

Antitrust Aspects of the “Access to Affordable Pharmaceuticals” Act: Incentives for Generics Out the Window?

Andrew H. Berks *

INTRODUCTION	1306
I. OVERVIEW OF THE HATCH-WAXMAN AMENDMENTS	1307
II. AAPA MODIFICATIONS TO HATCH-WAXMAN.....	1310
III. ANTITRUST ISSUES AROUND HATCH-WAXMAN	1314
IV. AGREEMENTS TO DELAY THE MARKETING OF GENERIC DRUGS	1317
A. <i>AGREEMENTS OUTSIDE THE SCOPE OF A PATENT GRANT AS AN ILLEGAL RESTRAINT OF TRADE</i>	1317
B. <i>AGREEMENTS WITHIN THE SCOPE OF THE PATENT GRANT DO NOT INCUR ANTITRUST LIABILITY</i>	1323
V. ANTITRUST ASPECTS OF THE 180-DAY EXCLUSIVITY AND DECLARATORY JUDGMENTS.....	1334
VI. THE END OF 180-DAY EXCLUSIVITY?.....	1341
VII. CONCLUSION.....	1347

* J.D. Candidate, Fordham University School of Law, 2007; Ph.D., Organic Chemistry, University of Colorado, Boulder, 1988; B.A., Chemistry, University of California, Santa Cruz, 1980. Email: berks@law.fordham.edu. The author gratefully acknowledges the support of the Journal staff for their criticism and assistance that have greatly improved this Note and brought it to fruition. Also, the author thanks his family and wife, Deloria, for her great support and patience during the preparation of this manuscript.

INTRODUCTION

The Hatch-Waxman amendments¹ were enacted by Congress in 1984 to ease the introduction of generic drugs into the market.² Since their enactment, the Hatch-Waxman amendments have stimulated a thriving generic drug industry and greatly improved access of lower cost drugs in the pharmaceutical marketplace.³ The generic drug industry segment is now an essential and indispensable part of the U.S. and international pharmaceutical industry.⁴ The Hatch-Waxman amendments provide for administrative procedures to streamline the approval of generic drug products, but certain aspects of the Hatch-Waxman amendments have created antitrust implications. This paper will discuss antitrust aspects of the most recent changes to the Hatch-Waxman amendments, in the “Medicare Prescription Drug, Improvement, and Modernization Act of 2003” (hereinafter, the “Medicare Modernization Act” or “MMA”), enacted December 8, 2003,⁵ which included the “Access to Affordable Pharmaceuticals” Act (“AAPA”).⁶

The AAPA amendments introduced significant modifications affecting the 180-day term of exclusivity given to first challenger of a listed patent, the 30-month stay of approval, as well as other changes to the Hatch-Waxman amendments.⁷ The AAPA also contains a provision requiring notification of the Federal Trade Commission (FTC) and Department of Justice (DOJ) for agreements between generic and innovator drug companies.⁸

¹ Pub. L. No. 98-417, 98 Stat. 1585 (1984). See *Apotex, Inc. v. Thompson*, 347 F.3d 1335, 1337 (Fed. Cir. 2003), for a general discussion of the Hatch-Waxman amendments.

² See generally A. Maureen Rouhi, *Beyond Hatch-Waxman, Legislative Action Seeks To Close Loopholes In U.S. Law That Delay Entry Of Generics Into The Market*, 80 (38) CHEM. ENGR. NEWS 53–59 (Sept. 23, 2002), available at <http://pubs.acs.org/cen/coverstory/8038/8038biogenerics2.html>. See also Anne Field, *Doctoring the Hatch-Waxman Act* (Aug. 2003), http://www.gsb.stanford.edu/news/research/pubpolicy_bulow_hatchwaxman_act.shtml (last visited July 29, 2006).

³ Rouhi, *supra* note 2.

⁴ *Id.*

⁵ Pub. L. No. 108-173, 117 Stat. 2065 (2003).

⁶ *Id.* at 2448–64 (Title XI of the MMA, subtitles A and B).

⁷ *Id.* (These provisions are in Title XI subtitle A of the MMA).

⁸ *Id.* (These provisions are in Title XI subtitle B of the MMA).

The patent laws have long engendered antitrust implications. The Hatch-Waxman amendments and AAPA modifications, because they affect patent rights, also invite a review of antitrust issues in light of the latest statutory scheme. This paper will summarize the Hatch-Waxman amendments and the AAPA amendments, and will discuss antitrust aspects of the Hatch-Waxman amendments. Several recent relevant cases addressing antitrust aspects of generic drug approvals are reviewed. The balancing of rights between the three principal market participants, patentee and New Drug Application (NDA) holders, generic market entrants, and the public, will be discussed from an antitrust perspective. Finally, future antitrust implications under the 2003 Act will be considered, with particular reference to the forfeiture provisions in the MMA. This paper concludes that the MMA amendments will cause substantial harm to the generic drug companies, more than they will aid the NDA holders, but that the greatest damage will be to the public, which will likely experience marketing delays in the introduction of lower cost drugs, because of reduced innovation in generic drug development.

I. OVERVIEW OF THE HATCH-WAXMAN AMENDMENTS

The overarching objective of generic drug development is to produce lower cost copies of marketed and effective drugs.⁹ The rules pertaining to drug approvals generally are codified in the “Food, Drug, and Cosmetic Act” (“FDCA”), at 21 U.S.C. §§ 301 *et. seq.* (2000).¹⁰ The Hatch-Waxman amendments provide for an “Abbreviated New Drug Application” (“ANDA”),¹¹ which allows a generic drug company to rely on the clinical data of the innovator

⁹ For general reviews of the Hatch-Waxman Act and related history, see Laba Karki, *Review of FDA Law Related to Pharmaceuticals: The Hatch-Waxman Act, Regulatory Amendments and Implications for Drug Patent Enforcement*, 87 J. PAT. & TRADEMARK OFF. SOC’Y 602 (2005) and Erika King Leitzan, *A Brief History of 180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act*, 59 FOOD & DRUG L.J. 287 (2004).

¹⁰ See *Bayer AG v. Elan Pharm. Research Corp.*, 212 F.3d 1241, 1244 (Fed. Cir. 2000).

¹¹ See *id.* The ANDA provisions are discussed in § 505(j) of the Food, Drug, and Cosmetic Act (“FDCA”). 21 U.S.C. § 355(j) (2000). There are also some aspects in the patent laws. See *Bayer AG*, 212 F.3d at 1245.

company. Innovator companies file a “New Drug Application” (“NDA”),¹² which requires, *inter alia*, toxicological and clinical data demonstrating safety and effectiveness. A generic drug company seeking to copy an innovator drug only has to show “bioequivalence” to gain approval for a generic drug ANDA.¹³

The Hatch-Waxman amendments provide for a system of patent listings for approved drugs listed under § 505(b) of the FDCA,¹⁴ covering the drug product, method of use, and formulations. The Food and Drug Administration (FDA) maintains this patent listing as part of the database “Approved Drug Products with Therapeutic Equivalence Evaluations,” commonly referred to as the “Orange Book.”¹⁵

Generic companies seeking to copy a listed drug must certify one of four statements concerning the patents on a listed drug: (i) the listed drug is not patented (a “paragraph I certification”); (ii) the listed drug’s patent has expired (a “paragraph II certification”); (iii) the generic drug will be marketed after the expiration date of the listed drug’s patent (a “paragraph III certification”); or (iv) the listed drug’s patent “is invalid or . . . it will not be infringed by the manufacture, use, or sale of the new drug” covered by the ANDA (a “paragraph IV certification”).¹⁶ In addition to the four patent certifications, there is an additional provision in that the listed patent covers an indication for which the drug is not approved.¹⁷ Most of the interesting features of generic drugs, as will be explained in more detail in this paper, involve the paragraph IV certification process.

¹² 21 U.S.C. § 355(b) (2000).

¹³ See *Bayer AG*, 212 F.3d at 1244 for a description of bioequivalence. Bioequivalence generally means that the extent and rate of absorption of the generic drug are not significantly different from that of the innovator drug. See 21 U.S.C. § 355(j)(8)(B)(i).

¹⁴ 21 U.S.C. § 355(b) (2000).

¹⁵ Available at <http://www.fda.gov/cder/ob/>. For general discussions of patent listings in the Orange Book, see the faq’s on the Orange Book web site, and also http://www.fda.gov/cder/about/smallbiz/generic_exclusivity.htm, and <http://www.fda.gov/cder/guidance/2576fnl.pdf>.

¹⁶ 21 U.S.C. § 355(j)(2)(A)(vii)(I)–(IV) (2000). See *Bayer AG*, *supra* note 10 at 1244–45.

¹⁷ 21 U.S.C. § 355(j)(2)(A)(vii) (2000). See *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1360–61 (Fed. Cir. 2003).

If an ANDA is certified under paragraph IV, the applicant must notify the patent's owner of the certification following a notice from the FDA that the application was accepted.¹⁸ This notification is essentially an invitation to be sued. A paragraph IV certification is deemed to be an act of patent infringement "if the purpose of such a submission is to obtain approval under the [FDCA] 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 a patent."¹⁹

If a listed drug's patent owner brings suit for patent infringement within 45 days of receiving the notice of a paragraph IV certification, then the ANDA is not approvable until the date a court determines invalidity or non-infringement, the date the patent expires, or 30 months from the date the patent holder receives notice of the ANDA paragraph IV certification (subject to judicial discretion), whichever occurs first.²⁰ This is the so-called "30 month stay" provision.

As an incentive for generic companies to challenge patents, the first ANDA applicant to file a paragraph IV certification is entitled to 180 days of exclusivity before another ANDA can be approved by the FDA.²¹ This is the so-called "First to File" provision. The 180-day exclusivity period begins on the start of the actual sale of the drug, rather than the date the FDA approves the ANDA.²²

Parts of the Hatch-Waxman amendments are also in the patent laws. As a quid pro quo to the relative ease of challenging listed patents and the exclusivity period afforded to generic drug companies making paragraph IV certifications, the innovator companies are entitled to a patent term extension on one patent per drug product to compensate for regulatory delays in the approval process.²³ Thus, the term of a patent which claims a product, a

¹⁸ 21 U.S.C. § 355(j)(2)(B) (superseded 2000). *See also* 21 C.F.R. §§ 314.52, 314.94.

¹⁹ 35 U.S.C. § 271(e)(2)(A) (2000).

²⁰ 21 U.S.C. § 355(j)(5)(B)(iii). *See* Allergan, Inc. v. Alcon Labs., 324 F.3d 1322, 1327 (Fed. Cir. 2003).

²¹ 21 U.S.C. § 355(j)(5)(B)(iv) (2000). *See also* Apotex, Inc. v. Thompson, 347 F.3d 1335, 1338 (Fed. Cir. 2003). For a general discussion of the 180-day exclusivity provision, see http://www.fda.gov/cder/about/smallbiz/generic_exclusivity.htm.

²² 21 U.S.C. § 355(j)(5)(B)(iv) (2000).

²³ 35 U.S.C. § 156 (2000).

1310 *FORDHAM INTELL. PROP. MEDIA & ENT. L.J.* [Vol. 16:1305

method of use, or a manufacturing process of a product that is subject to regulatory approval can be extended for up to five years,²⁴ with a maximum term extension following approval of 14 years.²⁵

Additionally, Congress legislatively overruled *Roche v. Bolar*²⁶ and provided that it shall not be an act of infringement to make and test a patented drug solely for the uses reasonably related to the development and submission of information for an Abbreviated New Drug Application (ANDA).²⁷

II. AAPA MODIFICATIONS TO HATCH-WAXMAN

In 2002 and 2003, the Federal Trade Commission published a pair of studies containing significant criticisms regarding generic drug approvals and the conduct of drug companies around Hatch-Waxman issues.²⁸ Both innovator companies and generic companies were accused of “gaming” the system to their advantage.²⁹ The major manipulations were NDA holder strategies to obtain multiple 30 month stays delaying ANDA approvals, by layering patent additions to the Orange Book,³⁰ and strategies by ANDA applicants and innovator drug

²⁴ 35 U.S.C. § 156(g)(6)(A) (2000). MANUAL OF PATENT EXAMINING PROCEDURE § 2758 (8th ed. 2005).

²⁵ 35 U.S.C. § 156(c)(3) (2000). *Merck & Co. v. Kessler*, 80 F.3d 1543, 1551 (Fed. Cir. 1996).

²⁶ 733 F.2d 858 (Fed. Cir.1984), *cert denied*, 469 U.S. 856 (1984).

²⁷ 35 U.S.C. § 271(e)(1). *Merck KGaA v. Integra Lifesciences I, Ltd.*, 125 S. Ct. 2372, 2380 (2005).

²⁸ FED. TRADE COMM’N, *GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY* (2002), *available at* <http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf> [hereinafter *FTC, GENERIC DRUG STUDY*]; FED. TRADE COMM’N, *TO PROMOTE INNOVATION: THE PROPER BALANCE OF COMPETITION AND PATENT LAW AND POLICY*, (2003), *available at* <http://www.ftc.gov/os/2003/10/innovationrpt.pdf> [hereinafter *FTC, INNOVATION STUDY*].

²⁹ *FTC, INNOVATION STUDY*, *supra* note 28, at ch. 3, p. 13. *See also* 149 CONG. REC. S8188 (daily ed. June 19, 2003). One of the more spectacular episodes leading to the FTC investigation involved the attempts by Bristol-Myers Squibb to fend off generic competition for buspirone. *See* FED. TRADE COMM’N., *IN THE MATTER OF BRISTOL-MYERS SQUIBB COMPANY* (2003) *available at* <http://www.ftc.gov/os/2003/03/bristolmyersanalysis.htm>, in the section discussing BuSpar [hereinafter *FTC, Bristol-Myers Squibb*].

³⁰ *FTC, GENERIC DRUG STUDY*, *supra* note 28, at ii.

companies to delay the start of the 180-day exclusivity.³¹ By failing to market generics timely, generic manufacturers could delay the 180-day exclusivity to a time of their choosing, delaying the introduction of a generic drug to the marketplace and delaying the introduction of other generic competitors.³²

The *Generic Drug Study*³³ made two major recommendations: that innovator drugs should be limited to one 30-month stay per drug,³⁴ and that innovator and generic drug companies should be required to file certain agreements with the FTC.³⁵ The discussion of the latter recommendation largely centers around the 180-day marketing exclusivity provision, because there were a number of cases where innovator and generic companies made deals affecting the exclusivity period.³⁶

Congress made drug reform a priority in 2003 and both the House and Senate passed bills H.R. 1 and S. 1. The final MMA legislation was enacted on December 8, 2003.³⁷ One key goal of the legislation was to reform prescription drug benefits for Medicare patients,³⁸ but Title XI of the Act, the AAPA, made substantial changes to the Hatch-Waxman provisions as well. Paragraph 5 of 21 U.S.C § 355(j), which covers most of the issues pertaining to paragraph IV certifications, was essentially completely rewritten, a new paragraph 5 was added to the patent

³¹ *Id.* at vii.

³² *Id.* at 57. Since the 180-day exclusivity clock does not start until the first to file generic drug company commences marketing of a generic drug, a failure to market prevents the approval of any other ANDA for that drug.

³³ *Id.*

³⁴ *Id.* at Exec. Summary, p. ii

³⁵ *Id.* at iv.

³⁶ *Id.* at vii.

³⁷ Medicare Prescription Drug, Improvement, & Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (2003).

³⁸ See CENTERS FOR MEDICARE AND MEDICAID SERVICES, MEDICARE MODERNIZATION ACT, available at http://www.acf.hhs.gov/programs/liheap/guidance/information_memoranda/im05-16.html (last visited July 28, 2006) (noting that the purpose of the MMA is to bring “more affordable health care, prescription drug coverage to all people with Medicare, expanded health plan options, improved health care access for rural Americans, and preventive care services, such as flu shots and mammograms.”). See also *Medicare Modernization Act*, U.S. DEP’T OF HEALTH & HUMAN SERVICES: HEALTHFINDER, <http://www.healthfinder.gov/docs/doc09265.htm> (last visited July 5, 2006).

laws at 35 U.S.C. § 271(e), and several other provisions were modified.

Under the AAPA amendments, the 30-month stay provision was modified to explicitly allow only a single stay for any drug.³⁹ This was accomplished by inserting language into the statute that an action for infringement under the Hatch-Waxman provisions can only be brought for patents listed prior to the filing of the ANDA.⁴⁰ The previous law had no similar limitation, and the innovator drug companies used this to their advantage by listing patents after an ANDA was filed, which permitted a separate stay for each listed patent. Thus, NDA holders could delay generic entry with layered patents, and additional infringement suits that would trigger multiple 30-month stays.⁴¹ According to the *Generic Drug Study*, this happened eight times between 1992 and 2000, with an additional stay beyond the first 30-month stay of 4–40 months.⁴²

The AAPA amendments provided a new set of forfeiture events, affecting the 180-day exclusivity. An ANDA applicant must now market the drug on the earlier of either 75 days after approval or 30 months after submission, or within 75 days of a decision from a court from which no appeal can be taken, or a settlement with a finding that the patent is invalid or not infringed, or else the exclusivity is forfeited.⁴³

Agreements between drug companies, either between innovator and generic or between generic and generic, must be reported to the FTC and the Attorney General.⁴⁴

³⁹ See generally U.S. FOOD & DRUG ADMINISTRATION, GUIDANCE FOR INDUSTRY LISTED DRUGS, 30-MONTH STAYS, & APPROVAL OF ANDAs AND 505(B)(2) APPLICATIONS UNDER HATCH-WAXMAN, AS AMENDED BY THE MEDICARE PRESCRIPTION DRUG, IMPROVEMENT & MODERNIZATION ACT OF 2003 QUESTIONS & ANSWERS, available at <http://www.fda.gov/cder/guidance/6174dft.htm> (discussing FDA Guidance on MMA changes to the Hatch-Waxman amendments).

⁴⁰ 21 U.S.C. § 355(j)(5)(B)(iii) (superseded 2003).

⁴¹ FTC, *GENERIC DRUG STUDY*, *supra* note 28, at 48.

⁴² *Id.*, *passim* (Table 4-3 lists drug stays extended beyond 30 months).

⁴³ 21 U.S.C. § 355(j)(5)(D) (superseded 2003).

⁴⁴ Medicare Prescription Drug Improvement & Modernization Act of 2003, Pub. L. No. 108-173, §§ 1111–1118, 117 Stat. 2066, 2461 (2003).

ANDA applicants, when filing paragraph IV certifications, must now notify the NDA holder within 20 days of the acceptance of filing by the FDA. Previously, there was no express time limit on when the NDA holder had to be notified.⁴⁵

The particulars of a civil action to obtain patent certainty, where a paragraph IV certification is made and the NDA holder does not sue the generic applicant within the 45-day notice period, are now more substantially spelled out.⁴⁶ The pre-MMA statute⁴⁷ expressly allowed for the filing of an action for a declaratory judgment under 28 U.S.C. § 2201. The major substantive change is that the ANDA applicant must offer confidential access to the ANDA to help the NDA holder in deciding if there is actionable infringement.⁴⁸ Presumably, this is intended to encourage suits or settlements between the parties.

The new law provides for a counterclaim to an infringement action claiming that a patent was improperly listed because the patent does not claim the approved drug product or an approved method of using the drug.⁴⁹

In a sense, there was a quid pro quo in the MMA, in that there was one factor strongly in favor of generic companies—the single 30-month stay change—and another factor presumed to be in favor of the NDA holders—the exclusivity forfeiture provisions. As will be seen, this Note suggests that the exclusivity forfeiture provisions in the MMA will likely damage most of the exclusivity awards for the generic drug companies. This will harm incentives for the generic drug companies more than it will help the innovator

⁴⁵ 21 U.S.C § 355(j)(2)(B)(ii)(I) (superseded 2003).

⁴⁶ 21 U.S.C § 355(j)(5)(C) (superseded 2003).

⁴⁷ 21 U.S.C § 355(j)(5)(B)(iii)(III) (repealed 2003)

⁴⁸ 21 U.S.C § 355(j)(5)(C)(i)(III) (superseded 2003).

⁴⁹ 21 U.S.C § 355(j)(5)(C)(ii) (superseded 2003). There is also an administrative procedure for listing a patent in the Orange Book, under 21 C.F.R. § 314.53(f), which permits anyone to petition the FDA that a patent was improperly listed. However, the FDA does not independently evaluate the patent information listed. The FDA will only request that the entity that listed the patent make the correction. *See also* FTC, *Generic Drug Study*, *supra* note 28, at 45 (“Box 4-2 Private Parties Have No Right to Seek the Delisting of a Patent in the Orange Book”) (discussing the attempts by Mylan to have a buspirone patent listed.).

companies or consumers, and more than the single 30-month stay will help the generic companies.

III. ANTITRUST ISSUES AROUND HATCH-WAXMAN

In many respects, the goals of antitrust and patent law seem to conflict.⁵⁰ Patent holders are afforded a twenty year monopoly by statute, based on the Constitutional authorization in Section 8 of Article I, on inventions examined by the U.S. Patent and Trademark Office that meet patentability criteria. On the other hand, the goal of antitrust is to promote competition and limit monopolies that can be unfair to consumers and competitors.⁵¹ However, these competing objectives are not necessarily or inherently in conflict, and in some ways are complimentary.⁵² As Lawrence Sullivan and Warren Grimes explain in their book *The Law of Antitrust: An Integrated Handbook*, intellectual property law and antitrust law are often perceived as conflicting, because intellectual property fosters the creation of market power and antitrust responds to market power abuses.⁵³ However, antitrust and intellectual property are more often complementary, because both systems advance consumer welfare resulting from efficient resource allocation, innovation, and technological progress.⁵⁴ Patents are recognized as playing a major role in innovation and benefits to consumers.⁵⁵ However, antitrust violations can occur, for example when patentees attempt to extend their legal monopoly beyond that which is permitted by patent law.⁵⁶

⁵⁰ See, e.g., LAWRENCE A. SULLIVAN & WARREN S. GRIMES, *THE LAW OF ANTITRUST: AN INTEGRATED HANDBOOK*, (West Group 2000), §§ 15.1, 15.3, p. 800, 813–15; Christine S. Paine, *Brand-Name Manufacturers Risk Antitrust Violations By Slowing Generic Production Through Patent Layering*, 33 SETON HALL L. REV. 479, 479–80 (2003); FTC, *INNOVATION STUDY*, *supra* note 28, at Exec. Summary, pp. 2–3.

⁵¹ See Paine, *supra* note 50.

⁵² See FTC, *INNOVATION STUDY*, *supra* note 28, at Exec. Summary, pp. 2–3.

⁵³ SULLIVAN & GRIMES, *supra* note 50, at 800–01.

⁵⁴ *Id.*

⁵⁵ See FTC, *INNOVATION STUDY*, *supra* note 28, at Exec. Summary, pp. 2–3.

⁵⁶ See *infra* notes 88–118 and accompanying text (discussing *Valley Drug Co. v. Geneva Pharm., Inc.*, 344 F.3d 1294 (11th Cir. 2003) (*Terazosin II*)); *infra* notes 169–208 and accompanying text (discussing *Schering* and *Upsher*).

The main impetus behind the AAPA, the abuses of the 30-month stay and the 180-day exclusivity provisions, can be analyzed in terms of antitrust law. The 30-month stay can raise questions of illegal monopolization, where attempts to extend the patent grant are questionable on antitrust grounds, as possible violations of Section 2 of the Sherman Act.⁵⁷ Additionally, the manipulations of the 180-day exclusivity period can raise questions of collusion between the generic manufacturers and the innovator drug companies, which are potential violations of Section 1 of the Sherman Act,⁵⁸ because these cases often involve agreements between the generic and innovator companies.⁵⁹

The 30-month stay period has been used in attempts to extend a patent monopoly that would otherwise expire, and therefore layering 30-month stays can raise antitrust concerns as illegal attempts to monopolize.⁶⁰ The 30-month stay was established to give the generic applicant and NDA holder the opportunity to resolve patent issues prior to commercial marketing.⁶¹ The 30-month stay is invoked if the NDA holder sues the generic applicant within 45 days of being notified of the ANDA filing with a paragraph IV certification.⁶² During this time, the FDA will not give final, marketing approval to the ANDA, unless the patent expires or there is a court decision that the patent is invalid or not infringed.⁶³ The innovator drug companies began exploiting the 30-month stay provision by layering patent listings in the Orange Book following the filing of an ANDA with a paragraph IV

⁵⁷ See FTC, INNOVATION STUDY, *supra* note 28, at ch. 1, pp. 3–4. Section 2 of the Sherman Act prohibits monopolies and attempts to monopolize. 15 U.S.C. § 2 (2000).

⁵⁸ “Every contract, combination in the form of trust or otherwise, or conspiracy, in restraint of trade or commerce among the several States, or with foreign nations, is hereby declared to be illegal.” 15 U.S.C. § 1 (2000).

⁵⁹ FTC, INNOVATION STUDY, *supra* note 28, at ch. 1, pp. 3–4. See also *infra* notes 76–86 and accompanying text (discussing *In re Cardizem CD Antitrust Litig.*, 332 F.3d 896, 903 (6th Cir. 2003)); *infra* notes 121–144 and accompanying text (discussing *In re Ciprofloxacin Hydrochloride Antitrust Litig.*, 363 F. Supp. 2d 514 (E.D.N.Y. 2005)).

⁶⁰ FTC, GENERIC DRUG STUDY, *supra* note 28, at 50 (Box 4-4), 55.

⁶¹ *Id.* at 39.

⁶² *Id.* See also discussion *supra*, Part II.

⁶³ *Aventis Pharms., Inc. v. Barr Labs., Inc.*, 335 F. Supp. 2d 558, 563 n.4 (D.N.J. 2004).

certification, which invoked successive 30-month stays.⁶⁴ In a number of cases, the stays extended well beyond 30 months.⁶⁵ Thus, the use of multiple 30-month stays potentially creates an unlawful monopoly that can be interpreted as extending patent rights beyond their statutory grants.⁶⁶

The 180-day exclusivity provision was created to incentivize generic drug companies to challenge innovator drug patents with paragraph IV certification filings.⁶⁷ These exclusivity periods are enormously profitable for the generic drug companies.⁶⁸ From an antitrust perspective, the exclusivity periods raise antitrust issues as horizontal restraints of trade, because NDA holders and ANDA applicants may be motivated to create anticompetitive deals and settlements involving the exclusivity period. The anticompetitive conduct was from both the generic and innovator companies. On the generic side, in some cases, generic companies “parked” their exclusivity by failing to market the generic drug in a timely manner.⁶⁹ Under the original Hatch-Waxman statute, the exclusivity did not begin until the generic company began to market the drug, and other ANDA applications were not approvable until the exclusivity period was over.⁷⁰ Thus, if a first filed ANDA with exclusivity failed to market the generic drug in a

⁶⁴ This is the subject of Chapter 4 of the FTC, *GENERIC DRUG STUDY*. *Supra* note 28, at 39.

⁶⁵ *Id.* See Table 4-3, p. 49 for a number of specific examples.

⁶⁶ *In re Buspirone Patent Litig.*, 185 F. Supp. 2d 363, 366 (S.D.N.Y. 2002). A related issue is whether there is an exemption from the antitrust laws provided to Orange Book listings under the *Noerr-Pennington* doctrine, and whether Orange Book listings are a petition to the government and thus immune from antitrust laws. *United Mine Workers of Am. v. Pennington*, 381 U.S. 657 (1965); *E. R.R. Presidents Conf. v. Noerr Motor Freight, Inc.*, 365 U.S. 127 (1961); *see also In re Buspirone*, *supra* at 368–69. The *Noerr-Pennington* doctrine exempts from antitrust liability efforts to persuade the government to take an action that would otherwise create a restraint or monopoly. *In re Buspirone*, *supra* at 368–69. The Southern District of New York has ruled that *Noerr-Pennington* does not apply to patent listings in the Orange Book. *See* FTC, *GENERIC DRUG STUDY*, *supra* note 28, at 46 (Box 4-3).

⁶⁷ *Minn. Mining & Mfg. Co. (3M) v. Barr Labs., Inc.*, 289 F.3d 775, 778 (Fed. Cir. 2002). *See also* Section II *supra*.

⁶⁸ Barr Laboratories, a leading generic drug company, reportedly earned \$311 million during the six month exclusivity period it had for fluoxetine. Rouhi, *supra* note 2, at 53–59.

⁶⁹ FTC, *GENERIC DRUG STUDY*, *supra* note 28, at 7.

⁷⁰ *Id.*

2006]

GENERIC INCENTIVES OUT THE WINDOW

1317

timely manner due to a settlement with the innovator company, generic copies would stay off the market entirely.⁷¹ On the innovator side, NDA holders have been tempted to enter into agreements with generic companies to pay the generics to defer marketing in order to keep generic competitors off the market.⁷²

Another feature of Hatch-Waxman are the declaratory judgment provisions, in which Congress attempted to create a cause of action for generic market entrants to clarify the patent landscape prior to marketing. As will be seen, these actions have become an important weapon for attacking the 180-day exclusivity period.⁷³

IV. AGREEMENTS TO DELAY THE MARKETING OF GENERIC DRUGS

A. *Agreements Outside the Scope of a Patent Grant As An Illegal Restraint of Trade*

As a consequence of the threat to innovator drugs by generic companies seeking the 180-day exclusivity period, the innovator companies, in several instances, approached generic companies with attempts to make deals to defer the introduction of the generic drug. Two significant recent cases in this area are *In re Cardizem CD Antitrust Litigation*⁷⁴ and *In re Ciprofloxacin Hydrochloride Antitrust Litigation*.⁷⁵

In the *Cardizem CD* case, an agreement held to be outside the statutory grant of a patent was condemned as a *per se* antitrust violation. Andrx Pharmaceuticals filed an ANDA to sell a generic copy of Cardizem CD, a once per day extended release form of diltiazem hydrochloride, a drug indicated for cardiovascular

⁷¹ *Id.*

⁷² *In re Cardizem CD Antitrust Litig.*, 332 F.3d 896, 903 (6th Cir. 2003).

⁷³ See *infra* notes 248–277 and accompanying text (discussing sertraline in *Teva Pharms. USA, Inc. v. Pfizer, Inc. (Teva v. Pfizer II)*, 395 F.3d 1324 (Fed. Cir. 2005) and *Teva Pharms. USA, Inc. v. FDA (Teva v. FDA III)*, 398 F. Supp. 2d 176 (D.D.C. 2005)).

⁷⁴ *In re Cardizem CD*, 332 F.3d at 896.

⁷⁵ *In re Ciprofloxacin Hydrochloride Antitrust Litig.*, 363 F. Supp. 2d 514 (E.D.N.Y. 2005).

disease.⁷⁶ Cardizem CD was manufactured by Hoechst Marion Roussel (“HMR,” now part of Sanofi-Aventis Pharmaceuticals). In September 1995, Andrx filed the first ANDA for Cardizem CD with a paragraph IV certification, entitling it to the 180-day exclusivity period once Andrx began marketing its copy of the drug.⁷⁷ The patent at issue, U.S. 5,470,584, (the ‘584 patent) claimed the dissolution profile of the extended release formulation.⁷⁸ HMR sued Andrx in January 1996 for patent infringement, triggering the 30-month stay of approval, which would expire in July 1998.⁷⁹ Andrx counterclaimed with antitrust and unfair competition allegations against HMR.⁸⁰

On September 15, 1997, the FDA tentatively approved Andrx’s ANDA, indicating that the drug could be marketed on the earlier date of a court decision favorable to Andrx on the infringement suit, or the expiry of the 30-month stay.⁸¹ However, on September 24, 1997, HMR and Andrx entered into an agreement, whereby Andrx agreed not to market its generic version of Cardizem CD until the earliest of: (1) a favorable and unappealable court decision that Andrx did not infringe the patent; (2) HMR and Andrx entered into a license agreement; or (3) HMR entered into a license agreement with a third party. Andrx further agreed to drop its antitrust and unfair competition claims against HMR, and it would retain its 180-day exclusivity. In return, HMR agreed to pay Andrx \$10 million per quarter after Andrx received final approval, and \$100 million, per year, less the quarterly payments, until the patent suit was resolved.⁸²

HMR began making payments to Andrx in July 1998, on the expiry of the statutory 30-month stay.⁸³ Andrx’s product was reformulated and received final approval for marketing in June 1999. By this time, HMR had paid Andrx \$89 million,⁸⁴ and the

⁷⁶ *In re Cardizem*, 332 F.3d at 901–02.

⁷⁷ *Id.* at 902.

⁷⁸ *Id.*

⁷⁹ *Id.* at 902.

⁸⁰ *Id.*

⁸¹ *Id.*

⁸² *Id.* at 903.

⁸³ *Id.*

⁸⁴ *Id.*

agreement delayed the introduction of a generic copy of Cardizem CD for 11 months.

A number of antitrust lawsuits were filed in this matter, as early as August, 1998, all of which were consolidated into the federal district court for the Eastern District of Michigan.⁸⁵ The central holding was that the agreement to delay the introduction of Andrx's generic version of Cardizem CD was a "classic example of a per se illegal restraint of trade," because Andrx had designed around the '584 patent.⁸⁶ Thus, the agreement fell outside the scope of the patent grant.⁸⁷

A similar situation occurred in *Valley Drug Company v. Geneva Pharmaceutical, Inc.* ("*Terazosin II*"),⁸⁸ where the court held that an agreement based on invalid patents was likewise illegal because the agreement was not based on valid patent claims. In *Terzosin II*,⁸⁹ patent validity was central to the antitrust analysis.

Terazosin, a drug for high blood pressure and benign prostatic hyperplasia, was first marketed by Abbott under the brand name Hytrin in 1987.⁹⁰ In 1993, Geneva Pharmaceuticals filed several ANDA's to manufacture a generic version of Terazosin. Then, in 1996, Abbott Laboratories obtained an additional patent, U.S. 5,504,207 (the "'207 patent"), claiming polymorphic forms of the drug substance,⁹¹ and Geneva filed a paragraph IV certification against that patent.⁹² Abbott sued Geneva for patent infringement,⁹³ and Geneva won a motion for summary judgment

⁸⁵ *Id.*

⁸⁶ *Id.* at 908. For a general discussion of *per se* restraints of trade, noting that a *per se* restraint is a horizontal restraint so "inherently anticompetitive" that inquiry into the harm caused is unnecessary, see *id.* at 907 (citing *Copperweld Corp. v. Independence Tube Corp.*, 467 U.S. 752, 768 (1984)).

⁸⁷ *In re Cardizem CD Antitrust Litig.*, 332 F.3d 896, 907-08 (6th Cir. 2003).

⁸⁸ *Valley Drug Co. v. Geneva Pharm., Inc. (Terazosin II)*, 344 F.3d 1294 (11th Cir. 2003).

⁸⁹ *Id.*

⁹⁰ *Id.* at 1298.

⁹¹ *In re Terazosin Hydrochloride Antitrust Litig. (Terazosin III)*, 352 F. Supp. 2d 1279, 1289 (S.D. Fla. 2005).

⁹² *Id.* at 1289.

⁹³ *Id.*

on a claim that the '207 patent was invalid because of an “on-sale bar” under 35 U.S.C. § 102(b).⁹⁴

Abbott and Geneva then entered into an agreement to defer marketing of Geneva’s Terazosin until either another generic entered the market or there was an appellate judgment.⁹⁵ Abbott agreed to pay into an escrow account \$4.5 million per month beginning in April, 1998, until the question was settled.⁹⁶ The agreement lasted until August of 1999, and most of the funds in the escrow account were returned to Abbott.⁹⁷ The Agreements were apparently terminated in response to an FTC investigation.⁹⁸ Geneva thereupon launched its generic Terazosin in August 1999.⁹⁹

Antitrust plaintiffs, which included drug wholesalers, drug store chains, health insurers, and individuals, brought suit alleging antitrust violations. Judge Seitz of the Southern District of Florida granted plaintiffs’ motion for partial summary judgment,¹⁰⁰ concluding that the Agreements were per se violations of section 1 of the Sherman Act because they were geographic market allocation agreements between horizontal competitors, essentially allocating the entire market to Abbott, who shared its profits with other cartel members during the life of the agreement.¹⁰¹ Judge Seitz’s opinion concluded that the “defendants’ horizontal market allocation agreements would tend to inhibit domestic output and price competition without creating efficiencies for American consumers, and the defendants have not adduced sufficient facts to place the illegality of their restraints in genuine dispute.”¹⁰²

⁹⁴ *Id.* at 1289–90.

⁹⁵ *Id.* at 1290–91.

⁹⁶ *Id.* at 1291.

⁹⁷ As of the termination date, there was \$49.5 million in the escrow account, and under the terms of the termination agreement, \$45 million was returned to Abbott. *Id.*

⁹⁸ *Valley Drug Co. v. Geneva Pharm., Inc. (Terazosin II)*, 344 F.3d 1294 (11th Cir. 2003).

⁹⁹ *In re Terazosin Hydrochloride Antitrust Litig. (Terazosin III)*, 352 F. Supp. 2d 1279, 1291 (S.D. Fla. 2005).

¹⁰⁰ *In re Terazosin Hydrochloride Antitrust Litig. (Terazosin D)*, 164 F. Supp. 2d 1340 (S.D. Fla. 2000).

¹⁰¹ *Terazosin II*, 344 F.3d at 1301.

¹⁰² *Terazosin I*, 164 F. Supp. 2d at 1354.

The court identified several elements of the agreement as anticompetitive, including Geneva's agreement not to market tablets and capsules of Terazosin until the agreement terminated, and Geneva's promise to aid Abbott in opposing the entry of other generic Terazosin products.¹⁰³ Defendants Geneva and Abbott appealed to the 11th Circuit, arguing that the district court erred in concluding that the Agreements were *per se* violations of the Sherman Act and that issues of material fact were still in dispute.¹⁰⁴ The defendants argued that there were pro-competitive justifications that warrant analysis under the rule of reason, and that patent litigation settlements must be analyzed under the rule-of-reason unless it is shown that the settlements were a sham.¹⁰⁵

The 11th Circuit reversed and remanded to the district court. They concluded:

[E]xposing settling parties to antitrust liability for the exclusionary effects of a settlement reasonably within the scope of the patent merely because the patent is subsequently declared invalid would undermine the patent incentives. Patent litigation is too complex and the results too uncertain for parties to accurately forecast whether enforcing the exclusionary right through settlement will expose them to treble damages if the patent immunity were destroyed by the mere invalidity of the patent.¹⁰⁶

Thus, the 11th Circuit concluded that a settlement within the scope of a valid patent could not be subject to *per se* antitrust condemnation.¹⁰⁷ Restricting settlement options would increase the cost of patent enforcement and impair incentives for disclosure and innovation.¹⁰⁸ Furthermore, this is in accordance with *Walker Process Equipment, Inc. v. Food Machine & Chemical Corporation*, which stated that permitting antitrust liability on a

¹⁰³ *Terazosin II*, 344 F.3d at 1301–02.

¹⁰⁴ *Id.* at 1303.

¹⁰⁵ *Id.*

¹⁰⁶ *Id.* at 1308.

¹⁰⁷ *Id.* at 1309, 1314.

¹⁰⁸ *Id.* at 1308.

mere showing of invalidity can “chill the disclosure of inventions” by obtaining patents because of fear of punitive consequences.¹⁰⁹

One of the most significant factors in *Terazosin II* is that the Court distinguished anticompetitive conduct within and without of the patent regime.¹¹⁰ Both *per se* and rule of reason analysis were noted to assess the anticompetitive effects of particular conduct, but this court concluded that in patent cases a different standard of analysis was needed, that assesses the extent to which anticompetitive conduct undermines innovation and disclosure, or the extent to which the patent laws shield patentees and potential infringers with whom they settle from antitrust liability.¹¹¹ Thus, this court held that there was a patent exception for antitrust liability, but that exception was limited by the terms of the patent and the statutory rights granted to the patentee.¹¹² In other words, the 11th Circuit seemed to be advocating for a special standard of review where the alleged restraints involve patented products.

The court stated that the appropriate issues on remand would likely involve an identification of the protection afforded by the patents, the relevant FDA law, and whether or not the agreements reflected a reasonable implementation of these factors.¹¹³

However, on remand, Judge Seitz of the Southern District of Florida again held, under the *Terazosin II* instructions, that the Agreements violated § 1 of the Sherman Act because the scope of the Agreements exceeded the scope of the protections afforded to Abbott under the '207 patent.¹¹⁴ The district court repeated the holding that the agreements were *per se* violations of § 1 of the Sherman Act because the horizontal market allocation was so obviously anticompetitive and was an unreasonable restraint of trade.¹¹⁵ The district court appeared to disregard the instruction of

¹⁰⁹ *Walker Process Equip., Inc. v. Food Mach. & Chem. Corp.*, 382 U.S. 172, 180 (1965).

¹¹⁰ *Terazosin II*, 344 F.3d at 1311 (citing to “accommodation of differing policies” of patent and non-patent exclusionary conduct in *Walker Process*, 382 U.S. 172).

¹¹¹ *Id.* at 1311.

¹¹² *Id.* at 1312.

¹¹³ *Id.*

¹¹⁴ *In re Terazosin Hydrochloride Antitrust Litig. (Terazosin III)*, 352 F. Supp. 2d 1279, 1319 (S.D. Fla. 2005).

¹¹⁵ *Id.*

a new standard of review, as suggested in *Terazosin II*, in making this decision. A major factor in this holding was the questionable validity of the '207 patent, which “was likely to be invalidated by the district court.”¹¹⁶ This opinion, that the '207 was likely invalid, was in turn a major factor in the holding that the agreements exceeded the scope of the patent, and that the agreements did not represent a reasonable interpretation of the patent protections.¹¹⁷

To date, this case tells us that basing a reverse payment agreement on a patent of questionable validity will likely incur a holding of an antitrust violation. Thus, this case to a large extent fulfills the hypothetical posed at the end of the *Ciprofloxacin* case,¹¹⁸ that reliance on a patent where the validity is questionable, and there was a strong case for invalidity, is a risky strategy. This puts generic companies in a bind, because they should balance the desire to zealously invalidate innovator patents with the possibility that they can make a deal with the innovator. If the case for invalidity case is too strong, the deal will be subject to antitrust liability. By contrast, if the generic company thought that a deal with an innovator was possible, they might not pursue an aggressive invalidity strategy, and would pursue some other colorable, but possibly less than zealous, strategy for getting an ANDA approval with a paragraph IV certification.

B. Agreements Within the Scope of the Patent Grant Do Not Incur Antitrust Liability

In contrast to the *Cardizem CD*¹¹⁹ and *Terazosin II*¹²⁰ cases, where agreements among innovator and generic drug companies outside the scope of patent claims incurred antitrust liability, other cases where the agreements were held to be within the scope of patent claims were upheld with no valid antitrust claims. In the case of *Ciprofloxacin*, an agreement between the innovator and a

¹¹⁶ *Id.* at 1317.

¹¹⁷ *Id.* at 1307–68.

¹¹⁸ *In re Ciprofloxacin Hydrochloride Antitrust Litig.*, 363 F. Supp. 2d 514 (E.D.N.Y. 2005). *See also infra* note 144 and accompanying text.

¹¹⁹ *In re Cardizem CD Antitrust Litig.*, 332 F.3d 896 (6th Cir. 2003).

¹²⁰ *Terazosin II*, 344 F.3d 1294 (11th Cir. 2003).

generic drug company was held to be within the claim scope, and the antitrust plaintiffs were unsuccessful.¹²¹ Ciprofloxacin is a quinolone antibacterial, used for the treatment of infections, and was first marketed in 1987 by Miles Laboratories, the U.S. predecessor to Bayer Pharmaceuticals. The main patent covering the product was U.S. 4,670,444 (the “444 patent”),¹²² expiry December 9, 2003.¹²³ Barr Laboratories filed an ANDA in October 1991, with a paragraph IV certification to the ‘444 patent, contending that it was invalid and unenforceable, and notified Bayer in December 1991 as required by the Hatch-Waxman amendments.¹²⁴ Bayer sued Barr in the Southern District of New York for patent infringement.¹²⁵ The 30-month stay would have expired in July 1994, but the parties agreed to extend the stay until the case was settled.¹²⁶

On January 8, 1997, Bayer and Barr settled just before trial,¹²⁷ with an agreement whereby Barr acknowledged the validity of the ‘444 patent,¹²⁸ and in return Bayer made an immediate payment to Barr of \$49.1 million, and quarterly payments of about \$15 million until the ‘444 patent expired.¹²⁹ Bayer ultimately paid Barr \$398 million under this agreement.¹³⁰

Antitrust plaintiffs, including unions, drug wholesalers, and individuals, sued alleging antitrust violations, arguing that the 1997 agreements violated § 1 of the Sherman Act.¹³¹ The plaintiffs

¹²¹ In re Ciprofloxacin Hydrochloride Antitrust Litig. (*Cipro III*), 363 F. Supp. 2d 514 (E.D.N.Y. 2005).

¹²² *Id.* at 518.

¹²³ *Id.* at 519.

¹²⁴ In re Ciprofloxacin Hydrochloride Antitrust Litig. (*Cipro I*), 166 F. Supp. 2d 740, 744 (E.D.N.Y. 2001).

¹²⁵ *Id.* The case has no citation for the original Hatch-Waxman action for patent infringement, filed in the Southern District of New York, Jan. 16, 1992, probably because the parties settled without a decision. *Id.* The Eastern District decision cited here was the antitrust action.

¹²⁶ *Id.*

¹²⁷ In re Ciprofloxacin Hydrochloride Antitrust Litig. (*Cipro III*), 363 F. Supp. 2d 514, 519 (E.D.N.Y. 2005).

¹²⁸ *Cipro I*, 166 F. Supp. 2d at 745.

¹²⁹ In re Ciprofloxacin Hydrochloride Antitrust Litig. (*Cipro II*), 261 F. Supp. 2d 188, 196 (E.D.N.Y. 2003).

¹³⁰ *Id.*

¹³¹ *Cipro III*, 363 F. Supp. 2d at 517.

alleged that “but for” the Agreements, generic ciprofloxacin would have appeared in 1997, many years earlier than it was actually marketed generically.¹³² Barr received tentative approval to market ciprofloxacin in January 1995, and reportedly received full approval in January 1997.¹³³ The payments here, termed “reverse,” “exit” or “exclusion payments,”¹³⁴ have an anticompetitive appearance because they appear to offer nothing by the recipient of the payments in return, other than staying off the market, which preserves a monopoly that would otherwise be extinguished. The defense was that the 1997 agreements did not extend the beyond the scope of the ’444 patent.¹³⁵

In the *Cipro II* decision, Judge David Trager of the Eastern District of New York held that there was no *per se* violation of section 1 of the Sherman Act by the Bayer-Barr agreements because the exclusionary effect of the agreements were within the scope of the ’444 patent.¹³⁶ However, the decision left open the possibility that a rule-of-reason analysis could find a Sherman Act violation.¹³⁷ In the *Cipro III* decision, Judge Trager held that in the ciprofloxacin market, Bayer had market power, but the ’444 patent gave Bayer the right to exclude others during the term of the patent,¹³⁸ and that a validity inquiry was not necessary because conduct within the scope of a patent is exempt from antitrust scrutiny.¹³⁹ Judge Trager noted that there was “no legal basis for restricting the rights of patentees to choose their enforcement vehicle” such as a settlement agreement or litigation of a

¹³² According to the FDA’s website, generic ciprofloxacin was not finally approved for marketing until June 9, 2004. *Ciprofloxacin: Label and Approval History*, DRUGS @ FDA, http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Label_ApprovalHistory#aphist (last visited July 29, 2006).

¹³³ *Cipro I*, 166 F. Supp. 2d at 744.

¹³⁴ *Cipro III*, 363 F. Supp. 2d at 520.

¹³⁵ *Id.* at 517.

¹³⁶ *In re Ciprofloxacin Hydrochloride Antitrust Litig. (Cipro II)*, 261 F. Supp. 2d 188, 196, 257 (E.D.N.Y. 2003).

¹³⁷ The rule-of-reason analysis was litigated in *Cipro III*. 363 F. Supp. 2d 514. A rule-of-reason analysis balances the alleged adverse effects of the conduct with its procompetitive benefits. *See id.* at 520 (discussing the application of a rule-of-reason analysis).

¹³⁸ *Id.* at 523–24.

¹³⁹ *Id.* at 530.

challenged patent.¹⁴⁰ The parties may sensibly conclude that either course of action was more appropriate.¹⁴¹ Since the plaintiffs did not challenge the validity of the '444 patent,¹⁴² it was presumed to be valid, the settlement was held to be proper and within the patent scope.¹⁴³ Because the plaintiffs did not show that the agreements had anti-competitive effects beyond the scope of the '444 patent, the rule of reason analysis failed.¹⁴⁴ Thus, the mere payment of money to keep an otherwise patented product off the market does not prove an anticompetitive or adverse effect on the market.

Significantly, Judge Trager's reasoning was predicated on a presumption of patent validity. Indeed, it is not clear if the original patent challenge at the Southern District of New York would have succeeded in invalidating the patent. One can infer that Judge Trager would have felt differently in a situation in which the patent facially appeared to be invalid. In the *Ciprofloxacin* litigation, the antitrust plaintiffs did not argue the validity of the patent, only the antitrust implications of the Agreements. In a case where the patent validity was in question presumably the outcome would be the opposite, since the monopoly of a patent ends if it is declared invalid, so any agreement to extend a facially invalid patent could be held to exceed the scope of the patent. The issue gets sticky, however, because patent validity, and indeed any judicial proceeding, engenders unpredictable outcomes.

A similar situation, where the validity of exclusionary agreements within the scope of valid patent claims was upheld, involved tamoxifen, a drug for breast cancer.¹⁴⁵ In 1987, Barr Laboratories filed the first ANDA for tamoxifen containing a

¹⁴⁰ *Id.* at 531–32.

¹⁴¹ *Id.* at 532 (citing *T & T Mfg. Co. v. A.T. Cross Co.*, 449 F. Supp. 813, 827 (D.R.I. 1978), *aff'd* 587 F.2d 533 (1st Cir. 1978), *cert. denied*, 441 U.S. 908 S. Ct. (2000)).

¹⁴² *Id.* at 531.

¹⁴³ *Id.* at 540.

¹⁴⁴ *Id.* at 541. In addition, Judge Trager held that consumers, who were antitrust plaintiffs in this case, had no standing to sue because “consumers . . . who may feel that they are being charged supracompetitive prices by the patentee have no cause of action to invalidate the patent.” *Id.*

¹⁴⁵ See generally *In re Tamoxifen Citrate Antitrust Litig. (Tamoxifen III)*, 429 F.3d 370 (2d Cir. 2005).

paragraph IV certification.¹⁴⁶ ICI¹⁴⁷ sued Barr for patent infringement, and in April 1992, the district court ruled that the ICI patent in the suit was invalid because ICI deliberately withheld critical information from the patent examiner (“*Tamoxifen I*”).¹⁴⁸

ICI appealed to the Federal Circuit, and in 1993, while the appeal was pending, the parties entered into a confidential agreement, whereby Zeneca, which had succeeded the patent ownership from ICI, agreed to pay Barr \$21 million, and in return Barr changed its patent certification to Paragraph III, meaning that Barr would wait until the expiry of the patent at issue in 2002 before marketing its copy of Tamoxifen.¹⁴⁹ During the term of the agreement, prior to the expiry of the patent in 2002, Barr agreed to market, under its label, Tamoxifen manufactured by Zeneca.¹⁵⁰ The parties also agreed that if the patent was held to be invalid or unenforceable in a litigation from another generic drug firm, that Barr would be able to change its patent certification back to paragraph IV to put itself back into the position it had been in during the initial litigation.¹⁵¹

The Zeneca-Barr agreement was contingent on the vacatur of the district court judgment in *Tamoxifen I*, and the Federal Circuit granted a joint motion to dismiss *Tamoxifen I*.¹⁵² Subsequently, three additional generic companies filed ANDA’s for Tamoxifen with paragraph IV certifications.¹⁵³ In each of the subsequent ANDA’s, Zeneca responded with a patent infringement suit, and in each case, the court rejected the attempts of the generic company to rely on the vacated *Tamoxifen I* decision, and in contrast to *Tamoxifen I*, upheld the validity of the Zeneca patent.¹⁵⁴

In 1998, Barr restored its paragraph IV certification, and invoked its entitlement to the 180-day exclusivity as the first

¹⁴⁶ *Id.* at 377.

¹⁴⁷ ICI is the predecessor in interest to Zeneca. *Id.* Zeneca is now AstraZeneca.

¹⁴⁸ *Id.* (citing *Imperial Chem. Indus., PLC v. Barr Labs., Inc.*, 795 F. Supp. 619, 626–27 (S.D.N.Y. 1992)).

¹⁴⁹ *Id.*

¹⁵⁰ *Id.*

¹⁵¹ *Id.* at 378.

¹⁵² *Id.*

¹⁵³ *Id.*

¹⁵⁴ *Id.* at 379.

generic company to file a paragraph IV certification.¹⁵⁵ Because this action precluded final approval of other ANDA's until the exclusivity period was over, this action prevented the FDA from approving other Tamoxifen copies.¹⁵⁶ Barr did not exercise its exclusivity and continued to market Zeneca's Tamoxifen under the 1993 agreement.¹⁵⁷ These actions were successful in preventing the introduction of generic Tamoxifen until the expiration of the patent in August 2002.¹⁵⁸

Some thirty antitrust lawsuits were filed by consumers and consumer groups challenging the validity of the 1993 agreement between Zeneca and Barr.¹⁵⁹ The key contention of the antitrust plaintiffs was that the agreement allowed Zeneca and Barr to circumvent the district court invalidation of the Zeneca patent in *Tamoxifen I*, which the plaintiffs asserted would have been affirmed at the Federal Circuit.¹⁶⁰ The affirmance would have triggered the 180 day exclusivity period, and other generic companies would have marketed lower cost Tamoxifen copies several years earlier than they actually entered the market.¹⁶¹

The defendants were granted a motion to dismiss the class action for failure to state a claim upon which relief could be granted, under Fed. R. Civ. 12(b)(6).¹⁶² The district court reasoned that a patent holder may settle with a potential infringer without offending the Sherman Act, provided that the agreement does act beyond the limits of the patent monopoly.¹⁶³

The antitrust plaintiffs appealed, but the Second Circuit upheld the district court.¹⁶⁴ The major findings were that the settlement

¹⁵⁵ *Id.*

¹⁵⁶ *Id.* at 380.

¹⁵⁷ *Id.*

¹⁵⁸ *Id.*

¹⁵⁹ *Id.* The suits were consolidated as a class action in the Eastern District of New York. *In re Tamoxifen Citrate Antitrust Litig. (Tamoxifen II)*, 277 F. Supp. 2d 121 (E.D.N.Y. 2003).

¹⁶⁰ *Tamoxifen III*, 429 F.3d at 380–81.

¹⁶¹ *Id.* at 379–80.

¹⁶² *Id.* at 381 (citing *Tamoxifen II*, 277 F. Supp. 2d at 140).

¹⁶³ *Id.* at 381.

¹⁶⁴ *Id.* at 405. The decision was a 2-1 plurality written by Judge Sack. Judge Pooler dissented, and would have reversed the motion to dismiss and remanded for trial. *Id.*

and vacatur of the *Tamoxifen I* litigation was not an antitrust violation,¹⁶⁵ that the reverse payments were proper in scope and size, in that under Hatch-Waxman, generic challengers gain considerable leverage, which redistributes risk assessments,¹⁶⁶ that the settlement agreement did not extend the patent monopoly,¹⁶⁷ and that Barr's claim to the 180 day exclusivity period was not an antitrust violation.¹⁶⁸ The key finding, for the purpose of this paper, of both the district court and appeal court, is that an agreement that does not exceed the scope of the patent grant will not create an antitrust violation.

Another significant reverse payments case with significant lessons for the industry involved extended release potassium chloride ("*Schering*").¹⁶⁹ As with *Terazosin* and *Tamoxifen*, the agreement here was held to be within the scope of valid patent claim, and therefore did not incur antitrust liability. In *Schering*, a delayed entry based on legitimate patent rights was held to be proper and procompetitive.

Schering marketed an extended release form of potassium chloride under the brand name "K-Dur 20," which used a formulation patented in U.S. 4,863,743 (the "'743 patent"), expiry September 5, 2006.¹⁷⁰ In 1995, Upsher-Smith Laboratories filed an ANDA for a generic version of K-Dur 20, called "Klor Con," with a paragraph IV certification against the '743 patent.¹⁷¹ Schering sued for patent infringement, but prior to trial in June 1997, the parties entered into a settlement, whereby Schering and Upsher agreed that Schering would license several Upsher drugs for an upfront payment, and in return, Upsher would not launch Klor Con until September 1, 2001.¹⁷² In particular, Schering was interested in the Upsher drug "Niacor," an extended release niacin

¹⁶⁵ *Id.* at 389.

¹⁶⁶ *Id.* at 391.

¹⁶⁷ *Id.* at 400.

¹⁶⁸ *Id.* at 401.

¹⁶⁹ *Schering-Plough Corp. v. FTC*, 402 F.3d 1056 (11th Cir. 2005), *reh'g en banc denied*, 147 Fed. Appx. 156 (11th Cir. 2005).

¹⁷⁰ *Id.* at 1067.

¹⁷¹ *Id.* at 1058–59.

¹⁷² *Id.* The basis for the entry date of Klor Con is not explained in the decision.

product used to reduce cholesterol.¹⁷³ When the agreement was finalized, Schering made a \$60 million upfront payment to Upsher, plus a \$10 million milestone payment and an agreement for royalty payments of 10% or 15% of sales for Niacor.¹⁷⁴

Another generic drug company, ESI Lederle, (“ESI”) also filed an ANDA for an extended release potassium chloride product.¹⁷⁵ Schering sued ESI, but the parties settled in December 1997, with ESI agreeing to delay the introduction of its product until January 1, 2004 in return for a fee of \$5 million, attributed to legal fees, plus an additional \$10 million only if ESI’s product was approved by a certain date.¹⁷⁶ In addition, Schering agreed to license two generic drugs, enalapril and buspirone, in exchange for a payment of \$15 million.¹⁷⁷

On March 30, 2001, the FTC filed an administrative complaint against Schering, Upsher, and ESI’s parent, American Home Products, alleging that the agreements were illegal restraints of trade and that Schering monopolized and conspired to monopolize the potassium supplement market.¹⁷⁸

The FTC complaint was tried before an Administrative Law Judge (“ALJ”), who dismissed the complaint, holding that the agreements were lawful settlements of the patent lawsuits.¹⁷⁹ The ALJ held that a finding that the settlements were anticompetitive required an assumption that either the ’743 patent was invalid or that the generic drugs would not have infringed the ’743 patent, and there was no basis for either assumption.¹⁸⁰ In addition, the ALJ held that the payments to Upsher and ESI were not anticompetitive per se, but legitimate payments based on patent rights.¹⁸¹ Finally, the ALJ dismissed as unproven the complaint

¹⁷³ *Id.* at 1059 n.3.

¹⁷⁴ *Id.* at 1060.

¹⁷⁵ *Id.*

¹⁷⁶ *Id.* at 1060–61.

¹⁷⁷ *Id.* at 1060–61 n.6.

¹⁷⁸ *Id.*

¹⁷⁹ *Id.* at 1060–61.

¹⁸⁰ *Id.*

¹⁸¹ *Id.*

that Schering maintained in illegal monopoly in the potassium chloride supplement market.¹⁸²

The FTC's counsel appealed this decision to the full Commission, which reversed the ALJ, holding that the agreements with Upsher and ESI violated the FTC Act and the Sherman Act.¹⁸³ The Commission did not rule on the per se legality of the payments, but concluded that the quid pro quo for the payment was a delay of generic market entry, which illegally harmed consumers.¹⁸⁴ In contrast to the ALJ's consideration of the patent rights at issue, the Commission used a "might have been" analysis of entry dates absent the challenged payments as determinative.¹⁸⁵ The Commission held that the payments to Upsher and ESI were not legitimate consideration for delaying market entry, so the Commission prohibited settlements whereby a generic drug company receives "anything of value" for delaying market development activities.¹⁸⁶ The only carve-out to this policy was a limited payment, not to exceed \$2 million, for litigation costs.¹⁸⁷

Schering and Upsher appealed this decision to the 11th Circuit.¹⁸⁸ The 11th Circuit applied the "substantial evidence" standard it developed in the *Terazosin II* case¹⁸⁹ and stated that neither a rule-of-reason nor per se analysis was appropriate for antitrust analysis in patent cases because patents by nature are exclusionary and anticompetitive.¹⁹⁰ The court repeated the opinion it expressed in *Terazosin II*,¹⁹¹ that in patent cases, antitrust liability requires an examination of (1) the exclusionary scope of the patent; (2) the extent to which agreements exceed the scope; and (3) the resulting anti-competitive effect.¹⁹² Thus, the

¹⁸² *Id.* at 1062.

¹⁸³ *Id.*

¹⁸⁴ *Id.*

¹⁸⁵ *Id.*

¹⁸⁶ *Id.*

¹⁸⁷ *Id.*

¹⁸⁸ *Id.*

¹⁸⁹ *Id.*

¹⁹⁰ *Id.* at 1065–66.

¹⁹¹ See *infra* notes 88–118 and accompanying text (discussing *Valley Drug Co. v. Geneva Pharm., Inc. (Terazosin II)*, 344 F.3d 1294 (11th Cir. 2003)).

¹⁹² *Schering-Plough Corp. v. FTC*, 402 F.3d 1056, 1066 (11th Cir. 2005), *reh'g en banc denied*, 147 Fed. Appx. 156 (11th Cir. 2005)(citing *Terazosin II*, 344 F.3d at 1312 n.15).

court held that because of the '743 patent, Schering had the right to exclude Upsher and ESI until either they proved the patent invalid or that their generic copies did not infringe the patent.¹⁹³ There was no basis for challenging the validity of the '743 patent, so it was considered valid.¹⁹⁴ Further, it appeared that both generic copies were infringing the '743 patent.¹⁹⁵ The FTC case turned on the substantiality of evidence supporting the FTC assertion that the challenged agreements restrict competition beyond the statutory exclusion of the '743 patent.¹⁹⁶ The 11th Circuit held that the evidence relied on by the ALJ was reliable,¹⁹⁷ that the challenged agreement expressly described the payments to Upsher as royalties,¹⁹⁸ and that the agreements did not exceed the scope of the '743 patent.¹⁹⁹ The court noted that the scope of the Schering-Upsher agreement demonstrated an efficient narrowness, and in not exceeding the scope of the '743 patent, was not anticompetitive.²⁰⁰ Thus, the court concluded that the settlements were proper and reversed the FTC.²⁰¹

This case highlights many important points that sharpen the balance between the exclusions of patents and the anticompetitive benefits of the antitrust regime. The FTC seemed unconcerned with Schering's patent rights in holding that the agreements were anticompetitive.²⁰² By contrast, the 11th Circuit noted that patentees "should not be in a worse position, by virtue of their patent rights, to negotiate and settle surrounding lawsuits."²⁰³ Further, "[b]y entering into the settlement agreements, Schering realized the full potential of its infringement suit—a determination that the '743 patent was valid and that ESI and Upsher would not

¹⁹³ *Id.* at 1068.

¹⁹⁴ *Id.*

¹⁹⁵ *Id.*

¹⁹⁶ *Id.*

¹⁹⁷ *Id.* at 1071.

¹⁹⁸ *Id.*

¹⁹⁹ *Id.* at 1072.

²⁰⁰ *Id.* at 1073.

²⁰¹ *Id.* at 1076.

²⁰² *Id.* at 1072 (noting that the FTC "refused to consider the underlying patent litigation.").

²⁰³ *Id.*

infringe.”²⁰⁴ Upsher and ESI obtained less than they would have had they won the suit, but there was no assurance of victory in court.²⁰⁵ As reiterated from *Terazosin II*, “[d]ue to the ‘asymmetrics of risk and large profits at stake, even a patentee confident in the validity of its patent might pay a potential infringer a substantial sum in settlement.’”²⁰⁶ In other words, the outcome of litigation is never assured. Further, the “caustic environment” of patent litigation can decrease innovation by “amplifying the period of uncertainty” around a drug manufacturers’ ability to bring a new or generic drug to market.²⁰⁷ Thus, the court held that patent settlements, such as the type in the *Schering* case, actually facilitate innovation and competition.²⁰⁸

This case has important lessons for drug companies. The guidance of *Schering* is that where a generic company files a paragraph IV certification, and there is a settlement involving payments to the generic company, then they can likely evade antitrust liability if they avoid the appearance of a simple payment to stay off the market. Innovator companies may want to make such payments to avoid the litigation risk of invalidating their patent, and generic companies want to receive them to avoid the litigation risk that they will lose and have to wait for other limiting patents or exclusivity to expire. Ways the appearance of a simple payoff can be avoided are expressions of a legitimate business purpose in the settlement agreement, evidence of diligence in establishing the business purpose, and a limitation on the scope of any agreement to the scope of the patent. The presence of a quid pro quo of the generic company offering something else to the innovator, such as a license to a developed product, will also be helpful in avoiding the appearance of a reverse payment.

²⁰⁴ *Id.* at 1075.

²⁰⁵ *Id.*

²⁰⁶ *Id.* at 1075.

²⁰⁷ *Id.*

²⁰⁸ *Id.*

V. ANTITRUST ASPECTS OF THE 180-DAY EXCLUSIVITY AND DECLARATORY JUDGMENTS

The Hatch-Waxman amendments, both pre- and post-MMA, provided for a trigger to the 180-day exclusivity on a judicial holding of invalidity or noninfringement.²⁰⁹ A recent example relating to this issue involved sertraline,²¹⁰ where a subsequent ANDA filer attempted to extinguish a 180-day exclusivity through a declaratory judgment action. Here, Teva Pharmaceuticals filed a declaratory judgment action in an attempt to make a showing of a judicial decision within the meaning of the FDCA, which triggers the 180-day exclusivity period.²¹¹ If the judicial declaration had been granted, the 180-day period would be triggered on the date of the decision rather than on an expiry of a limiting patent, and the exclusivity period would run and expire prior to the ability of the FDA to approve the first ANDA.²¹² The effect of this procedure is to deprive the first ANDA applicant of its exclusivity. There are arguments that this procedure could be a restraint of trade, by improperly depriving a party of an exclusionary right under the patent and food and drug laws. A contrary argument is the consumerist view in favor of bringing low cost competitors to market as quickly as possible, and that delays in the commencement of the 180-day exclusivity period are a restraint of trade that harms consumers.²¹³

This litigation involved sertraline, a major “SSRI” drug prescribed for depression and marketed under the brand name

²⁰⁹ 21 U.S.C. § 355(j)(5)(B)(iv)(II) (pre-MMA). *Teva Pharms. USA v. FDA (Teva v. FDA I)*, 182 F.3d 1003, 1007–08 (D.C. Cir. 1999). Under the MMA, there is a similar provision in the forfeiture provisions at 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(AA)–(BB). Under this provision, if a first filer otherwise entitled to 180-day exclusivity does not market the product within 75 days of an infringement action, a declaratory judgment action, or settlement agreement holding the patent to be invalid or not infringed (i.e., a trigger), the exclusivity is forfeited.

²¹⁰ *Teva Pharms. USA, Inc. v. Pfizer, Inc. (Teva v. Pfizer II)*, 395 F.3d 1324 (Fed. Cir. 2005).

²¹¹ *Id.* at 1328.

²¹² *Id.*

²¹³ The FTC and AARP filed amicus curiae briefs in support of Teva (to quash the exclusivity period), suggesting that the patent listings and settlements caused Teva economic injury. *Id.* at 1335.

“Zoloft.” The background is that Ivax Pharmaceuticals²¹⁴ had filed the first ANDA to manufacture generic sertraline in 1999 with a Paragraph III certification to U.S. patent 4,356,518 (the “518 patent”),²¹⁵ expiry June 30, 2006, which claims the sertraline chemical compound.²¹⁶ The paragraph III certification meant that Ivax did not intend to challenge the ’518 patent as not infringed or invalid. Ivax therefore agreed to wait until the expiry of the ’518 patent before launching its product.²¹⁷ In the same ANDA, Ivax filed a paragraph IV certification to the other patent at issue in this case, U.S. 5,248,699 (the “699 patent”), expiry September 28, 2010,²¹⁸ which claimed a novel crystalline form of sertraline and a method for preparing it.²¹⁹ Pfizer timely sued Ivax for infringement, but the parties settled in 2002, with Pfizer giving Ivax a royalty-bearing license on the ’699 patent.²²⁰ With this license, Ivax should be free to launch a generic sertraline on the expiration of the ’518 patent.²²¹ Ivax was the first generic pharmaceutical company to file an ANDA with a paragraph IV certification to the ’699 patent, so it should be entitled to the 180-day exclusivity period.²²²

Meanwhile, Teva Pharmaceuticals filed an ANDA to manufacture generic sertraline in July, 2002, with the same paragraph III and IV certifications that Ivax made.²²³ Teva notified Pfizer as required by the Hatch-Waxman amendments, but Pfizer did not sue Teva within the 45-day period as required by the Hatch-Waxman amendments.²²⁴ Thereafter, Teva filed a declaratory judgement action against Pfizer in the U.S. District Court for the District of Massachusetts, under 28 U.S.C.

²¹⁴ At the time of the ANDA filing, Ivax Pharmaceuticals was then known as Zenith Goldline Pharmaceuticals, Inc. *Id.* at 1330.

²¹⁵ *Id.*

²¹⁶ *Id.* at 1329.

²¹⁷ *Id.* at 1330.

²¹⁸ *Id.* at 1329.

²¹⁹ *Id.* Ivax’s specific non-infringement or invalidity allegations are not in the opinion discussed here.

²²⁰ *Id.* at 1330.

²²¹ *Id.*

²²² *Id.*

²²³ *Id.* at 1326–27.

²²⁴ *Id.* at 1327.

§ 2201(a),²²⁵ seeking a declaration that the Teva's ANDA did not infringe the '699 patent, or alternatively that the '699 patent was invalid.²²⁶ On December 8, 2003,²²⁷ the district court dismissed the case for lack of jurisdiction and failure to establish that an actual controversy existed between Teva and Pfizer.²²⁸ The court held that Teva failed to show Pfizer had taken actions giving rise to a "reasonable apprehension" that Pfizer would sue Teva for infringement of the '699 patent.²²⁹

Teva appealed the district court decision to the Federal Circuit, arguing that the district court erred in holding that there was no actual controversy between it and Pfizer as a matter of law.²³⁰ The majority on the panel affirmed the district court decision.²³¹

The district court applied a two-part test formulated by the Federal Circuit for analyzing a controversy in a declaratory judgment action.²³² Under the test, a declaratory judgment plaintiff must show both (1) an explicit threat by the patentee that creates a "reasonable apprehension" that it will be sued for infringement, and (2) that the plaintiff is engaging in infringing activities.²³³ The district court established that the second prong was satisfied by the filing of the ANDA, but that Teva failed to satisfy the reasonable apprehension prong.²³⁴ It is the latter holding that is the truly contentious point in this case.²³⁵ Teva argued essentially that listing the '699 in the Orange Book was tantamount to an explicit threat and the creation of a reasonable

²²⁵ *Id.* at 1331. Note that the pre-MMA Hatch-Waxman amendments statute, under which the Teva declaratory judgment action was first filed, expressly permits an ANDA applicant, not sued within 45 days by the NDA holder, to bring a suit under the declaratory judgment statute. 21 U.S.C. § 355(j)(5)(B)(iii) (2000).

²²⁶ *Id.* at 1330.

²²⁷ Note that this decision was issued the same day that the MMA was enacted into law.

²²⁸ *Teva Pharms. USA, Inc. v. Pfizer, Inc. (Teva v. Pfizer I)*, 69 U.S.P.Q.2d 1791 (D. Mass. 2003). See also *Teva v. Pfizer II*, 395 F.3d at 1327.

²²⁹ *Id.*

²³⁰ *Id.*

²³¹ *Id.* See also *id.* at 1338. The majority opinion was written by Judge Schall and joined by Judge Clavenger.

²³² *Id.* at 1330.

²³³ *Id.*

²³⁴ *Id.* at 1330–31.

²³⁵ *Id.* at 1332.

apprehension by an ANDA filer.²³⁶ Teva argued that the purpose for Orange Book patent listings is to put potential infringers on notice that the listed patents are central to the product, and that patents are listed in the Orange Book for the purpose of providing notice that such patents “could reasonably be asserted” in an infringement suit.²³⁷ However, these arguments were dismissed by the Federal Circuit majority, which held that Teva’s reliance on Orange Book patent listings was “misplaced,” and that such listings are merely the result of a statutory requirement.²³⁸ The majority stated: “[w]ithout more, Pfizer’s compliance with the Hatch-Waxman listing requirement should not be construed as a blanket threat to potential infringers . . . [m]ore is required for an actual controversy than the existence of an adversely held patent . . .”²³⁹ The court stated that under Article III of the Constitution, a declaratory judgment plaintiff had to show the creation of an actual controversy, not one that is “conjectural or hypothetical.”²⁴⁰

Teva also argued that the MMA amendments establish jurisdiction without regard to the reasonable apprehension prong of the two-part test.²⁴¹ The MMA amendments were applicable to this case because Congress provided that they would apply to any pending proceeding on or after the date of enactment, and the district court decision was issued the same day as the MMA was enacted.²⁴² However, the Federal Circuit majority held that the declaratory judgment provisions of the MMA Amendments did not alter its analysis, noting that “[w]e do not think that the cases cited by Teva support the proposition that the reasonable apprehension of suit prong of our traditional two-part test is not a constitutional requirement.”²⁴³ The majority further went on to cite the Conference Committee Report on H.R. 1 (the House version of the

²³⁶ *Id.*

²³⁷ *Id.*

²³⁸ *Id.* at 1333.

²³⁹ *Id.*

²⁴⁰ *Id.*

²⁴¹ *Id.* at 1334. *See also supra* notes 46–48 and accompanying text (discussing the declaratory judgment provisions of the MMA).

²⁴² *Id.*

²⁴³ *Id.* at 1335.

Medicare Amendments) as supporting the contention that Congress did not intend for the declaratory judgment provisions of the Medicare Amendments to alter the courts' interpretation of the constitutional requirements for a declaratory judgment action.²⁴⁴

Although antitrust issues are discussed only indirectly in this case, the issues provide valuable insights into the objectives of the parties. The FTC joined Teva with an amicus curiae that the 180-day exclusivity creates an economic injury, in that

if Pfizer had not obtained the '699 patent and listed it in the Orange Book, settled its litigation with Ivax, declined to sue Teva, and refused Teva's request for a covenant not to sue, Teva would have the opportunity to gain access to the Zolofit™ market during the 180-day period that will follow the expiration of the '518 patent.²⁴⁵

The FTC therefore suggests that Pfizer's conduct was monopolistic and an anticompetitive restraint of trade, suggesting that Pfizer vigorously defended its agreement to preserve its pricing power for an additional six months beyond the expiry of the '518 patent. However, the potential antitrust violations must be balanced with the rights conferred by valid patents, and the intent of the Hatch-Waxman amendments to incentivize generic companies to obtain 180-day exclusivities as a reward for filing successful paragraph IV certifications. Here, the '699 was a valid patent, and any ANDA applicant seeking to market sertraline on the expiry of the '518 patent had to show either non-infringement or invalidity with respect to the '699 patent. The burden of enforcing patent rights is on the patentee,²⁴⁶ and if Pfizer elected not to bring suit against Teva, that fact does not imply that the '699 patent is invalid. Thus, the 180-day exclusivity afforded to a first to file paragraph IV certifier is not a patent extension of an earlier expiring patent, but rather a bite out of the statutory monopoly of the patent to which the paragraph IV certification was made.

²⁴⁴ *Id.* at 1337. Teva petitioned for a rehearing *en banc*, but this was denied. Teva Pharms. USA, Inc. v. Pfizer Inc. (*Teva v. Pfizer III*), 405 F.3d 990 (Fed. Cir. 2005).

²⁴⁵ *Teva v. Pfizer II*, 395 F.3d at 1335.

²⁴⁶ *See Pfizer, Inc. v. Teva Pharms. USA, Inc.*, 429 F.3d 1364, 1372 (Fed. Cir. 2005).

A significant strategic consideration on Pfizer's part was the risk of losing a suit with Teva had Pfizer accepted the invitation and sued Teva. If Pfizer had engaged Teva and lost, the '699 patent could be invalidated completely. If this had happened, then Teva and other generic drug companies would have been able to enter the market immediately on the expiry of the '518 patent, and no exclusivity would have been awarded because Teva was not the first ANDA filer to make a paragraph IV certification against the '699 patent. Thus, this issue of patent certainty boils down to a risk-benefit analysis for Pfizer, balancing the risk of losing billions in sales that it could share during the exclusivity period with just a single competitor, with the chance of a successful outcome in litigation. As the 11th Circuit noted in *Terazosin II*, there is no assurance of the outcome of litigation, and the "asymmetries of risk" mitigates towards patentees of extremely valuable patents going to great lengths to avoid an infringement trial and the possibility that the patent will be declared invalid.²⁴⁷ Therefore, from an antitrust perspective, there is a good argument that Pfizer's strategy was a legitimate preservation of its patent rights, rather than an improper monopolistic or anticompetitive strategy.

A related fact pattern for litigation involving the hypocholesterolemic drug pravastatin ("*Pravastatin*") further illustrates the potential of declaratory judgment actions to destroy the 180-day exclusivity.²⁴⁸ In this episode, several generic drug companies filed ANDA's to market pravastatin following the expiry of U.S. 4,346,227 (the "'227 patent"), on April 20, 2006, with paragraph IV certifications to several later expiring patents listed in the Orange Book.²⁴⁹ None of the generic drug companies were sued by BMS.²⁵⁰ Teva was apparently the first to file and was entitled to 180-day exclusivity.²⁵¹ One of the other ANDA applicants, Apotex, sought assurances from BMS that it was not infringing the later expiring patents, and despite three letters from

²⁴⁷ *Valley Drug Co. v. Geneva Pharm., Inc. (Terazosin II)*, 344 F.3d 1294, 1310 (11th Cir. 2003).

²⁴⁸ *Teva Pharms. USA, Inc. v. FDA*, 398 F. Supp. 2d 176 (D.D.C. 2005).

²⁴⁹ *Id.* at 179.

²⁵⁰ *Id.* at 180.

²⁵¹ *Id.*

BMS indicating no intention to sue, Apotex filed a declaratory judgment action seeking judicial clarification that it was not infringing or that the patents were invalid or unenforceable.²⁵² The action was dismissed for lack of subject matter jurisdiction under a joint motion between the parties.²⁵³ The FDA then issued a decision maintaining that the 180-day clock started on the date of the BMS-Apotex dismissal, on August 22, 2004, and therefore expired on February 18, 2005, prior to the expiry of the '227 patent.²⁵⁴ Thus, the FDA proposed to deny Teva its exclusivity period. Teva sued the FDA in the D.C. District Court to preserve its exclusivity period and enjoin the FDA from approving other ANDA's during the exclusivity period to which it believed it was entitled. The court found that the decision was not a triggering court decision under the terms of the Hatch-Waxman statute, and granted Teva its injunction.²⁵⁵

The FDA relied on a pair of earlier decisions involving the drug ticlopidine²⁵⁶ in support of its position to deny Teva exclusivity. Interestingly, the parties in the ticlopidine litigation also involved Teva and Apotex, but in diametrically opposed positions. In the ticlopidine case, Apotex was first to file, and Teva was a subsequent filer and sought a declaratory judgement that it was not infringing. Roche, which owned ticlopidine, indicated that they would not sue Teva for infringement, and this representation was held to be an estoppel for the purposes of the statute. Ultimately in the ticlopidine case, Apotex lost its exclusivity as a result of the Teva action.²⁵⁷

The *Pravastatin* court distinguished several features of the Roche representations to not sue Teva over ticlopidine with the

²⁵² *Id.* at 179–80.

²⁵³ *Id.* at 180–81.

²⁵⁴ The FDA considered the BMS-Apotex dismissal to be a “decision of a court with respect to any ANDA, in which the court holds the relevant patent is invalid, unenforceable or not infringed” under 21 U.S.C. § 355(j)(5)(B)(iv)(II) (pre-MMA). Such a court decision is a triggering event for exclusivity. *Id.* at 181.

²⁵⁵ *Id.* at 192.

²⁵⁶ *Id.* See also *Teva Pharms. USA v. FDA (Teva v. FDA I)*, 182 F.3d 1003 (D.C. Cir. 1999) and *Teva Pharms. USA, Inc. v. FDA (Teva v. FDA II)*, 2000 U.S. App. LEXIS 38667, WL 1838303 (D.C. Cir. 2000) (unpublished opinion).

²⁵⁷ See *Teva v. FDA II*, 2000 U.S. App. LEXIS 38667.

BMS stipulation to not sue Apotex over pravastatin. In the ticlopidine case, the court had to make a predicate finding of fact, which was not necessary in the *Pravastatin* case.²⁵⁸ Thus, the BMS-Apotex dismissal was not a “decision of a court” under the Hatch-Waxman Act, so the 180 day exclusivity was not triggered by the dismissal.²⁵⁹ Therefore, the district court granted Teva’s motion for an injunction to preserve its exclusivity for pravastatin.²⁶⁰ This decision has been appealed to the D.C. Circuit.²⁶¹

This was an important holding, affirming the preservation of 180-day exclusivity periods that are critical to the generic drug industry. If a third party could extinguish an exclusivity period on the mere filing of a declaratory judgment action, regardless of its merit or the representations of the innovator company, then there would never be an exclusivity period again. Although consumer groups, and possibly the FTC, appear to be opposed to the 180-day exclusivity period, the exclusivity is an important incentive created by Congress in the Hatch-Waxman regime, to reward the first company to file an ANDA challenging innovator patents. The substantial profits derivable from the exclusivity period²⁶² are an important factor in the financial health of the generic drug industry. However, the 180-day exclusivity period is far from healthy.

VI. THE END OF 180-DAY EXCLUSIVITY?

A recurring theme in the cases discussed in this paper is the power of the 180-day exclusivity, as an incentive to the generic companies, and sometimes as a financial benchmark in the cases involving payments to generic companies to defer marketing. As discussed *supra*, Congress became very concerned over abuses,

²⁵⁸ *Teva Pharms. USA, Inc. v. FDA (Teva v. FDA III)*, 398 F. Supp. 2d 176, 191 (D.D.C. 2005).

²⁵⁹ *Id.* at 190–91.

²⁶⁰ *Id.* at 192.

²⁶¹ Case Docket number 05-5401, filed Nov. 16, 2005.

²⁶² *See, e.g., Teva v. FDA III*, 398 F. Supp. 2d at 180.

particularly involving the 180-day exclusivity period.²⁶³ Thus, Congress created substantial limits on the exclusivity period in the MMA with the new forfeiture provisions.

The forfeiture provisions have significant antitrust implications. While the new provisions are designed to avoid situations like that discussed *supra* in *Cardizem CD*, *Ciprofloxacin*, and *Terazosin*, where manipulations of the 180-day exclusivity led to allegations of anticompetitive conduct, the new provisions will have other, significant impacts on the generic drug industry.

The new rules seem designed to take away the incentive to file an ANDA earlier than 30 months before the expiry of exclusivity, and do not account for valid paragraph III certifications later than 30 months post filing. Prior to the MMA, generic companies often filed ANDA's many years in advance.²⁶⁴ Generic drug companies were incentivized to do this under the Hatch-Waxman amendments, which essentially made the filing of ANDA's with paragraph IV certifications a race to obtain the 180-day exclusivity, by rewarding only the first filer the exclusivity.²⁶⁵ However, the new statute essentially holds that the exclusivity period will be forfeited within 30 months of the filing of the ANDA, unless there is a judicial finding of patent invalidity or noninfringement.²⁶⁶ Exceptions allowing an earlier filing that preserve exclusivity are very limited. One possibility may be if a generic can successfully invalidate a main product patent in an infringement suit, which would avoid forfeiture events if the generic drug can be launched timely after a final court decision.²⁶⁷

²⁶³ See *supra* Part II (discussion of the forfeiture provisions).

²⁶⁴ See for example, the *Ciprofloxacin* discussion *supra*. Barr Laboratories filed its ANDA to the '444 patent, expiry December 2003, in October 1991, which was 12 years in advance.

²⁶⁵ *Teva Pharm. Indust., Ltd. v. FDA*, 355 F. Supp. 2d 111, 114 (D.D.C. 2004); *Pharmachemie B.V. v. Barr Laboratories, Inc.*, 276 F.3d 627, 629 (D.C. Cir. 2002).

²⁶⁶ See *supra* Part II (discussion of the forfeiture provisions).

²⁶⁷ In this scenario, 21 U.S.C. § 355(j)(5)(B)(iii)(I) or (II)(aa), will apply, and the ANDA will be approvable on the date of a court decision of invalidity or noninfringement, and forfeiture provision 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(AA) applies, so a forfeiture event be triggered if the generic drug is not marketed within 75 days of the decision of a court from which no appeal can be taken.

Another exception may be if the generic company files a declaratory judgment action, which constitutes a legal action under the forfeiture statute and defers the trigger until the action is settled.²⁶⁸ Another exception may be if the generic company and NDA holder settle without a concession on the validity of the patent by the NDA holder, and without promise by the NDA holder to not sue the generic company. This situation is essentially a grant of a license to use the patent that would otherwise be litigated, and does not trigger exclusivity under the forfeiture provision,²⁶⁹ since there would be no finding of patent invalidity or noninfringement. There are pitfalls with the settlement option, such as the chance that a third party generic company will challenge the patent.²⁷⁰ Thus the MMA forfeiture events do not account for a legitimate paragraph III certification far in advance of the ANDA filing. This situation threatens to take away from the generic companies many cases of exclusivity that would have been awarded under the pre-MMA statute.

For example, as an illustration of the time lines under the new rules, consider the *Teva* case involving sertraline discussed *supra*.²⁷¹ If the Ivax and Teva ANDA's were originally filed under the AAPA provisions, Ivax would have forfeited its exclusivity because the product would not have been marketed within 30 months of the original filing,²⁷² or within 75 days of the settlement granting the '699 license.²⁷³ Therefore, under the AAPA regime, if a generic company had wished to file a paragraph IV certification against the '699 patent, they could not have done so until December 31, 2003, 30 months prior to the expiry of the '699 patent on June 30, 2006. If any generic company filed a

²⁶⁸ 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb). However, note that in this scenario the generic company has little control over the timing of the settlement of the case.

²⁶⁹ 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(BB).

²⁷⁰ See *infra* note 276 and accompanying text.

²⁷¹ *Teva Pharms. USA, Inc. v. Pfizer, Inc. (Teva v. Pfizer II)*, 395 F.3d 1324 (Fed. Cir. 2005).

²⁷² The exact date of the Ivax ANDA is not given in *Teva v. Pfizer II*, 395 F.3d at 1330; the date is only given as "1999." Thus, the latest possible 30-month date is June 30, 2003. The exclusivity based on the '518 patent, which was not challenged by Ivax or Teva, expires June 30, 2006. *Id.*

²⁷³ The date of the Pfizer license to Ivax is only given as "2002." *Id.*

paragraph IV certification earlier, then exclusivity would be forfeited for all generic companies.²⁷⁴

Alternatively, Pfizer could have provided a license to Ivax for the '699 patent, which would not trigger the forfeiture provisions.²⁷⁵ However, this is not a fool proof alternative, because it does not prevent another company from challenging the '699 patent. If a challenge was successful, that would have taken away Ivax's exclusivity.²⁷⁶ In that case, Ivax would not have accrued the reward of the 180-day exclusivity period as an incentive for being the first to file an ANDA with a paragraph IV certification. A later challenger would not get an exclusivity period either. On the expiration of the '699 patent, in this hypothetical, most likely multiple generic copies would be introduced simultaneously, causing very rapid price erosion.²⁷⁷ While this may have short term benefits for consumers, it is damaging to the incentives for the generic drug industry.

Another problem with the settlement and license hypothetical is that it puts too much control over the process in the hands of the innovator company. A generic company approaching an innovator company for a license to circumvent the forfeiture provisions may have no indication of the innovator's willingness to license later expiring patents, and also will have no idea of generic competitors' activity affecting any agreement. A generic company can thus make a substantial investment, and the innovator may simply

²⁷⁴ See 21 U.S.C. § 355(j)(5)(B)(iv)(I), stating that if a previous ANDA with a paragraph IV certification was filed, then the ANDA approval will be delayed 180 days. If the exclusivity of the first ANDA filer is forfeited, then no company is entitled to any exclusivity.

²⁷⁵ 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(BB). See also *supra* note 269 and accompanying text.

²⁷⁶ The exclusivity would be extinguished in this scenario because the patent being challenged would be invalidated by a party other than the first applicant to file a paragraph IV certification, far in advance of the judicial decision. Under 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(AA), exclusivity is forfeited if the drug is not marketed within 75 days of a decision of invalidity by a court from which no appeal can be taken, on a challenge by any party. In this scenario, if the marketing date is constrained to a future time months or years after such a decision, exclusivity is destroyed.

²⁷⁷ See A. Maureen Rouhi, *Generic Tide is Rising*, 80 (38) *Chemical and Engineering News* 37-51 (2002), available at <http://pubs.acs.org/cen/coverstory/8038/8038biogenerics1.html> (discussing the price erosion in innovator drugs once generics are introduced to the market).

refuse to deal. Perhaps the refusal would be due to a prior generic company concluding a confidential licensing arrangement. There could be any number of other reasons, rational or not. Moreover, this concept invites ANDA applicants and innovator drug companies to make deals, which in the antitrust regime are horizontal market allocations but for the patent involved. It was concern over just these kinds of deals, affecting the 180-day exclusivity, that led to the FTC investigations and the AAPA itself.

Innovator companies could conceivably hold an auction, where exclusivity would be based on a factor other than the first party to develop the drug, which was the original intent of the Hatch-Waxman amendments.²⁷⁸ Prior to the enactment of the forfeiture provisions, free market forces determined which company was first to market. The FDA made public the existence of an ANDA with a paragraph IV certification, so a generic company would at least know prior to ANDA filing if they were not first to file. With the forfeiture provisions, there is now a cloud over the whole process.

The 180-day exclusivity period benefits the innovator companies too, by tempering the rapid price erosion that would otherwise occur if multiple generics entered the market simultaneously.²⁷⁹ This suggests that the innovator companies may have an incentive to work with the generic companies to maintain exclusivity periods,²⁸⁰ but it also can leave the generic companies subject to arbitrary or capricious choices by the innovators, rather than letting unbiased market forces determine the exclusivity period.

Benefit or harm to the public is always an element of an antitrust analysis.²⁸¹ The benefit to the public from the new forfeiture provisions, assuming exclusivity periods become rare, will only lie in the rapid price erosion once generics enter the

²⁷⁸ *Supra* note 265.

²⁷⁹ *Supra* note 277.

²⁸⁰ This statement may be obvious in light of the episodes discussed *supra*, such as *Caridizem CD*, *Terazosin*, *Ciprofloxacin*, etc., but the meaning here is that innovator companies have an interest in their generic rivals' exclusivity periods even if there are no antitrust issues, such as anticompetitive dealing, in order to moderate price erosion after generic entry into the market.

²⁸¹ See SULLIVAN & GRIMES, *supra* note 50, at 12–13, discussing the importance of consumer welfare goals in antitrust analysis.

market.²⁸² Conversely, if generic and innovator companies rush into each others arms, the cooperation will tend to benefit larger generic companies, who can afford the legal resources and cost of license deals. This could be interpreted as an anticompetitive effect, favoring only those generic companies with a substantial capital structure, not necessarily those that are more innovative. Innovation should be the appropriate determinative factor.

If exclusivity periods become rare in the new regime, the forfeiture rules may tend to harm consumers by delaying the introduction of generic drugs, because the generic drug companies will have less incentive to innovate and file paragraph IV certifications without the benefit of the exclusivity period. Thus, consumers may have to wait longer before they realize the benefits of the price erosion. This delay may translate to a lengthened exclusivity of the brand name drugs.

This situation seems to have taken away the original intent of the Hatch-Waxman statute to incentivize generic companies to file ANDA's with paragraph IV certifications, because of the diminished prospects for exclusivity. The legislative record of the forfeiture provisions indicates that Congress was concerned with collusion between the innovator and generic companies by delaying the commencement of the exclusivity.²⁸³ Although the Congressional record mentions no specific cases, it appears they had in mind situations like *Cardizem CD* or *Terazosin*, where there were agreements to delay the start of the exclusivity period, which in addition to perceived unfair profits to both the innovator and generic company, also delayed the introduction of other generic competitors, and was perceived to harm consumers. However, the way the legislation turned out, important incentives for generic drug companies to innovate, by designing bioequivalent copies of known effective medications, and racing to file patent challenges and ANDA's as soon as possible, have apparently been significantly harmed.

In many cases, generic drugs are not simply copy cat versions of marketed products, but rather require significant investment and

²⁸² *Supra* note 277.

²⁸³ 149 CONG. REC. S15746 (daily ed. Nov. 24, 2003).

development. The potential damage to the generic drug industry threatens to harm consumers and reduce the diversity of business interests manufacturing drugs. The potential misallocation of resources is antithetical to the goals of antitrust law.²⁸⁴ That is an undesirable outcome.

VII. CONCLUSION

The AAPA provisions of the Medicare Modernization Act were promulgated largely in response to antitrust concerns around the original Hatch-Waxman amendments, particularly in the area of perceived abuses in the 30-month stay of effectiveness on the filing of a paragraph IV certification, and perceived harm from collusive agreements between innovator and generic companies, often involving horizontal territorial restraints and manipulations of the 180-day exclusivity period. While in some respects, such as the limit in the AAPA amendments of a single 30-month stay per drug, the amendments seem to have leveled the playing field and provided benefits to both generic drug companies and consumers, while still being fair to innovator drug companies, in other respects, particularly the 180-day exclusivity forfeiture provisions, it seems that the new amendments will harm the generic and innovator drug companies substantially. The trajectory of cases from *Cardizem CD* to *Terazosin* to *Schering* suggested that the courts had worked out a rational and predictable set of rules, essentially holding that agreements within the scope of patent rights are acceptable and not challengeable on antitrust grounds, and agreements outside that scope will incur antitrust liability. It seems that Congress, in its implementation of the AAPA, may have misunderstood patent rights and incentives to innovate by coming down too hard with the forfeiture provisions that will disincentivize and harm the generic drug industry. Generic drugs do not grow on trees, and in the end consumers will lose if either the innovator or generic drug industries are excessively harmed by the new statutes.

²⁸⁴ SULLIVAN & GRIMES, *supra* note 50, at 19.