsuperscript{108}

The Federal Circuit framed the question as whether experiments that do not supply information for submission to the FDA, but rather identified the best drug candidate to subject to future clinical testing, are exempt from liability for infringement under § 271(e)(1).\textsuperscript{109} Stated more broadly, the issue was whether the "safe harbor" reaches back down the chain of experimentation to embrace the identification and development of new drugs that will be subject to FDA approval.\textsuperscript{110}

After reviewing the legislative history of § 271(e)(1), the Federal Circuit concluded that the focus of the exemption is the provision of information to the FDA.\textsuperscript{111} It reasoned that, while the term "reasonably" permits some activities that are not themselves the experiments that produce FDA information, the exemption does not extend to general biomedical research to identify new pharmaceutical compounds.\textsuperscript{112} As stated by the court, "[t]he FDA has no interest in the hunt for drugs that may or may not later undergo clinical testing for FDA approval."\textsuperscript{113}

The Federal Circuit agreed with Merck that the damage award was not supported by substantial evidence.\textsuperscript{114} According to the court,
the record evidence on a hypothetical license negotiation simply did not support the jury's damage award.115

Judge Newman concurred-in-part and dissented-in-part, focusing on the common law research exemption and § 271(e)(1).116 According to Judge Newman, the Scripps/Merck activities were either exempt exploratory research or immunized by § 271(e)(1):

It would be strange to create an intervening kind of limbo, between exploratory research subject to exemption, and the FDA statutory immunity, where the patent is infringed and the activity can be prohibited. That would defeat the purposes of both exemptions; the law does not favor such an illogical outcome.117

B. § 271(e)(2) and Method-of-Use Patents

In Warner-Lambert Co. v. Apotex Corp.,118 the Federal Circuit considered, as a matter of first impression, whether it is an act of infringement under 35 U.S.C. § 271(e)(2)(A) to submit an ANDA seeking approval to make, use, or sell a drug for an approved use if any other use of the drug is claimed in a patent, or if it is only an act of infringement to submit an ANDA seeking approval to make, use, or sell a drug if the drug or the use for which FDA approval is sought is claimed in a patent.119 Section 271(e)(2)(A) provides in pertinent part as follows:

It shall be an act of infringement to submit . . . an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act . . . for a drug claimed in a patent or the use of which is claimed in a patent . . . if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug . . . claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.120

The Federal Circuit concluded that it is not an act of infringement to submit an ANDA for approval to market a drug for a use when neither the drug nor that use is covered by an existing

115. Id. at 872.
117. Id. at 877.
118. 316 F.3d 1348 (Fed. Cir. 2003).
patent, and the patent at issue is for a use not approved under the NDA.\textsuperscript{121}

Warner-Lambert is the owner of several patents related to gabapentin, a cyclic amino acid compound.\textsuperscript{122} In 1993, Warner-Lambert obtained approval of an NDA to market gabapentin for use in "adjunctive therapy in the treatment of partial seizures with or without secondary generalization in adults with epilepsy."\textsuperscript{123} Apotex filed an ANDA seeking approval for the same indication, including a paragraph IV certification for two patents of Warner-Lambert referred to as the "monohydrate patent" and the "neurodegenerative method patent."\textsuperscript{124} Notwithstanding Apotex's position in its paragraph IV notice that the neurodegenerative method patent did not claim a method of using gabapentin and its derivatives for partial seizure, Warner-Lambert filed suit, alleging that Apotex's submission of its ANDA was an act of infringement of that patent under § 271(e)(2)(A).\textsuperscript{125}

In Warner-Lambert's view, a patent claiming a use of a drug is infringed by the filing of an ANDA irrespective of whether approval is sought to market the drug for the patented use.\textsuperscript{126} After reviewing the Hatch-Waxman Amendments and their legislative history, the court concluded that Congress did not intend for it to be an act of infringement to submit an ANDA for a drug if just any use of that drug was claimed in a patent and the applicant sought approval of its ANDA prior to the expiration of that patent.\textsuperscript{127} Rather, Congress intended to limit actions for infringement of method-of-use patents under § 271(e)(2)(A) to "controlling use patents," or patents that claim an approved use of a drug.\textsuperscript{128} Since Apotex was not submitting an application to sell a drug for treatment of neurodegenerative diseases, it was entitled to summary judgment of noninfringement.\textsuperscript{129}

\textsuperscript{121} Warner-Lambert, 316 F.3d at 1354–55.
\textsuperscript{122} Id. at 1351–52.
\textsuperscript{123} Id. at 1352.
\textsuperscript{124} Id. In filing its ANDA, Apotex sought approval to market generic gabapentin upon expiration of Warner-Lambert’s “epilepsy method patent.” Id. The claim under the monohydrate patent was the subject of a summary judgment of noninfringement and not an issue on appeal. Id. at 1353 n.1.
\textsuperscript{125} Warner-Lambert, 316 F.3d at 1353.
\textsuperscript{126} Id. at 1355.
\textsuperscript{127} Id. at 1358–59.
\textsuperscript{128} Id. at 1362.
\textsuperscript{129} Id.
The Federal Circuit also rejected Warner-Lambert's assertion of inducement of infringement under § 271(b) based on its argument that gabapentin was being prescribed for off-label uses, including for the treatment of neurodegenerative diseases. The court concluded that, in the absence of any evidence that Apotex has or will promote or encourage doctors to infringe the neurodegenerative method patent, there was no genuine issue of material fact on inducement of infringement.

In Allergan, Inc. v. Alcon Laboratories, Inc., the Federal Circuit affirmed the district court's grant of summary judgment of noninfringement. Citing Warner-Lambert, the court held that the action for induced infringement brought by Allergan was not cognizable under 35 U.S.C. § 271(e)(2). However, all three judges expressed their disapproval of Warner-Lambert.

Allergan obtained FDA approval for the use of brimonidine for reducing intraocular pressure. That use, as well as brimonidine, is unpatented and in the public domain. After further research, Allergan discovered that brimonidine was also effective in treating patients with neurodegeneration of the optic nerve. Allergan obtained two patents on the use of brimonidine to treat ocular neural injuries, and listed both in the Orange Book. Later, Alcon and Bausch & Lomb filed ANDAs to market generic versions of brimonidine for use in lowering intraocular pressure.

Allergan filed suit for infringement under 35 U.S.C. § 271(e)(2), contending that if Alcon and Bausch & Lomb obtained approval for their ANDAs, they would induce doctors to infringe by prescribing

130. Id. at 1363–64.
131. Warner-Lambert, 316 F.3d at 1364. For more on generic gabapentin, see TorPharm, Inc. v. Thompson, 260 F. Supp. 2d 69 (D.D.C. 2003) discussed infra Part IV.C.
132. 324 F.3d 1322 (Fed. Cir. 2003), cert. denied, 124 S.Ct. 813 (2003) ("Allergan"). Finnegan Henderson represented Allergan before the Federal Circuit. See also Alcon Labs., Inc. v. Allergan, Inc., 256 F. Supp. 2d 1080, 1085 (C.D. Cal. 2003) (granting motions for summary judgment of noninfringement eight days before Allergan was decided, noting that Warner-Lambert confirmed in the court's mind that its analysis was correct).
133. Allergan, 324 F.3d at 1324.
135. Allergan, 324 F.3d at 1324.
136. See id. at 1334–46.
137. Id. at 1327.
138. Id.
139. Id.
140. Id. at 1328.
Alcon and Bausch & Lomb denied induced infringement by asserting that their ANDAs were for a use of the drug that is different from the use of the drug claimed in the asserted patent.143

The district court granted summary judgment, holding that the filing of an ANDA does not provide a predicate for a method-of-use patent holder to sue an ANDA applicant for induced infringement.144 In addition, the district court found that, since there was yet to be any third-party infringement, the question of inducing infringement would be entirely too speculative and run afoul of the case or controversy requirement of Article III of the Constitution.145

Holding that the case was controlled by Warner-Lambert, the Federal Circuit affirmed the summary judgment of noninfringement.146 However, the court disagreed with the rationale of the district court, noting that the language of § 271(e)(2) does not limit the reach of the statute to direct infringement actions to the exclusion of actions for induced infringement.147 The court further concluded that, while a § 271(e)(2) induced infringement claim may be speculative, it is not sufficiently so to contravene the case or controversy requirement.148

Judge Schall, joined by Judge Clevenger, wrote a concurring opinion disputing the holding of the Court’s precedent in Warner-Lambert.149 Judge Schall noted that the plain language of § 271(e)(2) compels the conclusion that an action for infringement may lie based on the filing of an ANDA for a drug whose use is patented, even if approval for the patented use is not sought in the ANDA.150 Writing separately, Judge Linn stated that the court in Warner-Lambert had overstepped its bounds in interpreting Congress’s intent by making

142. *Id.* at 1328. The Federal Circuit noted that the FDA does not prohibit doctors from prescribing a drug for an unapproved use, and it does not prohibit patients from using a drug for an unapproved use. *Id.* at 1324 n.1.

143. *Id.* at 1328.


145. *Id.* at 1227, 1231.

146. *Id.* at 1321.

147. *Id.* at 1331.

148. *Id.* at 1331–32. The Federal Circuit also rejected Allergan’s alternative argument that § 271(e)(2) provides a direct cause of action based simply upon the filing of the ANDA. *Id.* at 1334 n.9.

149. *Id.* at 1334.

150. *Id.* at 1335.
policy choices that were inconsistent with the plain language of the statute.\footnote{151}

C. Battle of the Generics—TorPharm and Purepac

Entitlement to the 180-day exclusivity period was at issue in TorPharm v. Thompson\footnote{152} and the related predecessor case Purepac v. Thompson.\footnote{153} TorPharm and Purepac had submitted rival ANDAs for the drug gabapentin, which the FDA had earlier approved for the treatment of epilepsy.\footnote{154} The United States District Court for the District of Columbia held that Purepac alone was entitled to the 180-day exclusivity to market generic gabapentin.\footnote{155}

Warner-Lambert had submitted several patents in connection with the FDA approval of gabapentin for the treatment of epilepsy.\footnote{156} Of particular significance were U.S. Patent No. 4,084,479 ("the '479 patent") for a method of using the drug to treat neurodegenerative diseases and U.S. Patent No. 6,054,482 ("the '482 patent"), a drug composition patent, which was submitted to the FDA on April 25, 2000, after Warner-Lambert’s approval for gabapentin.\footnote{157}

In March 1998, Purepac submitted an ANDA to market a generic version of gabapentin for the treatment of epilepsy.\footnote{158} Purepac submitted a section viii statement on the '479 patent when it submitted its ANDA and, on May 26, 2000, amended its application to include a paragraph IV certification for the newly submitted '482 patent.\footnote{159} Purepac, however, did not mail its required notice to Warner-Lambert until June 13, 2000.\footnote{160} On April 20, 1998, TorPharm submitted its rival gabapentin ANDA.\footnote{161} On June 13, 2000, TorPharm mailed a section viii statement and paragraph IV certification for the '479 patent, which were received by the FDA on

\footnotesize{\begin{itemize}
  \item \footnotetext{151}{Allergan, 324 F.3d at 1345–46.}
  \item \footnotetext{152}{260 F. Supp. 2d 69 (D.D.C. 2003).}
  \item \footnotetext{153}{238 F. Supp. 2d 191 (D.D.C. 2002).}
  \item \footnotetext{154}{TorPharm, 260 F. Supp. 2d at 74–75.}
  \item \footnotetext{155}{Id. at 86.}
  \item \footnotetext{156}{Id. at 74.}
  \item \footnotetext{157}{Id.}
  \item \footnotetext{158}{Id.}
  \item \footnotetext{159}{Id.}
  \item \footnotetext{160}{TorPharm, 260 F. Supp. 2d at 78.}
  \item \footnotetext{161}{Id. at 75.}
\end{itemize}}
June 16. TorPharm sent its notice to Warner-Lambert on the same day (June 13) it mailed its certification to the FDA.

In Purepac, the district court considered the FDA's decision not to approve Purepac's ANDAs because they contained section viii statements regarding the '479 patent. The district court ruled in favor of Purepac, holding that the FDA's decision "impermissibly disregarded both Warner-Lambert's and the agency's own understanding of the coverage claimed by that patent." However, the district court declined to go further and require the FDA to reject TorPharm's paragraph IV certification to the '479 patent, stating that it would leave "this delicate question" for the FDA to resolve in the first instance. On remand, the FDA gave Purepac the exclusive right to sell gabapentin free from generic competition for 180 days, deciding that Purepac had exclusivity with respect to the '482 patent but that no ANDA applicant was eligible for the 180-day exclusivity with respect to the '479 patent.

TorPharm vigorously objected to the FDA's decision and filed suit, along with a request for a preliminary injunction, on February 14, 2003. TorPharm argued that it was entitled to exclusivity on the '482 patent because it was the first ANDA applicant to comply with the statutory mandate that notice shall be provided to the NDA holder (and patent owner) at the same time that the applicant amends its application to include a paragraph IV certification. While Purepac did not provide notice to Warner-Lambert at the same time it offered its amended certification to the FDA, the appropriate remedy determined by the FDA was simply delaying the operative date of the certification to the date notice was sent. The FDA also determined that the operative date (assuming notice has been sent) for the filing of an amended certification is the day the certification is received by the FDA (i.e., June 16 for the TorPharm certification). The district court found that these decisions by the FDA on the '482 patent were

162. Id. at 75, 78.
163. Id. at 78.
165. Id. at 212.
166. Id. at 211.
167. TorPharm, 260 F. Supp. 2d at 76, 78.
168. Id. at 79.
169. Id.
170. Id. at 80.
171. Id. at 81.
reasonable and affirmed the 180-day exclusivity awarded to Purepac based on that patent. 172

Concerning the '479 patent, the district court stated that the FDA had two options once TorPharm's paragraph IV certification was deemed improper in light of Purepac's section viii statement. 173 It could have required TorPharm to submit its own section viii statement to replace the rejected paragraph IV certification or it could have done as it did and removed the patent from the Orange Book altogether, the delisting regulation posing no impediment to striking the patent from the agency's records. 174 The district court concluded that, for exclusivity purposes, there was no functional difference between these options, and that either way TorPharm's claim to exclusivity based on the '479 patent was extinguished. 175

D. Antitrust Issues—In re Cardizem and Valley Drug

In In re Cardizem, 176 the Court of Appeals for the Sixth Circuit considered the antitrust implications of an agreement by a generic drug manufacturer (Andrx) to refrain from marketing its generic version of Cardizem CD after receiving FDA approval in exchange for quarterly payments of $10 million. 177 Plaintiffs, direct and indirect purchasers of Cardizem CD, alleged that the agreement between Hoescht Marion Roussel, Inc. ("HMR") (now Aventis Pharmaceuticals) and Andrx was a violation of federal and state antitrust laws. 178 The foundation of the plaintiffs' claims was that, but for the agreement, Andrx would have brought its generic product to market once it received FDA approval and at a lower price than the patented Cardizem CD sold by HMR. 179

172. Id. at 86.
173. TorPharm, 260 F. Supp. 2d at 85. The district court noted that the FDA has long taken the position that paragraph IV certifications and section viii statements are mutually exclusive. Id. at 83.
174. Id. at 85. Under agency regulations, because the patent had been the subject of a lawsuit based on a paragraph IV certification, it could be delisted only if no ANDA applicant was, at the time of delisting, entitled to exclusivity based on that patent. Id. at 82; 21 C.F.R. § 314.94(a)(12)(viii)(B) (West, WESTLAW through Mar. 12, 2004).
175. TorPharm, 260 F. Supp. 2d at 85. TorPharm and Purepac were also cited by the FDA as supporting its construction of the statute with respect to method-of-use patents. FDA Approval Applications, supra note 43, at 36,681–82.
177. Id. at 899–900.
178. Id. at 900.
179. Id. at 904.
The agreement arose out of a patent infringement suit by HMR triggered by Andrx's filing of an ANDA and a paragraph IV certification with respect to the patents listed as covering Cardizem CD.\(^{180}\) The agreement was entered into before the expiration of the statutory 30-month waiting period.\(^{181}\) Upon final approval of the Andrx ANDA, HMR began making quarterly payments of $10 million to Andrx and Andrx refrained from bringing its generic product to market.\(^{182}\) Approximately one year later, the parties settled the infringement suit and terminated the agreement, and Andrx began marketing its generic product with its 180-day period of market exclusivity.\(^{183}\)

The district court granted the plaintiffs' motion for partial summary judgment and certified two questions for interlocutory appeal: (1) whether plaintiffs had properly pled antitrust injury, and (2) whether the agreement between HMR and Andrx constituted a restraint of trade that was illegal \textit{per se} under section 1 of the Sherman Antitrust Act, 15 U.S.C. § 1, and under the corresponding state antitrust laws.\(^{184}\) The Sixth Circuit held that the plaintiffs had properly pled antitrust injury and concluded that the agreement at issue was a horizontal market allocation agreement and, as such, \textit{per se} illegal under the Sherman Act and corresponding state antitrust laws.\(^{185}\)

In \textit{Valley Drug Co. v. Geneva Pharmaceuticals, Inc.},\(^{186}\) the Court of Appeals for the Eleventh Circuit considered the terms of agreements similar to the agreement in \textit{Cardizem}, and reversed and remanded the district court's conclusion that the agreements at issue constituted \textit{per se} violations of the antitrust laws.\(^{187}\) According to the Eleventh Circuit, an antitrust analysis cannot ignore the scope of the patent exclusion when the exclusionary power of a patent is implicated.\(^{188}\) It respectfully disagreed with the Sixth Circuit's \textit{Cardizem} opinion to the extent it suggests that a settlement of patent

\begin{itemize}
\item 180. \textit{Id.} at 902.
\item 181. \textit{Id.}
\item 182. \textit{Cardizem}, 332 F.3d at 903.
\item 183. \textit{Id.}
\item 184. \textit{Id.} at 900.
\item 185. \textit{Id.} The court noted, however, that its holding did not resolve the issues of causation and damages, both of which would have to be established before the plaintiffs could succeed on their claim for treble damages under the Clayton Act. \textit{Id.} at 909.
\item 186. 344 F.3d 1294 (11th Cir. 2003).
\item 187. \textit{Id.} at 1306, 1310 n.25.
\item 188. \textit{Id.} at 1310.
\end{itemize}
litigation was a *per se* violation of the antitrust laws merely because it involves a generic's agreement to delay marketing until resolution of the patent infringement case in exchange for exit payments.189

V. CONCLUSION

The tension between the desired support for pioneering drug development and the public's demand for low-cost generics will continue to spur activity in the regulatory, legislative, and judicial arenas. Such activity will undoubtedly require further clarification and refinement, through litigation or otherwise. As a result, the desired balance of the competing policy interests originally sought by the Hatch-Waxman Amendments will remain in flux for some time. Stay tuned.

---

189. *Id.* at 1311 n.26.