VIRGINIA JOURNAL OF LAW & TECHNOLOGY

SUMMER 2015 UNIVERSITY OF VIRGINIA VOL. 19, NO. 03

Roberts Was Wrong: Increased Antitrust Scrutiny after FTC v. Actavis Has Accelerated Generic Competition

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ABSTRACT

In *Federal Trade Commission v. Actavis*, the Supreme Court ruled that reverse-payment settlements between pharmaceutical patent holders and generic manufacturers are subject to heightened antitrust scrutiny. In a vigorous dissent, Chief Justice John Roberts suggested that greater antitrust scrutiny may actually harm competition by discouraging generics from challenging pioneers' patents in the first place. This Article finds that, contrary to Roberts's prediction, the number of Paragraph IV challenges actually increased by twenty percent in the year following *Actavis*. To restore the incentive balance between pioneers and generics, this Article argues that the Federal Trade Commission should be required to prove patent invalidity before bringing an antitrust suit. This Article also urges the Federal Drug Administration to adopt more transparent disclosure policies, Congress to amend the Hatch-Waxman Act to include a "rolling exclusivity" procedure, and courts to adopt a more coherent framework for evaluating settlements between patentees and generic challengers.

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> The irony of all this is that the majority's decision may very well discourage generics from challenging pharmaceutical patents . . . . Taking the prospect of settlements off the table . . . puts a damper on the generic's expected value going into litigation, and decreases its incentive to sue in the first place.
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> - Chief Justice John Roberts[1]

I. INTRODUCTION

Pharmaceutical companies invent more than just drugs—they have also invented creative legal strategies for protecting those drugs. Representative Henry Waxman has quipped that "some of the most outstanding research happening at certain brand-name drug companies is in the field of law."[2] One such innovation is the so-called reverse-payment settlement, which often occurs after a pioneer drug manufacturer sues a generic drug manufacturer for patent infringement.[3] In these agreements, the patentee agrees to pay

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[1] FTC v. Actavis, Inc., 133 S. Ct. 2223, 2247 (2013) (Roberts, C.J., dissenting).

[2] Press Release, Henry A. Waxman, Representative Henry A. Waxman on the Delay of Approval of Generic Drugs (Nov. 20, 2001) (attributing this quote as a comment by an anonymous "drug company official"), *available at* http://www.citizen.org/congress/reform/drug_patents/bmsg/articles.cfm?ID=6496.

[3] *See Actavis*, 133 S. Ct. at 2227. The Court explained that reverse-payment settlements occur in the following scenario:

Company A sues Company B for patent infringement. The two companies settle under terms that require (1) Company B, the claimed infringer, not to produce the patented product until the patent's term expires, and (2) Company A, the patentee, to pay B many millions of dollars. Because the

the generic competitor—often millions of dollars annually—in exchange for the generic agreeing to delay marketing its copy of the patentee's drug.[4] These types of settlements have been highly scrutinized for their anticompetitive effects and underscore the tension between antitrust law and patent law.[5] The antitrust laws were designed to prevent the willful acquisition of monopoly power.[6] In direct conflict with this is patent law, which was designed to give limited monopolies to inventors for a limited period of time.[7] Reverse-payment settlements exacerbate this tension because they arguably allow pharmaceutical pioneers to unfairly extend the scope of their monopolies beyond the limited period envisioned by the patent laws and the Hatch-Waxman Act, which established a system whereby generic manufacturers can seek to market generic equivalents of a pioneer's patented drug prior to the patent's expiration.[8] Such payments arguably allow pioneers to avoid

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settlement requires the patentee to pay the alleged infringer, rather than the other way around, this kind of settlement agreement is often called a "reverse payment" settlement agreement.

Id. at 2227. A "pioneer" drug manufacturer is one that researches, develops, and sells a brand-name drug; a "generic" drug manufacturer is one that sells a drug "bioequivalent" to the pioneer's brand-name drug. *Id.* at 2228. For the purposes of this Article, "pioneer" is synonymous with "pioneer drug manufacturer" and "generic" is synonymous with "generic drug manufacturer."

[4] *Id.* at 2227.

[5] *See* Herbert J. Hovenkamp, *Competition for Innovation* (U Iowa Legal Studies, Research Paper No. 13-26, Oct. 26, 2012) *available at* http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2008953.

[6] *See* Herbert J. Hovenkamp (U Iowa College of Law), *Antitrust and Patent Law Analysis of Pharmaceutical Reverse Payment Settlements*, (Jan. 15, 2011), *available at* http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1741162.

[7] MARGRETH BARRETT, INTELLECTUAL PROPERTY: CASES AND MATERIALS 124 (4th ed. 2011).

[8] Hovenkamp, *supra* note 5; 21 U.S.C. § 355(j)(2)(A)(vii)(IV) (2012).

competition by sharing their monopoly profits with the generic challenger.[9]

After more than a decade of criticism of reverse-payment settlements by academics, consumer groups, and state and federal governments, the Supreme Court finally addressed the legality of reverse-payment settlements in the 2013 decision, *FTC v. Actavis*.[10] The Federal Trade Commission (FTC) argued that reverse-payment settlements harm generic competition and that such settlements should be banned.[11] The Court declined to find such settlements presumptively illegal, as argued for by the FTC, but also declined to uphold prior appellate court cases that found such settlements to be effectively *per se* legal under the antitrust laws.[12] Instead, the Court took the middle ground and held that reverse-payment settlements should be analyzed using the holistic "rule of reason" analysis to determine whether they violate antitrust laws.[13] The Court reasoned that these agreements pose a genuine risk of creating adverse effects on competition, and therefore may sometimes violate antitrust laws.[14] Consequently, the FTC should not be prevented from bringing antitrust suits against parties who enter into reverse-payment settlements.[15]

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[9] *See* Andrew A. Caffrey, III & Jonathan M. Rotter, Note, *Consumer Protection, Patents and Procedure: Generic Drug Market Entry and the Need to Reform the Hatch-Waxman Act*, 9 VA. J.L. & TECH. 1, 3 (2004).
[10] *See generally* FTC v. Actavis, Inc., 133 S. Ct. 2223 (2013).
[11] *See generally* FTC v. Watson Pharmaceuticals, Inc., 677 F.3d 1298 (11th Cir. 2012).
[12] *Actavis*, 133 S. Ct. at 2237.
[13] *Id.* at 2236.
[14] *Id.*
[15] *Id.* at 2238.

In his vigorous dissent in *Actavis*, Chief Justice John Roberts suggested that greater antitrust scrutiny may actually harm competition.[16] He reasoned that, because litigation is both very costly and very risky, taking the prospect of settlements off the table may discourage generics from challenging pioneers' patents in the first place.[17] Ultimately, this would harm consumers, since reducing the number of challenges by generic manufacturers against the patents of brand-name companies will decrease competition and, in turn, accessibility to affordable drugs.[18]

This Article investigates whether the number of patent challenges has indeed decreased since *Actavis*, per Chief Justice Roberts' prediction. Part II provides background information on patent law and antitrust law, and particularly the tension between the two. Part III describes the role of generic drug manufacturers in the pharmaceutical industry, including explanations of the Hatch-Waxman Act, Paragraph IV certifications, and why reverse-payment settlements are problematic. Part IV reviews the Supreme Court opinion in *Actavis*. Part V first presents the results of the Authors' empirical study, which reveal that, contrary to Chief Justice Roberts' prediction, there was in fact an increase in the number of patent challenges in the twelve-month interval following

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[16] *Id.* at 2247 (Roberts, C.J., dissenting).

[17] *Id.* "Patent litigation is costly, time consuming, and uncertain . . . . Generics 'enter this risky terrain only after careful analysis of the potential gains if they prevail and the potential exposure if they lose.'" *Id.* (citation omitted).

[18] Purepac Pharm. Co. v. TorPharm, Inc., 354 F.3d 877, 879 (D.C. Cir. 2004) (explaining that "[i]n order to encourage paragraph IV challenges, thereby increasing the availability of low-cost generic drugs, . . . [the first Paragraph IV ANDA filer] has the right to sell its drug without competition [from other generic entrants] for 180 days.").

Actavis, as compared to filings in preceding twelve-month intervals. Part V then analyzes the possible explanations for this increase in generic challenges and the practical implications of these findings for the pharmaceutical industry. Finally, Part VI discusses reforms that Congress, the courts, and the Food and Drug Administration (FDA) can implement in order to restore the balance between pioneers' incentive to develop new drugs and generics' incentive to bring cheaper copies of those drugs to market.

II. THE TENSION BETWEEN PATENT LAW AND ANTITRUST LAW IN THE PHARMACEUTICAL INDUSTRY

Because the *Actavis* decision was guided by both patent law and antitrust law, it is useful to begin with an analysis of the relationship between these two bodies of law, particularly in the context of how these laws are applied to the pharmaceutical industry.[19] Patent protection aims to strike a delicate balance between incentivizing innovation and ensuring the free flow of information to the public.[20] The patent system stems from the Patent and Copyright Clause of the Constitution, which affords Congress the power "[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."[21] In enacting patent laws

[19] *See* FTC v. Actavis, Inc., 133 S. Ct. 2223, 2227 (2013) (discussing the legal theories underlying both patent law and antitrust law).
[20] *See* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., No. 12-398, slip op. at 11 (U.S. June 13, 2013).
[21] U.S. CONST. art. I, § 8, cl. 8.

pursuant to this power, Congress contemplated a carefully-crafted bargain wherein inventors disclose their works in exchange for a limited period of market exclusivity.[22] The pharmaceutical industry is one of the few industries that require patent protection to ensure the profitability of their innovative products.[23] Because the drug discovery process has a high failure rate,[24] enormous costs are associated with

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[22] *See* Pfaff v. Wells Elecs., Inc., 525 U.S. 55, 63 (1998). In Pfaff, the D.C. Circuit wrote:

[T]he patent system represents a carefully-crafted bargain that encourages both the creation and the public disclosure of new and useful advances in technology, in return for an exclusive monopoly for a limited period of time. The balance between the interest in motivating innovation and enlightenment by rewarding invention with patent protection on the one hand, and the interest in avoiding monopolies that unnecessarily stifle competition on the other, has been a feature of the federal patent laws since their inception.

See also 35 U.S.C. § 154(a)(1) (2006) ("Every patent shall contain a . . . grant to the patentee . . . of the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States or importing the invention into the United States . . . ."); 35 U.S.C. § 154(a)(2) (stating that the term of protection for utility patents is twenty years from the effective filing date of the patent application).

[23] WESLEY M. COHEN ET AL., NAT'L BUREAU OF ECON. RESEARCH, PROTECTING THEIR INTELLECTUAL ASSETS: APPROPRIABILITY CONDITIONS AND WHY U.S. MANUFACTURING FIRMS PATENT (OR NOT) 23–25, NBER Working Paper No. 7552 (Feb. 2000), (reporting that, according to a 1994 survey, the pharmaceutical industry is one of the rare sectors that uses patents to appropriate rents); *see also* FED. TRADE COMM'N, ANTICIPATING THE 21ST CENTURY: COMPETITION IN THE NEW HIGH-TECH, GLOBAL MARKETPLACE, ch. 6, at 7 (1996) (describing a study demonstrating that approximately only forty percent of pharmaceutical inventions would have been developed in the absence of patent protection), *available at* http://www.nber.org/papers/w7552.pdf.

[24] *See* J. Fred Pritchard et al., *Making Better Drugs: Decision Gates in Non-Clinical Drug Development*, 2 NATURE REVS. DRUG DISCOVERY 542, 542 (2003) (describing failure risks associated with drug discovery).

identification, development, and testing of new drugs candidates.[25] Appropriate patent protection allows drug developers to shoulder these risks and recoup the financial losses incurred during research and development by granting them exclusionary rights for a limited time.[26]

In contrast, the purpose of antitrust law is to promote fair competition and protect consumers by regulating the conduct and organization of business corporations.[27] The antitrust laws serve to (1) restrict the formation of cartels and other "restraints of trade"; (2) restrict the mergers and acquisitions of organizations that could substantially lessen competition; and (3) prohibit the abuse of monopoly power.[28] The FTC, the Department of Justice, and private parties may

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[25] *See* Joseph A. DiMasia & Henry G. Grabowski, *The Cost of Biopharmaceutical R&D: Is Biotech Different?*, 28 MANAGERIAL & DECISION ECON. 469, 477 (2007) (calculating average research and development costs of $1.318 billion per new molecule approved by the Food and Drug Administration).

[26] *Pfaff*, 525 U.S. at 63; Matthew Avery, Note, *Continuing Abuse of the Hatch-Waxman Act by Pharmaceutical Patent Holders and the Failure of the 2003 Amendments*, 60 HASTINGS L.J. 171, 172 (2008).

[27] The main antitrust statutes are the Sherman Act of 1890, the Clayton Act of 1914, and the Federal Trade Commission Act of 1914. William Markham, *An Overview of Antitrust Law*, LAW OFFICES OF WILLIAM MARKHAM (2010), http://www.markhamlawfirm.com/law-articles/antitrust-law-san-diego/.

[28] Monopoly power is defined as "the ability of a firm or group of firms within a market to profitably charge prices above the competitive level for a sustained period of time." Philip Nelson, *Monopoly Power, Market Definition, and the* Cellophane *Fallacy*, ECONOMISTS INCORPORATED, http://justice.gov/atr/public/hearings/single_firm/docs/222008.htm (last visited Jan. 19, 2015).

bring actions in court to enforce the antitrust laws.[29] In the pharmaceutical context, antitrust concerns primarily revolve around actions by both brand-name manufacturers and generics that cause delays in the marketing of generic drugs.

In light of the foregoing, some would argue that the basic function of antitrust law directly conflicts with that of patent law.[30] Antitrust law promotes fair competition whereas patent law restricts competition for a limited period.[31] While the relationship between the two laws is arguably more nuanced, the legal community agrees that the two are definitely in tension, as evidenced by the fact that antitrust laws carve out many exceptions for patent holders.[32] Notwithstanding this tension, some experts contend that the legal theories undergirding patent law and antitrust law can be reconciled.[33] Both serve the utilitarian purpose of benefitting the public, whether by protecting consumers in antitrust law or by

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[29] To bring an antitrust claim, a private party must have been "injured in his business or property by reason of anything forbidden in the antitrust laws." 15 U.S.C. § 15 (2006).

[30] *See* Thomas Cheng, *Putting Innovation Incentives Back in the Patent-Antitrust Interface*, 11 NW. J. TECH. & INTELL. PROP. 385, 386 (2013).

[31] *See id*.

[32] Traditionally, patent law has provided immunity from antitrust liability, so long as the patent holder acts within the scope of his patent. William J. Newsom, *Exceeding the Scope of the Patent: Solving the Reverse Payment Settlement Problem through Antitrust Enforcement and Regulatory Reform*, 1 HASTINGS SCI. AND TECH. L.J. 201, 201 (2009); *see also In re* Tamoxifen Citrate Antitrust Litig., 429 F.3d 370, 392 (2d Cir. 2005).

[33] Atari Games Corp. v. Nintendo of Am., 897 F.2d 1572, 1576 (Fed. Cir. 1990); *see also* R. Hewitt Pate, *Refusals to Deal and Intellectual Property Rights*, 10 GEO. MASON L. REV. 429, 429 (2002) (Stating that "[i]ntellectual property and antitrust laws share a common objective—to encourage innovation industry, and competition.").

ensuring widespread access to innovation in patent law.[34] Moreover, while patents are sometimes construed as "limited monopolies," they do not necessarily grant the patent holder monopoly power in any market.[35] Most products incorporate hundreds, if not thousands, of inventions, each covered by a patent.[36] Thus, any single patent would be unlikely to cover all aspects of the product and likely could not be used to exclude all competitors from the market for that product. Patents, therefore, generally do not result in a monopoly in practice, and in turn do not necessarily conflict with antitrust law's anti-monopoly provisions.[37]

In the pharmaceutical industry, however, each new drug is usually only covered by a small number of patents, with some drugs relying on just a single patent for protection.[38] Any

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[34] *See* Hovenkamp, *supra* note 5; *see also* Cheng, *supra* note 31, at 408.

[35] Illinois Tool Works, Inc., v. Indep. Ink, Inc., 547 U.S. 28 (2006); *see also* Robert D. Gunderman and John M. Hammond, *What is a Patent? The Limited Monopoly*, THE ROCHESTER ENGINEER, Dec. 2005, http://www.patent-innovations.com/documents/200512LimitedMonopoly-WhatisaPatent.pdf.

[36] J. Strother Moore, *Industrially Sponsored University Research in Information Technology: Some Recommendations Regarding Intellectual Property Agreements*, THE UNIVERSITY OF TEXAS AT AUSTIN (Oct. 1, 2002), *available at* http://www.cs.utexas.edu/users/moore/publications/ip-memo.pdf.

[37] Dale B. Halling, *The Myth that Patents are a Monopoly*, STATE OF INNOVATION (May 31, 2009, 06:35 AM), http://hallingblog.com/the-myth-that-patents-are-a-monopoly/ (explaining that patents only grant a negative right to exclude, not the right to sell, so there is not necessarily a monopoly when a patent exists).

[38] Claude Barfield & John E. Calfee, *Patents Pending*, THE AMERICAN (Feb. 2008), *available at* http://www.american.com/archive/2008/january-february-magazine-contents/patents-pending (noting that a small number of patents can provide the foundation for years of research and development in the pharmaceutical industry).

single pharmaceutical patent is much more likely to cover most (if not all) aspects of a drug product, and therefore could be used to exclude all competitors from the market for that product. Pharmaceutical patents thus often result in an effective monopoly for brand-name manufacturers.[39] Additionally, most new drugs are covered by other forms of market exclusivity recognized by the Food, Drug, and Cosmetic Act (FDCA), regardless of whether a patent exists.[40] These industry-specific circumstances make the tension between antitrust law and patent law particularly acute in the pharmaceutical industry.[41] Consequently, some commentators argue that actions by pharmaceutical patent holders that hinder generic competition should be closely examined for possible antitrust violations.[42]

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[39] *Id.*

[40] These additional forms of exclusivity include: (i) 5-year New Chemical Entity Exclusivity; (ii) 3-year new clinical investigation exclusivity for an original NDA; (iii) 3-year new clinical investigation exclusivity for a supplemental NDA; (iv) 10-year window exclusivity; (v) 2-year window exclusivity; (vi) 5-year Generating Antibiotic Incentives Now Act exclusivity; (vii) 6-month pediatric exclusivity; (viii) 5-year enantiomer exclusivity; (ix) QI Act antibiotic exclusivity; (x) 180-day generic drug exclusivity; (xi) 7-year orphan drug exclusivity. Kurt Karst, *FDA Law Blog's 30 for 30 Hatch-Waxman 30th Anniversary Trivia: The Answers*, FDA LAW BLOG (Sept. 23, 2014), http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2014/09/our-30-for-30-hatch-waxman-30th-anniversary-trivia-the-answers.html. Note that if the new drug is also covered by a patent, some of these additional forms of exclusivity run coextensive with patent terms, while others (such as pediatric exclusivity) are added on at the end of the patent term. However, since patents usually run longer than most of these exclusivity terms, having a patent is often just a way to extend an NDA holder's exclusivity term.

[41] Avery, *supra* note 26, at 172; Hovenkamp, *supra* note 5.

[42] Avery, *supra* note 26, at 172.

A. The Role of Generic Drug Manufacturers in the Pharmaceutical Industry

Drugs are regulated by a complex framework codified in the FDCA and enforced by the FDA.[43] In 1984, the Hatch-Waxman Act amended the FDCA to prescribe the process for pharmaceutical manufacturers to file an Abbreviated New Drug Application (ANDA) to expedite approval of a generic drug.[44] Under Hatch-Waxman, the first generic manufacturer to file an ANDA with a Paragraph IV certification for a particular drug is rewarded with 180 days of exclusive rights to market its copy of the brand-name drug.[45] However, this process subjects the generic challengers to patent infringement liability, and the brand-name manufacturer will almost always sue the generic challenger.[46] These lawsuits often settle, and result in reverse-payment settlements, where the pioneer pays the generic competitor millions of dollars to delay market entry.[47] In recent years, reverse-payment settlements have come under scrutiny for potentially violating the antitrust laws.[48] This section will describe the legislative history of the Hatch-Waxman Act, detail Paragraph IV challenges, and explain why reverse-payment settlements are problematic.

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[43] 21 U.S.C. § 301 et seq. (2012).
[44] Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 [hereinafter *Hatch-Waxman Act* or *Hatch-Waxman*] (codified as amended at 35 U.S.C. §§ 271(e), 156 (2012) and 21 U.S.C. § 355(j)).
[45] 21 U.S.C. § 355(j)(5)(B)(iv).
[46] 35 U.S.C. § 271(e)(2)(A) ("It shall be an act of infringement to submit . . . an [ANDA] for a drug claimed in a patent or the use of which is claimed in a patent . . . .").
[47] FTC v. Actavis, Inc., 133 S. Ct. 2223, 2227 (2013).
[48] *See* Hovenkamp, *supra* note 6.

B. Legislative History of the Hatch-Waxman Act

Before marketing a new prescription drug, a pioneer pharmaceutical company must conduct extensive testing on its drug to obtain marketing approval from the FDA.[49] The pharmaceutical company must conduct clinical human trials to generate data on the drug's safety, efficacy, pharmacology, and toxicology.[50] At that point, the pioneer can file a New Drug Application (NDA), which must include "detailed reports of all animal studies and clinical testing done with the drug, reports of any adverse reactions, and any other pertinent information from worldwide scientific literature."[51]

After the pioneer drug is approved by the FDA, a generic drug manufacturer can obtain similar marketing approval through the use of streamlined "piggybacking" procedures.[52] Pursuant to the Hatch-Waxman Act, the generic can file an ANDA specifying that the generic drug is bioequivalent to and has the same active ingredient and basic pharmacokinetics as its name-brand counterpart.[53] Critically,

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[49] *See* 21 U.S.C. § 355(a) ("No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application . . . is effective with respect to such drug.").

[50] 21 C.F.R. § 312.23 (2013).

[51] Pennington Parker Landen, *Federal Preemption and the Drug Industry: Can Courts Co-Regulate?*, 43 FOOD DRUG COSM. L.J. 85, 100 (1988); *see also* 21 U.S.C. § 355(a)-(b); 21 C.F.R. § 314.50 (2013).

[52] James Brett, *Committee Update: Supreme Court Rules for Generic Drug Manufacturers*, THE NEW ENGLAND COUNCIL (Apr. 19, 2012), http://newenglandcouncil.com/assets/HC-Update-04-19-12.pdf (describing ANDAs as "piggybacking" on brands' NDAs).

[53] 21 U.S.C. § 355(j)(2)(A)(ii)-(iv). A generic drug is bioequivalent to a listed drug if the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed

the generic applicant is not required to provide independent proof of safety and efficacy, and can instead rely on the pioneer's clinical trial data.[54] The Hatch-Waxman scheme ensures the quality of generic drugs, simplifies the generic approval process, eliminates duplicative research costs associated with clinical trials, and accelerates consumer access to affordable drugs.[55]

Prior to the Hatch-Waxman Act, generic drug manufacturers had to satisfy the same safety and efficacy requirements as new drug applicants before obtaining marketing approval.[56] Generic manufacturers could not use the data from the approved NDA, and were forced instead to conduct their own costly and duplicative clinical trials.[57] This requirement proved unfeasible for many generic manufacturers

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drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses. *Id.* at § 355(j)(8)(B).

[54] 21 U.S.C. § 355(j)(2)(A).

[55] *See* Requirements for Submission of In Vivo Bioequivalence Data, 68 Fed. Reg. 61,640, 61,645 (proposed Oct. 29, 2003) (to be codified at 21 C.F.R. pts. 314 & 320) (reporting estimates of ANDA preparation and filing costs between $300,000 and $1,000,000); Thomas Chen, Note, *Authorized Generics: A Prescription for Hatch-Waxman Reform*, 93 VA. L. REV. 459, 464 (2007); H.R. REP. NO. 98-857 (1984) (explaining that a primary purpose of the Hatch-Waxman Act is to foster competition in the pharmaceutical industry, and thereby increase access to affordable drugs, by expediting generic entry); *see also* FDA, Office of Generic Drugs Home Page, http://www.fda.gov/drugs/resourcesforyou/consumers/questionsanswers/ucm100100.htm (last visited May 20, 2014) (explaining that "[a]lthough generic drugs are chemically identical to their branded counterparts, they are typically sold at substantial discounts from the branded price.").

[56] Avery, *supra* note 26, at 174 (citation omitted).

[57] *Id.*

and deterred them from seeking marketing approval.[58] As a result, pioneer drug manufacturers faced very little competition and were able to essentially monopolize the market, even after their patents expired, to the arguable detriment of consumers.[59] The Hatch-Waxman Act sought to rectify this inequity by expediting generic drug entry into the pharmaceutical market.[60]

It is important to note that obtaining FDA approval is quite different from obtaining a patent. FDA approval of a new drug confers exclusive marketing rights to a pioneer drug company.[61] On the other hand, patents conferring limited exclusion power can be granted anywhere along the development lifeline of a drug—before, concurrently with, or even after NDA approval.[62] While not all FDA-approved drugs are patented, pioneers almost always seek patents for their drugs to protect their inventions and ensure they can recover the exorbitant losses incurred during research and development.[63]

C. Paragraph IV Certifications

The Hatch-Waxman Act also sets forth special procedures for resolving patent-related disputes.[64] When filing

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[58] *Id.*
[59] *Id.* at 175 (explaining that "before the Hatch-Waxman Act was passed, the FDA estimated there were approximately 150 brand-name drugs on the market with expired patents but not generic equivalents.") (citation omitted).
[60] H.R. REP. NO. 98-857.
[61] FDA, U.S. Dept. of Health and Human Services Homepage, http://www.fda.gov/Drugs/DevelopmentApproval Process/ucm079031.htm (last visited May 20, 2014).
[62] *Id.*
[63] Avery, *supra* note 26, at 171 (citation omitted).
[64] *Id.* at 176.

an ANDA, the generic manufacture must make one of the following certifications for each patent covering the pioneer's brand-name drug: (I) that the pioneer drug is not patented or that patent information has not been filed; (II) that the patent has expired; (III) that the patent will expire on a specified date, and the generic drug will not enter the market until that date passes; or (IV) that the patent is invalid or will not be infringed by the manufacture, use, or sale of the generic drug in question.[65] These are commonly referred to as Paragraph I, II, III, and IV certifications, respectively.

A Paragraph IV filing, which is the most common way for generics to challenge the patents of brand-name manufacturers, automatically constitutes patent infringement, and the patentee has forty-five days to file suit after receiving notice of the application.[66] If an infringement action is not filed within that time, the FDA may issue final approval of the ANDA immediately.[67] However, if suit is brought during the forty-five day window, the FDA is barred from approving the ANDA for thirty months.[68] This special feature of the Hatch-Waxman Act is called the "thirty-month stay" and was designed to protect NDA holders with valid drug patents.[69] During the stay, the FDA can only tentatively approve the ANDA, which then can become effective immediately upon expiration of the stay.[70] Consequently, the patentee typically

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[65] *Id.*; *see also* 21 U.S.C. § 355(j)(2)(A)(vii)(I)-(IV).
[66] 35 U.S.C. § 271(e)(2)(A) ("It shall be an act of infringement to submit . . . an [ANDA] for a drug claimed in a patent or the use of which is claimed in a patent . . . .").
[67] 21 U.S.C. § 355(j)(5(B)(iii).
[68] *Id.*
[69] H.R. REP. NO. 98-857, pt. I, at 28.
[70] 21 U.S.C. § 355(j)(5)(B)(iv)(II)(dd).

does not face generic competition while the infringement suit is in progress.[71]

The 180-day marketing exclusivity period is a second special feature of the Hatch-Waxman Act invoked by a Paragraph IV challenge.[72] Under this provision, the first generic to file a Paragraph IV ANDA is granted 180 days of market exclusivity.[73] The exclusivity period is triggered by the first commercial marketing of the drug by the first ANDA applicant.[74] The FDA will not approve later-filed ANDAs for the same drug until the exclusivity period expires.[75] Therefore, the first filer's copy will be the only generic on the market for 180 days, allowing it to charge a substantially higher price than if multiple generics were on the market.[76] By rewarding first filers for undertaking the costs and risks of patent litigation, the marketing exclusivity period therefore incentivizes generic manufacturers to challenge suspect FDA-approved, patented drugs.[77] Indeed, the very purpose of the exclusivity period is to

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[71] H.R. REP. NO. 98-857, pt. I, at 28.
[72] 21 U.S.C. § 355(j)(5)(A)-(B).
[73] 21 U.S.C. § 355(j)(5)(B)(iv).
[74] 21 U.S.C. § 355(j)(5)(B)(iv).
[75] Avery, *supra* note 26, at 178.
[76] *Id.*
[77] *Id.*; *see also* Janssen Pharmaceutica, N.V. v. Apotex, Inc., 540 F.3d 1353, 1357 (2008) (explaining that "Congress decided to give generic pharmaceutical companies a 180-day exclusivity period as an incentive to challenge suspect Orange Book listed patents."); *see also* Diane E. Bieri, *Implications of FTC v. Actavis: A Reasonable Approach to Evaluating Reverse Payment Settlements*, 15 MINN. J.L. SCI. & TECH. 135, 141 (2014) (demonstrating the efficacy of the market exclusivity period at incentivizing patent challenges—a generic will file a Paragraph IV challenge even if it believes it only has a three percent chance of success).

encourage Paragraph IV filings, and thereby spur generic competition to increase the availability of low-cost drugs.[78]

D. The Problem of Reverse-Payment Settlements

Paragraph IV challenges frequently result in a phenomenon called "reverse-payment settlements" that highlight the tension between antitrust law and patent law.[79] In these agreements, the pioneer will typically pay the generic competitor millions of dollars to delay production of the generic drug until a later date (often until right before the pioneer drug's patent expires).[80] They are called "reverse-payments" because they involve payments from the patent holder to the alleged infringer (i.e., the generic challenger).[81] Occurring almost exclusively in the pharmaceutical industry,

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[78] Purepac Pharm. Co. v. TorPharm, Inc., 354 F.3d 877, 879 (D.C. Cir. 2004) ("In order to encourage paragraph IV challenges, thereby increasing the availability of low-cost generic drugs, . . . [the first Paragraph IV ANDA filer] has the right to sell its drug without competition [from other generic entrants] for 180 days."); *see also* C. Scott Hemphill, *Paying for Delay: Pharmaceutical Patent Settlement as a Regulatory Design Problem*, 81 N.Y.U. L. REV. 1553, 1605 (2006) (noting the importance of the 180-day exclusivity period for decreasing the free-rider problem and concomitantly incentivizing challenges of Orange Book-listed patents).

[79] Anne-Marie C. Yvon, *Settlements Between Brand and Generic Pharmaceutical Companies: A Reasonable Antitrust Analysis of Reverse Payments*, 75 FORDHAM L. REV. 1883, 1885 (2006).

[80] FTC V. Actavis, Inc., 133 S. Ct. 2223, 2227; Matthew Avery & Mary Nguyen, *The Roadblock for Generic Drugs: Declaratory Judgment Jurisdiction for Later Generic Challengers*, 15 N.C. J.L. & TECH. 1, 8-9 (2013).

[81] *Actavis*, 133 S. Ct. at 2227. More derisively, these types of settlements are often referred to as "pay-for-delay" settlements by politicians and other critics of the practice.

reverse-payment settlements were formed in record numbers in fiscal year 2012.[82]

Reverse-payment settlements, also known as pay-for-delay settlements, have been widely criticized as clear efforts to thwart competition in the pharmaceutical markets.[83] These agreements enable pioneers to circumvent the trigger of the 180-day market exclusivity period and thereby keep generics off the market.[84] By strategically sharing their monopoly profits with generic challengers, patentees can avoid competition and drive up the prices of their products.[85] Moreover, reverse-payment settlements create a roadblock to generic entry.[86] When the first filer settles instead of entering the market, the 180-day exclusivity period is never triggered; as a result, other generics also never enter the market because the FDA cannot approve later-filed ANDAs.[87] The Federal Trade Commission (FTC) estimates that reverse-payment settlements cost drug consumers about $3.5 billion per year.[88] Some scholars contend that antitrust laws can effectively

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[82] Press Release, Federal Trade Commission, FTC Study: In FY 2012, Branded Drug Firms Significantly Increased the Use of Potential Pay-for-Delay Settlements to Keep Generic Competitors off the Market (Jan. 17, 2013), http://www.ftc.gov/news-events/press-releases/2013/01/ftc-study-fy-2012-branded-drug-firms-significantly-increased.

[83] Newsom, *supra* note 32, at 201.

[84] Avery, *supra* note 26, at 181 (citing Holly Soehnge, *The Drug Price Competition and Patent Term Restoration Act of 1984: Fine-Tuning the Balance Between the Interests of Pioneer and Generic Drug Manufacturers*, 58 FOOD & DRUG L.J. 51, 74 (2003)).

[85] *Id.*

[86] *Id.*

[87] *Id.*

[88] FTC v. Watson Pharms., Inc., 677 F.3d 1298, 1302 (11th Cir. 2012).

remedy this consumer harm, a possibility that was addressed by the Supreme Court in *Actavis*.[89]

In response to the antitrust litigation spawned by the reverse-payment loophole described above, the FTC initiated a study to examine whether the Hatch-Waxman 180-day market exclusivity provision facilitated anti-competitive behavior.[90] The FTC released its report in July 2002 and recommended that the Hatch-Waxman Act be amended to require pioneer drug companies to inform the Department of Justice and the FTC of any agreements relating to the manufacture, marketing, or sale of a generic drug, or to the 180-day market exclusivity.[91]

Responding to the FTC study and pressure from the Executive Branch,[92] in 2003 Congress amended the FDCA by enacting the Medicare Prescription Drug, Improvement, and Modernization Act (MMA) in order to, *inter alia*, curb the abuse of the 180-day exclusivity period.[93] In particular, Congress added provisions whereby the first Paragraph IV ANDA applicant will forfeit its rights to the 180-day exclusivity period if a specified "forfeiture event" occurs.[94]

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[89] Newsom, *supra* note 32, at 201.
[90] FED. TRADE COMM'N, GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY, at i (July 2002) (reporting challenges involving 130 drugs between 1984 and 2000).
[91] *Id.* at vi.
[92] *See* President George W. Bush, Remarks by the President on Prescription Drugs (Oct. 21, 2002), *available at* http://whitehouse.gov/news/releases/2002/10/print/20021021-2.html (proposing new FDA regulations to expedite generic drug approvals).
[93] Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (2003) [hereinafter *Medicare Modernization Act* or *MMA*] (effective Dec. 8, 2003).
[94] *See* 21 U.S.C. § 355(j)(5)(D).

And in an attempt to thwart possible anticompetitive settlements between pioneers and generic challengers, the MMA also provides that most settlement agreements between a patent holder and a Paragraph IV ANDA applicant must be filed with both the Federal Trade Commission and the Department of Justice.[95]

Unfortunately, these provisions of the MMA proved to be almost completely ineffective at closing others, and failed to address some abuses altogether.[96] The forfeiture provisions state that the first filer's 180-day exclusivity is lost if, *inter alia*, there is a "failure to market" event.[97] But this "failure to market" provision is almost never triggered because all elements of the complicated provision are not satisfied by the typical reverse-payment settlement.[98] As for the reporting requirement, Congress incorrectly assumed that the FTC would be able to stop pay-for-delay settlements.[99] Instead, this harmful practice proceeded unabated in light of a split among the federal circuit courts of appeals on whether such payments were antitrust violations.[100] Two circuits allowed reverse-payment settlements absent direct evidence of patent invalidity

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[95] *Id.* § 1112.
[96] Avery, *supra* note 26, at 188.
[97] *Id.* § 355(j)(5)(D)(i)-(ii).
[98] Avery et al., *supra* note 80, at 10.
[99] Avery, *supra* note 26, at 190.
[100] *See* FED. TRADE COMM'N, AGREEMENTS FILED WITH THE FEDERAL TRADE COMMISSION UNDER THE MEDICARE PRESCRIPTION DRUG, IMPROVEMENT, AND MODERNIZATION ACT OF 2003: SUMMARY OF AGREEMENTS FILED IN FY 2007 2 (2008), *available at* https://www.ftc.gov/reports/agreements-filed-federal-trade-commission-under-medicare-prescription-drug-improvement-3 (finding that forty-two percent of settlement agreements between pioneers and generic manufacturers during fiscal year 2007 included some form of reverse payment).

or infringement,[101] while other circuits have deemed such settlements *per se* illegal.[102] In light of these decisions, the general rule seemed to be that for a reverse-payment settlement to be found legal, its terms must stay within the scope of the patent—that is, the settlement must not extend the patent holder's monopoly beyond the normal patent term.[103] In response, the FTC brought cases in an effort to create a split among the circuits and thereby force review by the U.S. Supreme Court, which was eventually granted in the case of *FTC v. Actavis*.[104]

III. FEDERAL TRADE COMMISSION V. ACTAVIS: A BRIEF REVIEW

In *Actavis*, the Supreme Court held that reverse-payment settlement agreements may violate the antitrust laws

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[101] *See In re* Tamoxifen Citrate Antitrust Litig., 466 F.3d 187, 187 (2d Cir. 2006), *cert. denied sub nom.* Joblove v. Barr Labs, Inc., 127 S. Ct. 3001 (2007); Schering-Plough Corp. v. FTC, 402 F.3d 1056, 1076 (11th Cir.), *cert. denied* 126 S. Ct. 2929 (2005); Valley Drug Co. v. Geneva Pharm., Inc., 344 F.3d 1294, 1304, 1312-13 (11th Cir. 2003), *cert. denied*, 543 U.S. 939 (2004).

[102] *See In re* Cardizem CD Antitrust Litig., 332 F.3d 896, 908 (6th Cir. 2003), *cert. denied sub nom.* Andrx Pharms., Inc. v. Kroger Co., 543 U.S. 939 (2004); Andrx Pharms., Inc. v. Biovail Corp. Int'l, 256 F.3d 799, 809-12 (D.C. Cir. 2001) (dicta), *cert. denied*, 535 U.S. 931 (2002).

[103] Yana Pechersky, Note, *To Achieve Closure of the Hatch-Waxman Act's Loopholes, Legislative Action Is Unnecessary: Generic Manufacturers Are Able to Hold Their Own*, 25 CARDOZO ARTS & ENT. L.J. 775, 795 (2007).

[104] *See* Avery, *supra* note 26, at 190; SETH SILBER, CLIENT ALERT: FTC SUES CEPHALON FOR "REVERSE PAYMENT" PATENT SETTLEMENTS WITH FOUR GENERIC PHARMACEUTICAL FIRMS 4 (2008), http://www.wsgr.com/publications/pdfsearch/clientalert_cephalon.pdf.

under a holistic "rule of reason" analysis.[105] The Court rejected both the traditional scope-of-the-patent test, which made most reverse-payment settlement agreements presumptively lawful, and the FTC's proposal to make such settlements presumptively unlawful.[106] Instead, the Court took the middle ground and held that courts reviewing such agreements should apply the rule of reason, but left it to the lower courts to determine what types of settlements would actually be antitrust violations.[107]

The defendants in the case included brand-name manufacturer Solvay Pharmaceuticals and several generic drug manufacturers who had formed reverse-payment settlements.[108] In 2003, Solvay obtained a patent for AndroGel (testosterone gel), a blockbuster therapy for treating low testosterone.[109] Shortly thereafter, generic manufacturers Actavis and Paddock filed ANDAs seeking FDA approval to sell a generic version of AndroGel and certified under Paragraph IV that Solvay's patent was invalid and that their generic version did not infringe it.[110] In response, Solvay sued Actavis and Paddock for patent infringement.[111]

The FDA eventually approved Actavis's first-to-file generic product, but instead of bringing its drug to market, Actavis entered into a reverse-payment settlement with Solvay.[112] Under the terms of the settlement, Actavis agreed to

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[105] FTC v. Actavis, Inc., 133 S. Ct. 2223, 2238 (2013).
[106] *Id.*
[107] *Id.*
[108] *Id.* at 2229.
[109] *Id.*
[110] *Id.*
[111] *Id.*
[112] *Id.* at 2230.

not market its generic drug until August 31, 2015, sixty-five months before Solvay's patent expired.[113] Additionally, Actavis agreed to promote brand-name AndroGel to urologists.[114] Two other generics, Paddock and Par Pharmaceuticals, formed similar agreements with Solvay.[115] In exchange for delaying market entry, Solvay agreed to pay millions of dollars to each generic—$12 million in total to Paddock, $60 million in total to Par, and an estimated $19-$30 million annually for nine years to Actavis.[116]

In January 2009, the FTC filed suit against Solvay and the generics, alleging that the companies engaged in anticompetitive behavior in violation of both the Sherman Act and the FTC Act.[117] The District Court dismissed the FTC's complaint, finding no antitrust violation.[118] On appeal, the Eleventh Circuit affirmed, opining that "absent sham litigation or fraud in obtaining a patent, a reverse-payment settlement is immune from antitrust attack so long as its anticompetitive effects fall within the scope of the exclusionary potential of the patent."[119] This reasoning describes the so-called scope-of-the-patent approach endorsed by most federal courts at the time.[120] The Eleventh Circuit ruled that patent holders are exempt from

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[113] *Id.*
[114] *Id.*
[115] *Id.* at 2229.
[116] *Id.*
[117] *Id.* at 2230 (stating that the FTC alleged that respondents violated section 5 of the FTC Act by "unlawfully agreeing to abandon their patent challenges, to refrain from launching their low-cost generic drugs, and to share in Solvay's monopoly profits."); *See* 15 U.S.C. §§ 1, 45.
[118] *In re* Androgel Antitrust Litigation (No. II), 687 F. Supp. 2d 1371, 1382 (N.D. Ga. 2010).
[119] FTC v. Watson Pharms., 677 F.3d 1298, 1312 (11th Cir. 2012).
[120] FTC v. Actavis, Inc., 133 S. Ct. 2223, 2230.

the antitrust principle that typically proscribes agreements where one company pays a competitor to delay market entry.[121] The presence of a patent, the court reasoned, confers a lawful right to exclude others from the market.[122] Further, this holding was consistent with the public policy favoring settlement over litigation.[123]

On June 17, 2013, the Supreme Court reversed the Eleventh Circuit's holding in a 5-3 decision.[124] The majority opinion by Justice Breyer declined to find reverse-payment settlements presumptively illegal, but ruled that the FTC could not be prevented from bringing an antitrust suit against the defendants.[125] Reverse-payment settlements were found to pose a "potential for genuine adverse effects on competition," and thus may sometimes violate antitrust laws.[126] In rejecting the scope-of-the-patent test, the Court noted that "patent and antitrust policies are both relevant in determining the 'scope of the patent monopoly'—and consequently antitrust law immunity—that is conferred by a patent."[127] The Court further suggested that the public interest in accessibility to affordable drugs outweighed the Eleventh Circuit's policy argument favoring settlement.[128] In a dissent that will be further discussed in Part IV.A, *infra*, Chief Justice Roberts endorsed the scope-of-the-patent test[129] and expressed concern that the

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[121] *Id.*
[122] *Id.*
[123] *Id.*
[124] *Id.* at 2238 (Justice Alito took no part in the case).
[125] *Id.* at 2227.
[126] *Id.* at 2234.
[127] *Id.* at 2231.
[128] *Id.* at 2237.
[129] *Id.* at 2238 (Roberts, C.J., dissenting) (explaining that a patent "provides an exception to antitrust law, and the scope of the patent—*i.e.*, the rights

majority opinion may have detrimental effects on generic competition.[130]

Importantly, *Actavis* deviates sharply from prior antitrust cases and creates a new path to liability for generics and pioneers alike.[131] Moving forward, reverse-payment settlements will face heightened antitrust scrutiny, and must survive the multi-factored rule-of-reason analysis to remain valid.[132] This suggests that a settlement will only be legal to the extent that patent law policy disfavoring competition offsets antitrust law policy favoring competition.[133] Perhaps the single most important factor in this analysis is the size and scale of the payment in relation to the patentee's anticipated litigation costs.[134] According to the Court, a massive payment may signify a weak patent that will likely be invalidated in litigation.[135] Other factors indicating anticompetitive effects

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conferred by the patent—forms the zone within which the patent holder may operate without facing antitrust liability.").

[130] *Id.* at 2247 (Roberts, C.J., dissenting) ("The irony of this all is that the majority's decision may very well discourage generics from challenging pharmaceutical patents in the first place.").

[131] Mark Botti & Jessica Hoke, *Redefining the Border between Intellectual Property and Antitrust: Implications of* FTC v. Actavis, BLOOMBERG BNA (2013), http://www.bna.com/redefining-the-border-between-intellectual-property-and-antitrust/ ("Fundamentally, the majority's move away from the scope of the patent test towards a more antitrust-focused analysis will impact not only reverse-payment settlements, but may shape other significant antitrust issues involving intellectual property.").

[132] *Actavis*, 133 S. Ct. at 2236.

[133] *Id.* (explaining that traditional antitrust factors to consider in the rule-of-reason approach include likely anticompetitive effects, redeeming virtues, market power, and potentially offsetting legal considerations present in the circumstances).

[134] *Id.*

[135] *Id.* (explaining that an excessively large payment can serve as a "workable surrogate" for the patent's weakness).

include the settlement's "independence from other services for which it might represent payment" and the "lack of any other convincing [procompetitive] justification."[136] However, *Actavis* failed to provide any useful guidance for how to apply these factors, instead leaving it to lower courts to create a workable process for evaluating reverse-payment settlements.[137]

IV. CRITIQUE OF *ACTAVIS*: AN EMPIRICAL STUDY

Chief Justice Roberts's dissent to *Actavis* voiced, among other issues, his concern that the majority's decision may have unintended anticompetitive effects in the pharmaceutical industry.[138] This Article investigates the validity of this argument by collecting data on the number of Paragraph IV challenges filed since *Actavis*.[139] Data compiled from the FDA's website reveals that the number of ANDAs filed with Paragraph IV certifications has increased in the twelve months since *Actavis*, as compared to filings in the preceding four years.[140] These empirical findings are a leading indicator that, contrary to Chief Justice Roberts's dissent, generic competition appears to have actually accelerated in the

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[136] *Id.* at 2237.
[137] *Id.* at 2238.
[138] *Id.* at 2247 (Roberts, C.J., dissenting).
[139] *Id.* Note that it is beyond the scope of this Article to analyze all points raised in Chief Justice Roberts's dissent.
[140] *See* Appendix 1; *Paragraph IV Patent Certifications*, U.S. FOOD AND DRUG ADMINISTRATION (April 21, 2014), http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/UCM293268.pdf [hereinafter *FDA, Paragraph IV Database*].

wake of the *Actavis* decision.[141] While more Paragraph IV challenges are being filed, it is not clear whether more generic drugs are actually entering the market.[142] Nonetheless, the increase in Paragraph IV filings suggests that generics are at least attempting to compete and that their incentive to challenge pioneers' patents has grown. In the long run, this may increase consumer access to affordable drugs, but also may threaten pioneers' incentives to make the massive investments necessary to identify, develop, and test new drugs candidates.[143]

A. Chief Justice Roberts's Dissent to *Actavis*

In a vigorous dissent to *Actavis*, Chief Justice Roberts suggested that heightened antitrust scrutiny could actually hurt rather than encourage competition.[144] He reasoned that generic companies are sensitive to the costs and risks of litigation, and consequently generics may be unwilling to face such risks if the prospect of being paid millions in reverse-payment

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[141] A "leading indicator" is one that signals a future event. *What Are Leading, Lagging, and Coincident Indicators? What Are They for?*, INVESTOPEDIA (Feb. 26, 2009), http://www.investopedia.com/ask/answers/177.asp.

[142] Note that it is not clear whether more generic drugs are actually entering the market after *Actavis* because, on average, the FDA takes about thirty-six months (3 years) to approve an ANDA, and only about twenty-four months have lapsed since *Actavis*. Bob Pollock, *June Approval Times for ANDAs – A Snapshot in Time*, LACHMAN CONSULTANTS (Aug. 19, 2013), http://www.lachmanconsultants.com/june-approval-times-for-andas-a-snapshot-in-time.asp.

[143] Purepac Pharm. Co. v. TorPharm, Inc., 354 F.3d 877, 879 (D.C. Cir. 2004) (explaining the importance of Paragraph IV challenges in increasing the availability of low-cost generic drugs).

[144] *Actavis*, 133 S. Ct. at 2247 (Roberts, C.J., dissenting).

settlements is taken away.[145] Although no generic manufacturer has expressly admitted this, given the uncertainty and complexity of litigation, it is likely safe to assume that the promise of handsome settlements played some role in incentivizing generic challenges.[146] However, *Actavis* makes it far more difficult to form valid reverse-payment settlements by subjecting these agreements to greater antitrust scrutiny.[147] Chief Justice Roberts postulated that the decision, therefore, may discourage generics from challenging pioneers' patents in the first place.[148] In a press release on *Actavis*, the Generic Pharmaceutical Association (GPhA) echoed a similar concern: "[T]he Court's ruling will require generic companies to take on a greater administrative burden to pursue a patent challenge, potentially lowering the number of challenges. As a result, consumers may have access to fewer generic options."[149]

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[145] *Id.* (stating that generics enter the "risky terrain" of litigation "only after careful analysis of the potential gains if they prevail and the potential exposure if they lose." (internal quotation marks omitted) (citation omitted)). Although beyond the scope of this paper, Chief Justice Roberts's theory that generic companies are particularly sensitive to the costs of litigation seems deeply flawed. Actavis is a global pharmaceutical manufacturer with a market capitalization of $67 billion and selling over 300 different generic drugs in the United States. The possibility of losing a few million dollars in an ANDA lawsuit is likely a *de minimis* risk for this generic giant.

[146] *Id.*

[147] *See id.* at 2223.

[148] *Id.* at 2247 (Roberts, C.J., dissenting).

[149] Kurt R. Karst, *Supreme Court Rules in Androgel Patent Settlement Agreement Case; Holds that Agreements are Subject to Antitrust Scrutiny, but Not Presumptively Unlawful*, FDA LAW BLOG (June 17, 2013), http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2013/06/supreme-court-rules-in-androgel-patent-settlement-agreement-case-holds-that-agreements-are-subject-t.html.

B. *Actavis* May Encourage Generics to File Paragraph IV Challenges

This independent empirical study investigates whether *Actavis* has in fact discouraged generics from challenging pharmaceutical patents per Chief Justice Roberts's prediction. Specifically, the Authors investigated whether the number of first-filed Paragraph IV challenges has decreased since *Actavis* was decided on June 17, 2013. The study uses publicly-disclosed records from the FDA's database of Paragraph IV filings, which lists the filing dates of every first-filed Paragraph IV challenge received by the Office of Generic Drugs (OGD) since March 2004.[150] These filing dates were collected and analyzed to determine the total number of Paragraph IV challenges filed in the twelve months since *Actavis*, as compared to filings in the four preceding twelve-month intervals.[151] This Article assumes that the number of ANDAs filed with Paragraph IV certifications is a reliable metric for the

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[150] The FDA lists only one first-filer of a "substantially complete" Paragraph IV certification for a particular drug; therefore, this study does not include data on multiple first-filers or any later filers of Paragraph IV ANDAs. *Paragraph IV Patent Certifications*, U.S. FOOD AND DRUG ADMINISTRATION (Jan. 20, 2015), http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm047676.htm. Also note that the FDA does not disclose the identity of the first Paragraph IV applicant for confidentiality reasons. Bob Pollock, *OK, What's Going on Here?*, LACHMAN CONSULTANTS (Feb. 12, 2013), http://www.lachmanconsultants.com/ok-whats-going-on-here.asp (explaining that the creation of the Paragraph IV Database was a "compromise solution" that maintains the confidentiality of the applicant while alerting firms of a first-to-file application's existence).

[151] Note that, at the time of writing, only about nineteen months had passed since the *Actavis* decision, so it was not possible to collect data for a sixth twelve-month interval.

level of generic-pioneer competition in the field.[152] Every Paragraph IV ANDA is inherently a challenge to the pioneer's patent and an effort to increase competition by entering the market prior to patent expiry.[153] Additionally, Paragraph IV filings are a precursor to reverse-payment settlements, and thus decreased reverse-payment settlements should correlate with decreased Paragraph IV filings.[154] Because *Actavis* is expected to reduce the number of reverse-payment settlements, the decision may also affect the number of patent challenges via Paragraph IV ANDAs.[155] The hypothesis is that there will be fewer Paragraph IV challenges after *Actavis* because the decision presumably reduced generics' incentive to file such

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[152] Purepac Pharm. Co. v. TorPharm, Inc., 354 F.3d 877, 879 (D.C. Cir. 2004) (noting that Paragraph IV challenges are linked to increased availability of low-cost generic drugs).

[153] *See id.* (explaining the importance of Paragraph IV challenges in increasing the availability of low-cost generic drugs). Note that patent challenges facilitate competition so long as they do not result in a reverse-payment settlement. *See* Newsom, *supra* note 32.

[154] In other words, if there is a decrease in the number of reverse-payment settlements, we should expect to see a decrease in the number of Paragraph IV challenges. *See Supreme Court Holds that the Use of "Reverse Payment" Settlement Agreements to Resolve Patent Infringement Litigation are Not Exempt from Antitrust Scrutiny*, CHADBOURNE & PARK LLP (June 26, 2013), http://www.chadbourne.com/files/Publication/4e43062e-6aac-49e4-96fa-007d1ca50bc3/Presentation/PublicationAttachment/ce92e4cc-4515-4d76-9c7f-0db3e94c5a8e/Actavis_Reverse_Payment_ca(Evans).pdf.

[155] Zachary Glantz & Jonathan Goddard, *FTC v. Watson Pharmaceuticals, Inc.*, LEGAL INFORMATION INSTITUTE (2012), *available at* http://www.law.cornell.edu/supct/cert/12-416 ("Watson argues that a prohibition on reverse settlements would reduce the number of settlements in general, which in turn would make generic manufacturers, fearing expensive litigation, less likely to attempt to sell generic drugs. Watson contends that such a prohibition would reduce innovation in the pharmaceutical industry.").

challenges by subjecting reverse-payment settlements to heightened antitrust scrutiny.

However, this hypothesis is completely contradicted by the evidence collected from the FDA. The findings of this empirical study indicate an increase in the number of first-filed Paragraph IV challenges in the twelve months since *Actavis*, as compared to filings in preceding twelve-month intervals. [156] In the four-year period leading up to *Actavis*, from June 17, 2009 to June 16, 2013, the total number of Paragraph IV applications steadily declined from ninety-one challenges in the first year down to only fifty-four challenges in the fourth year (see Table 1, below).[157] However, in the twelve months after the decision (June 17, 2013 through June 16, 2014), sixty-five challenges were filed—a twenty percent increase from the previous twelve-month interval.[158]

	Interval 1 6/2009 – 6/2010	**Interval 2 6/2010-6/2011**	**Interval 3 6/2011-6/2012**	**Interval 4 6/2012-6/2013**	**Interval 5 6/2013-6/2014**
Number of First-Filer Paragraph IV Challenges	91	81	55	54	65

Table 1

[156] *FDA, Paragraph IV Database*, *supra* note 140; *see also* Appendix 1, *infra* (displaying a summary of the findings of the empirical study).
[157] *See* Appendices 4-7; *see also* FDA, Paragraph IV Database, *supra* note 140.
[158] *See* Appendix 8; *see also* FDA, Paragraph IV Database, *supra* note 140.

The post-*Actavis* spike observed in Interval 5 is in dramatic contrast with the downward trend in Paragraph IV challenges observed prior to the *Actavis* decision.[159] While this post-decision increase in Paragraph IV filings is not definitive proof, it is compelling evidence that the *Actavis* decision has incentivized generics to challenge pioneers' patents.[160]

C. Refining the Causation Argument

In order to determine whether *Actavis* directly caused the observed increase in Paragraph IV challenges, the Authors analyzed other possible reasons for the uptick. In particular, the increased filings could have also been caused by an increase in the number of new drugs eligible for Paragraph IV challenge in the twelve months after *Actavis*.[161] Under the Hatch-Waxman Act, generic manufactures cannot file a Paragraph IV ANDA seeking to copy a New Chemical Entity (NCE) until four years

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[159] *See* Appendix 1; *see also* FDA, Paragraph IV Database, *supra* note 140.

[160] *See What Are Leading, Lagging, and Coincident Indicators? What Are They for?*, INVESTOPEDIA (Feb. 26, 2009), http://www.investopedia.com/ask/answers/177.asp.

[161] Other factors that may be of interest but are beyond the scope of this Article include: (1) the proportion of Paragraph IV challenges that actually led to patents being invalidated in litigation; and (2) the subject matter of patents that are more likely to be challenged via Paragraph IV. *Supreme Court Hears Oral Argument in "Pay-for-Delay" Patent Settlement Antitrust Case*, MCDERMOTT WILL & EMERY (Mar. 26, 2013), http://www.mwe.com/Supreme-Court-Hears-Oral-Argument-in-Pay-for-Delay-Patent-Settlement-Antitrust-Case-03-26-2013/?PublicationTypes= d9093adb-e95d-4f19-819a-f0bb5170ab6d (discussing Justice Kennedy's concern that "your test is the same for a very weak patent as a very strong patent . . . that doesn't make a lot of sense.") (internal quotation marks omitted).

after the FDA grants marketing approval to the NCE.[162] The general presumption in practice is that most NDAs are for NCEs, as generic companies frequently challenge drugs on the four-year anniversary of the challenged NDA's approval. Therefore, an increase in NDAs approved in the twelve-month interval four years prior to *Actavis* (Interval 1) could account for an increase in Paragraph IV challenges in the twelve months after *Actavis* (Interval 5).

Our research reveals that there was, in fact, an increase in NDA approvals during the relevant time period. During the twelve-month interval four years before the *Actavis* decision (Interval 1), ninety-eight NDAs were approved; in the twelve-month interval five years before *Actavis* (Interval 0), only seventy-four NDAs were approved.[163] Thus, the number of drugs eligible for Paragraph IV challenges increased by 32.4% post-*Actavis*, while the number of Paragraph IV challenges increased by only 20%.[164]

However, upon closer inspection, NDA approvals four years before *Actavis* are not a reliable predictor of Paragraph

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[162] An NCE is a drug that contains no active moiety that has been approved by the FDA in any other application submitted under section 505(b) of the FDCA. 21 U.S.C. § 355(c)(3)(E)(ii), (j)(5)(F)(ii).

[163] *See* Appendix 2 (also showing that eighty NDAs were eligible for Paragraph IV challenge in Interval 3, 115 NDAs were eligible in Interval 2, and eighty-six NDAs were eligible in Interval 1); *see also CDER Drug and Biologic Approvals for Calendar Years 2008 & 2009*, U.S. FOOD AND DRUG ADMINISTRATION (2009), http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/NDAandBLAApprovalReports/ucm373413.htm.

[164] *See* Appendix 3 for a line graph comparing the number of first-filer Paragraph IV challenges to the number of NDAs eligible for Paragraph IV challenge.

IV challenges. If the rise in eligible NDAs was the sole reason for the rise in Paragraph IV filings, all the NDAs challenged by ANDAs listed in Interval 5 would have been approved in Interval 1 (*i.e.*, the twelve-month period four years before Interval 5). This is because we expect that each ANDA filed during Interval 5 should have been filed on the four-year anniversary of the challenged NDA's approval. However, only 17.9% of these NDAs were approved four years before Interval 5.[165] That only a small fraction of the Paragraph IV filings were against newly eligible NDAs suggests that the rise in NDA approvals alone cannot account for the rise in Paragraph IV filings after *Actavis*. Consequently, we can assume that *Actavis* must have been a factor in causing the rise in Paragraph IV filings. Moreover, further research reveals that only a fraction of NDAs are for NCEs.[166] The statutory rule that NDAs can only be challenged four years after approval applies only for NCEs; because most NDAs are not for NCEs, the increase in newly eligible NDAs cannot fully explain the post-*Actavis* spike in Paragraph IV ANDAs.[167]

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[165] Only twelve out of the sixty-seven (17.9%) challenged NDAs were approved within the twelve-month period four years before Interval 5. *See* Appendix 8, sixth column.

[166] In 2009, only 28.9% of NDAs were for New Molecular Entities (NMEs), which include both NCEs and biological entities; in 2010, only 22.6% of NDAs were for NMEs; in 2011, only 30.3% of NDAs were for NMEs. *Summary of NDA Approvals & Receipts, 1938 to the Present*, U.S. FOOD AND DRUG ADMINISTRATION (Jan. 18, 2013), http://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/SummaryofNDAApprovalsReceipts1938tothepresent/default.htm.

[167] This is because our data in Appendix 1 includes challenges to NCEs and non-NCEs alike.

D. Implications of Findings

The findings of this empirical study could have far-reaching implications for both drug manufacturers and consumers. The study reveals that there was a twenty percent increase in first-filer Paragraph IV challenges in the twelve months after *Actavis*.[168] Importantly, this represents a reversal in the steady downward trend in first-filed Paragraph IV ANDAs before *Actavis*, from which we can conclude at least that *Actavis* did not discourage generic competition, contrary to Chief Justice Roberts's prediction.[169] Furthermore, *Actavis* may have actually accelerated generic competition, although the limited data available from the FDA makes it difficult to determine this with certainty.

First, at the very minimum, these findings indicate that Chief Justice Roberts's fears that *Actavis* would discourage generic competition are misplaced. Instead, generics' incentive to challenge pioneers' patents is clearly still intact.[170] It is possible that these settlements occur "so far down the line" after Paragraph IV ANDAs are filed that the prospect of forming a reverse-payment settlement does not even factor into generics' decision to challenge pioneer patents.[171] Generics' primary motivation is simply to enter the market as soon as possible, not enter into a settlement.[172] If these assumptions are

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[168] The twenty-five percent increase is as compared to the twelve-month interval before *Actavis*.
[169] *See* Appendix 1 (showing that 92, 81, 55, 53, and 66 Paragraph IV challenges were filed in Intervals 1, 2, 3, 4, and 5, respectively).
[170] *See* Appendix 1.
[171] Interview with Kurt R. Karst, Partner, Hyman, Phelps & McNamara, in Wash., D.C. (Jan. 16, 2015).
[172] *Id.*; *see also* Andrew Regan & Charles Miller, *Meeting of the Minds – Hatch-Waxman Litigation Post-Actavis: Crafting a Pro-Competitive*

true, then *Actavis* may have had no significant effect on generic competition.[173] Alternatively, generics may be undeterred by the heightened antitrust scrutiny created by *Actavis* because they know liability may be avoided by forming valuable alternative non-monetary settlements.[174] Furthermore, generic manufacturers are still presumably driven to seek the prize of the 180-day exclusivity period and market entry, which has not been changed by *Actavis*, and may in fact be even easier to achieve now that reverse-payment settlements will not be blocking generic entry.

Second, it is possible—but also harder to prove—that *Actavis* caused the increase in Paragraph IV filings observed in the year following the decision (Interval 5), either in whole or in part. For reasons that will be discussed in Part V, *infra*, there are some undisclosed statistics that could alter the results of our study.[175] Without access to this data, we can only speculate as to whether *Actavis* did in fact stimulate generic competition. Nonetheless, having eliminated one alternate cause for our findings,[176] we can confidently say that *Actavis* was at least one cause of the uptick in challenges, and thus the decision had

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Settlement Agreement, 6 LANDSLIDE 1, 4 (Sept/Oct. 2013) ("What generics really want is market entry.").

[173] Recall that "generic competition" is measured by Paragraph IV filings here. *Id.*

[174] Daryl Lim, *Reverse Payments: Life After* Actavis, 45 INT'L REV. INT. PROP. & COMPETITION 1, 3 (Nov. 2013) (explaining that because *Actavis* only explicitly discussed monetary payments, many pharmaceutical companies have responded by entering settlements that exchange services rather than money).

[175] *See infra* Part V.B. Specifically, we only had access to Paragraph IV data for first-filers, not later filers or multiple first-filers. Therefore, our findings may be different if this undisclosed data was available.

[176] *See supra* Part IV.C.

the intended effect of promoting competition by generics.[177] This is based on the assumption that Paragraph IV challenges are conducive to competition in the pharmaceutical industry.[178] The stated purpose of the 180-day exclusivity period granted to the first filer of a Paragraph IV ANDA is to incentivize generics to challenge suspect *Orange-Book*-listed patents and thereby increase generic-pioneer competition.[179] Increased Paragraph IV challenges therefore should eventually translate into more generics on the market and more affordable drugs for consumers.[180]

Under either of the two scenarios presented above, generics have the upper-hand over pioneers. Even before *Actavis*, the Hatch-Waxman Act was recognized as "pro-generic," essentially allowing generic manufacturers to challenge a pioneer's patents without the expense of first actually making an infringing product or the risk of accruing damages.[181] Instead, Paragraph IV challenges place almost all

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[177] *See* Appendix 1 (demonstrating that Paragraph IV filings have increased after *Actavis*).

[178] Janssen Pharmaceutica, N.V. v. Apotex, Inc., 540 F.3d 1353, 1357 (2008).

[179] *See id.* at 1361 (explaining that "Congress decided to give generic pharmaceutical companies a 180-day exclusivity period as an incentive to challenge suspect Orange Book listed patents."); *see also* Purepac Pharm. Co. v. TorPharm, Inc., 354 F.3d 877, 879 (D.C. Cir. 2004).

[180] *See* Avery, *supra* note 26, at 175 (Edwards, J., dissenting) (citing Abbott Labs. v. Young, 920 F.2d 984, 991 (D.C. Cir. 1990)).

[181] Matthew J. Higgins & Stuart J. H. Graham. *Balancing Innovation and Access: Patent Challenges Tip the Scales*, 326 SCIENCE 370 (Oct. 16, 2009), *available at* http://www.sciencemag.org/content/326/5951/370.full (explaining that the Hatch-Waxman Act has tipped the balance away from the incentives needed to support innovation); *see also* Monika Ermert, *Conference Debates Strategic Patenting, Innovation, and Public Health*, INTELLECTUAL PROPERTY WATCH (May 21, 2010), http://www.ip-

the risk on pioneers, who face the possibility of losing their entire market share overnight by having their patents invalidated at trial.[182] Mitigating this enormous risk is likely what drove many pioneers to form reverse-payment settlements.[183] But *Actavis* has now made it much more difficult for pioneers and generics to form valid reverse-payment settlements, and arguably robbed pioneers of their prerogative to settle.[184] The majority opinion was largely based on the misconception that a large reverse-payment settlement signals a weak patent that will likely be invalidated in litigation.[185] In reality, many patentees will settle even if they have no doubts about their patents' validity, in order to avoid the risk of invalidation at trial.[186] The ability to settle is

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watch.org/2010/05/21/conference-debates-strategic-patenting-innovation-public-health/ ("The Hatch-Waxman Act had been seen as pro-generic because it allowed the generic drug companies 'to sue at any time, to challenge the validity of the patent' without big risk.").

[182] White Paper Report: United States Patent Invalidity Study 2012, MORGAN LEWIS (2012), *available at* http://www.morganlewis.com/~/media/files/publication/presentation/speech/smyth_uspatentinvalidity_sept12 (stating that from 2007 to 2011 an average of only 14% of cases held challenged patent claims valid).

[183] Newsom, *supra* note 32, at 229 (explaining that pioneer drug manufacturers stand to lose much more by invalidation of a patent than generic drug manufacturers stand to gain, and therefore, it is "no surprise" that Hatch-Waxman settlements more commonly involve a reverse payment).

[184] FTC v. Actavis, Inc., 133 S. Ct. 2223, 2247 (2013).

[185] *Id.* at 2236 (explaining that an excessively large payment can serve as a "workable surrogate" for the patent's weakness).

[186] *See* Avery, *supra* note 26, at 195 ("A generic company with a weak case may nonetheless have a strong incentive to file a Paragraph IV ANDA, and a patent holder with a strong case still runs an enormous risk by proceeding to trial. In high-stakes litigation, the party with the most to lose has the greatest incentive to settle. But even where a patent holder believes it has a 90% chance of succeeding in litigation, the expected value associated with

therefore a crucial tool in pioneers' risk-management and business strategy. The number of reverse-payment settlements has decreased from forty in fiscal year 2012 (October 1, 2011 to September 30, 2012) to only twenty-nine in fiscal year 2013 (October 1, 2012 to September 30, 2013), suggesting that *Actavis* has in fact encroached upon pioneers' ability to settle.[187] Because Paragraph IV challenges have increased post-*Actavis*, and because *Actavis* may be deterring reverse-payment settlements, pioneers are facing more patent challenges along with a diminished ability to manage risk through settlement. In the long run, this could threaten pioneers' incentive to develop new life-saving drugs and bring them to market.[188]

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the 10% risk of losing is so substantial that it is arguably justified for the patentee to pay the ANDA applicant to settle as a means of risk management, especially where the patentee is risk averse.") *See also Actavis*, 133 S. Ct. at 2244 (Roberts, C.J., dissenting) (explaining that even a risk-averse patent holder that is ninety-five percent certain of his patent's validity may pay a large sum in order to avoid litigation and that five percent risk of a finding of invalidity).

[187] *Agreements Filed with the Federal Trade Commission under the Medicare Prescription Drug, Improvement, and Modernization Act of 2003: Overview of Agreements Filed in Fiscal Year 2013: A Report by the Bureau of Competition*, FEDERAL TRADE COMMISSION (Dec. https://www.ftc.gov/reports/agreements-filed-federal-trade-commission-under-medicare-prescription-drug-improvement-8. Note, however, that the FTC itself recognized that it is too soon to draw meaningful conclusions regarding the effects of *Actavis* on reverse-payment settlements. This is because fiscal year 2013 (Oct. 1, 2012 through Sept. 30, 2013) only covers the first three months after the *Actavis* decision. The FTC has not yet released its report on generic/brand-name settlement agreements for fiscal year 2014, which presumably will show a continued decline in the number of reverse-payment settlements.

[188] *But see* Ben Hirschler, *Pharma and Biotech on a Roll as Drug Approvals Hit 18-year High*, REUTERS (Jan. 1, 2015), http://www.reuters.com/article/2015/01/01/pharmaceuticals-approvals-idUSL6N0UE2C120150101 (stating that the FDA approved 41 novel drugs in 2014, versus 27 in 2013). Note the

Generic manufacturers may also be incentivized to bring Paragraph IV challenges because they know patent holders are now caught between a rock and a hard place—either the pioneer risks patent invalidation at trial or antitrust liability by settling.[189] Generics may expect that, with the threat of patent invalidation at trial and without the ability to easily settle, pioneers are less likely to respond with patent infringement actions.[190] This would allow generics to enter the market much more quickly and cheaply, and thus may explain

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fact that drug approvals have hit an 18-year high just shows that pioneers' incentive to innovate has not yet been diminished. Because only about two years have passed since *Actavis*, repercussions for pioneers' incentive to innovate may not manifest until much further down the line. At this point, all we know is that pioneers' ability to settle effectively has been compromised, and this could be the first step towards decreased innovation in the future.

[189] The risk of patent invalidation is even higher in the post-AIA world where the generic challenger can file an *inter partes* review (IPR) in response to a patent infringement action, where the Patent Trial and Appeal Board (PTAB) is essentially a "death squad" for patents, finding invalidity in the vast majority of cases. *See* Eliot Williams & May Eaton, *Surviving PTAB as a Patent Owner: Protecting Your Portfolio from the PTAB "Death Squads"*, BAKER BOTTS (Nov. 2014), http://www.bakerbotts.com/file_upload/Post-GrantReport10b2014-SurvivingPTABTrialsAsAPatentOwner.htm (stating that as of early October 2014, the PTAB has invalidated more than three-quarters of all claims as to which it has instituted an IPR and issued a final written decision).

[190] To investigate the validity of this argument, we would need to see what percent of Paragraph IV challenges filed in Interval 5 actually resulted in lawsuits, as compared to the percentage of Paragraph IV lawsuits targeted at ANDAs filed in previous intervals. However, because the FDA's Paragraph IV Database does not publish the ANDA No. of each listed drug for confidentiality reasons, it is very difficult to compile accurate information regarding which Paragraph IV ANDAs have been subject to suit by pioneers. This inquiry is therefore beyond the scope of this Article.

the sudden influx of Paragraph IV filings.[191] Overall, by undermining pioneers' ability to settle, *Actavis* has tilted the scales even further in favor of generics at the expense of pioneers.

V. FIXING THE POST-*ACTAVIS* WORLD

Given the compelling evidence that *Actavis* is accelerating generic competition, the next logical step is to restore the balance back towards brand-name manufacturers.[192] One way to accomplish this is to address the "elephant in the room"—to require the FTC to prove patent invalidity before bringing an antitrust claim.[193] This would temper the effects of *Actavis* by making it easier for pioneers to settle with generic challengers. In turn, this would reinstate pioneers' ability to effectively manage risk and recoup losses, thereby preserving their incentive to innovate. Furthermore, Congress should address the major criticism of reverse-payment settlements by amending the Hatch-Waxman act to allow for the 180-day exclusivity period to be granted on a "rolling" basis. This would still preserve the rights of pioneers to settle, while

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[191] A generic entering the market before a trial decision on the merits is referred to as "launching at risk," and is not uncommon, especially for more aggressive generic manufacturers like Teva Pharmaceuticals. *See* Joseph O'Malley et al., *Failure to Launch*, INTELLECTUAL PROPERTY MAGAZINE 30 (Apr. 2011), http://www.paulhastings.com/assets/publications/1877.pdf (explaining that, since 2007, more and more generics are launching at risk).

[192] Restoring pioneers' incentive to innovate will ultimately ensure that life-saving drugs continue to enter the market. *See supra* IV.D.

[193] James O'Connell, *Editor's Note: The Elephant Remains*, 1 ANTITRUST 5, 6 (Fall 2013) (quoting Justice Scalia in oral arguments for *Actavis*: "And to say you can consider every other factor other than the strength of the patent is—is to leave—leave out the—elephant in the room.").

preventing a single settlement from acting as a roadblock to all generic competition. This Article also calls for the FDA to increase transparency with respect to ANDA filings. In conducting this study, significant amounts of data on ANDA filings were not available to the Authors due to the FDA's strict confidentiality policies. The FDA should increase its transparency to allow generics and pioneers alike to make informed industry decisions. Finally, the increased Paragraph IV filings could stem in part from uncertainty in the wake of *Actavis*. To impart clarity and ensure that pioneers are not unduly deterred from settling, lower courts should devise a coherent analytical framework for evaluating the validity of settlements in Hatch-Waxman cases.[194]

A. Require the FTC to Prove Patent Invalidity Before Bringing Antitrust Claims

Our study reveals that Paragraph IV filings increased considerably in the year after *Actavis*, in sharp contrast to the downward trend in the years leading up to the decision.[195] If the number of Paragraph IV filings continues to trend upward, pioneers' incentive to innovate could be severely undercut.[196] One way to effectively restore the balance would be to make it easier for pioneers to form valid settlements. This Article therefore calls for legislative action to require the FTC to prove

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[194] *See* Lim, *supra* note 174.

[195] *See infra* Part IV.B; *see also* Appendix 1.

[196] If pioneers continue to face more and more Paragraph IV challenges (generic competition), they will not be able to as easily recoup the tremendous losses associated with the research and development of new drug candidates. Without these monopoly profits, pioneers' incentive to innovate may be diminished. *See supra* Part IV.D.

the invalidity of the underlying patent before arguing that a particular reverse-payment settlement violates the antitrust laws. This would enable pioneers to settle when it is in their best interest, and spend their resources on innovating rather than litigating.

One strong justification for elevating the FTC's burden of proof is the fact that a large reverse-payment settlement does not necessarily signify a weak patent. *Actavis* was based in part on the flawed assumption that "the size of the unexplained reverse payment can provide a workable surrogate for a patent's weakness, all without forcing a court to conduct a detailed exploration of the validity of the patent itself."[197] The Court reasoned that if a patentee knows the patent is likely invalid, there is more incentive to enter into an agreement that ensures the patent's validity is never challenged in court.[198] However, this rationale completely abrogates the property rights of the patent holder. Patents are presumed to be valid. But under the pretext of "increasing competition," the FTC has attempted to ignore the rights of pharmaceutical patentees by boldly claiming that pharmaceutical companies do not deserve any such presumption of validity because they have "weak" patents, and that they would not settle otherwise.

During oral arguments for *Actavis*, Justice Scalia criticized the FTC's argument by pointing out that "say[ing] you can consider every other factor other than the strength of the patent is—is to leave—leave out the—elephant in the room."[199] While Justice Scalia joined Chief Justice Roberts's

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[197] FTC v. Actavis, Inc. 133 S. Ct. 2223, 2236 (2013).
[198] *Id.*
[199] Transcript of Oral Argument at 38, FTC v. Actavis, Inc. 133 S. Ct. 2223 (2013) (No. 12-416).

dissent, the majority in *Actavis* adopted the FTC's flawed reasoning, which ignores the practical realities of high-stakes patent litigation.[200] Most pioneers have extensive product portfolios and are faced with the multiple Paragraph IV challenges at once—and the more successful a product is, the more generic challenges it will face.[201] Therefore, pioneers often enter into settlements even when the company has little doubt regarding the validity of its patents.[202] Considering this, a payment from a brand-name company to a generic challenger should merely be viewed as a means of mitigating risk rather than a concession of patent weakness.[203] Instead, courts should hold the FTC to its burden of proof by requiring it to prove the challenged patent is invalid rather than relying on a surrogate that is not in fact "workable." Logistically, this could be accomplished by either resolving patent validity as a threshold issue in an antitrust case or requiring the FTC to bring an *inter partes* review (IPR) action prior to the antitrust case.[204] Either solution would address the elephant in the room—that the validity of the underlying patents must be fully evaluated

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[200] Bieri, *supra* note 77, at 139.
[201] Bieri, *supra* note 77, at 142.
[202] *See* Avery, *supra* note 26; *see also Actavis*, 133 S. Ct. at 2247 (Roberts, C.J., dissenting).
[203] Bieri, *supra* note 77, at 142 ("Under these circumstances, it should not be surprising—nor should it be seen as an admission of weak patents—that many pharmaceutical innovators quite reasonably choose to settle some Hatch-Waxman challenges, even on terms that include providing considerable value to a generic competitor.").
[204] Gabrielle LaHatte, *Reverse Payments: When the Federal Trade Commission Can Attack the Validity of Underlying Patents*, 2 CASE W. RESERVE J.L. TECH. & INTERNET 37, 61 (2011), *available at* http://law.case.edu/journals/JOLTI/Documents/2%20Case%20W.%20Res.%20J.%20L.%20Tech.%20&%20Internet%2037-1.pdf (noting that the government has standing to challenge the validity of a patent when the patent holder is accused of violating antitrust law).

before a court can determine whether a settlement is actually an unreasonable restraint of trade in violation of the antitrust laws.

B. Increase FDA Disclosure of ANDA Filings

Unfortunately, several relevant data points for this study were unavailable due to the FDA's confidentiality policies and administrative delays. In 2004 the FDA released a limited database of information related to Paragraph IV filings as a "compromise solution" between the Agency and drug makers, which maintains the confidentiality of generic applicants while alerting other generics that a first-to-file application exists for a particular drug.[205] The FDA continues to update this Paragraph IV database, but it still only provides minimal information, excluding both the generic applicant's name and the FDA-assigned ANDA number.[206] More critically, the database only lists when the first Paragraph IV challenge was filed for a particular drug, but does not indicate the number of first filers (*i.e.*, if there were joint first filers), or the number of later filers. The FDA's *Orange Book* does provide information on approved later-filed Paragraph IV applications, but does not list the associated filing dates.[207]

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[205] Bob Pollock, *OK, What's Going on Here?*, LACHMAN CONSULTANTS (Feb. 12, 2013), http://www.lachmanconsultants.com/ok-whats-going-on-here.asp.

[206] FDA, Paragraph IV Database, *supra* note 140.

[207] The "*Orange Book*" is the common name for the FDA publication *Approved Drug Products with Therapeutic Equivalence Evaluations*, which is published monthly. *Office of Generic Drugs, Food & Drug Admin., Approved Drug Products with Therapeutic Equivalence Evaluations* (2015) [hereinafter *Orange Book*], *available at* http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/UCM071436.pdf .The FDCA requires a patent holder to include in its NDA "the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with

Having access to these statistics could entirely change the outcome of this study. For example, although our data shows an increase in the total number of NDAs being challenged by first-filers, we are unable to determine if the total number of Paragraph IV ANDAs has increased. If there are fewer joint first-filers, that could mean that the total number of generic challengers per drug has actually decreased, which may actually lead to less generic competition. Similarly, we were unable to determine the number of later filers post-*Actavis*. As such, our study is limited to analyzing only first filers of Paragraph IV ANDAs. Moreover, many drugs listed in the *Orange Book* have blank spaces under the "Date of Submission" column,[208] and there is a considerable delay between the actual date of submission and the date the drug is posted on the FDA's database.[209]

In order to draw more meaningful conclusions regarding the state of generic competition post-*Actavis*, access to this undisclosed data is crucial. This Article thus calls for the FDA to disclose more complete data of ANDA filings and to update the Paragraph IV database on a timelier basis. The FDA

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respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug." 21 U.S.C. § 355(b)(1). The patent numbers and expiration dates are then published in the *Orange Book*. Process patents and certain composition of matter patents are precluded from being listed in the *Orange Book*, though generic manufacturers may still be sued for infringing these unlisted patents.

[208] *See generally Orange Book*, *supra* note 207.

[209] This lag could also skew our data, since, for example, some Paragraph IV filings that were submitted during Interval 5 may not yet appear in the Database. Bob Pollock, *June Approval Times for ANDAs – A Snapshot in Time*, LACHMAN CONSULTANTS (Aug. 19, 2013), http://www.lachmanconsultants.com/june-approval-times-for-andas-a-snapshot-in-time.asp.

can still easily protect the identities of generic challengers by posting only the ANDA number and the date of submission of each ANDA. Disclosure of these filings—even without the identities of the generic applicants—would allow for a more accurate study, and would ultimately help pharmaceutical companies make informed business decisions.

C. Amend the Hatch-Waxman Act to Include a "Rolling Exclusivity" Procedure

Notwithstanding the increase in Paragraph IV challenges, more generic drugs may not actually be reaching the market. Non-monetary settlements between pioneers and the first ANDA filers may still roadblock generic entry while avoiding antitrust liability under *Actavis*. If the pioneer and the first filer enter into a settlement agreement (non-monetary or otherwise) where the generic agrees not to enter the market, the 180-day exclusivity period will not run and generic entry will still be bottlenecked because FDA cannot approve later-filed ANDAs.[210] This problem of penalizing later filers could be fixed by creating "rolling exclusivity."[211] Congress should revise the Hatch-Waxman Act so that if the first Paragraph IV challenger settles and does not enter the market, the 180-day exclusivity would instead be granted to the next challenger, and so on if the next challenger also settles.[212] By having the exclusivity period roll over after each settlement, it would only be awarded to the first *successful* generic challenger. This would arguably simplify the Hatch-Waxman Act and deter

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[210] Avery, *supra* note 26, at 181.
[211] *See* Avery, *supra* note 26, at 194.
[212] Ashlee B. Mehl, Note, *The Hatch-Waxman Act and Market Exclusivity for Generic Drug Manufacturers: An Entitlement or an Incentive?*, 81 CHI.-KENT. L. REV. 649, 674 (2006).

improper settlements (including both reverse-payment settlements that violate *Actavis* and other types of settlements that may delay generic entry) since it would be less feasible for the patent holder to enter such settlements with multiple generic challengers.[213]

D. Structure a Coherent Framework for Evaluating Reverse-Payment Settlements

Actavis only listed a few vague factors to be considered in assessing reverse-payment settlements, delegating the exact structuring of the analysis to lower courts.[214] Chief Justice Roberts criticized this "unruly" rule-of-reason standard in his dissent, wishing "[g]ood luck" to the district courts that must apply it.[215] Consequently, the increased Paragraph IV challenges may stem in part from uncertainty surrounding the presently underdeveloped rule-of-reason test.[216] Pharmaceutical patent holders are simply unsure of what types of settlements are still legal and, therefore, are hesitant to enter into those agreements in the first place.[217] It follows that

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[213] Avery, *supra* note 26, at 194.
[214] FTC v. Actavis, 133 S. Ct. 2223, 2238.
[215] *Id.* at 2245 (Roberts, C.J., dissenting).
[216] Bradley C. Graveline & Jennifer M. Driscoll-Chippendale, FTC v. Actavis: *What Does It Mean for Reverse Payment Settlements*, SHEPPARD MULLIN (July 2, 2013), *available at* http://www.mondaq.com/unitedstates/x/248122/Patent/FTC+v+Actavis+What+Does+It+Mean+for+ReversePayment ("The Actavis decision will generate increased uncertainty for parties contemplating reverse-payment settlements and absorb judicial resources as courts struggle to balance whether the procompetitive justifications of these agreements outweigh any anticompetitive effects.").
[217] *Id.* Furthermore, because the FTC has been so aggressive in filing antitrust claims, pioneers may be deterred from entering into any type of settlement, even if they think the settlement is lawful under *Actavis*, for fear of being sued by the government. *See* Carl Hittinger & Jeffrey Duffy, *FTC*

generic manufacturers are encouraged to aggressively file Paragraph IV challenges because they believe that pioneers have no tools remaining to stop generics from entering the market. Brand-name companies will still avoid trials and the risk of having their patents invalidated, and post-*Actavis* they now have to avoid settlements and the risk of antitrust liability.[218] To ensure that pioneers are not unduly deterred from settling, lower courts should develop a clear legal framework for analyzing reverse-payment settlements.[219]

The *Actavis* majority opinion explicitly identified the three most important factors in its rule-of-reason test: (1) the size of the reverse-payment settlement "in relation to the payor's anticipated future litigation costs"; (2) the "independence" of the payment "from other services for which it might represent payment;" and (3) the "lack of any other convincing [procompetitive] justification."[220] Other factors discussed in the decision include: (1) whether or not the payment has the "potential for adverse effects on competition;" (2) whether there are any legitimate justifications that could counterbalance or offset any anticompetitive effects; (3) the likelihood of the payment to result in anticompetitive harm to

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Aggressively Pressing 'Antitrust Trumps IP' Theme, THE LEGAL INTELLIGENCER (Dec. 1, 2014), http://www.thelegalintelligencer.com/id=1202677554124/FTC-Aggressively-Pressing-Antitrust-Trumps-IP-Theme?slreturn=20150102142808 (describing the FTC's "crusade against 'reverse-payment' patent infringement settlements in the pharmaceuticals sector.").

[218] *See infra* Part IV.D.

[219] Alexander Krueger, *Implementing* Actavis: *Three Tips for Future Courts Assessing Reverse Patent Settlements Under Rule of Reason Analysis*, 15 MINN. J.L. SCI. & TECH. 116, 117 (2014).

[220] *Actavis*, 133 S. Ct. at 2237 (noting that these factors tend to indicate the likelihood that a reverse-payment settlement would have anticompetitive effects).

the market; (4) the administrative feasibility of assessing a patent's validity or whether it has been infringed; and (5) the intent of the settling parties.[221] However, the court provided no guidance on how to weigh these factors or how to determine if they are satisfied or not, leaving it to the lower courts to sort out the mess.

Since *Actavis*, some district courts have attempted to simplify the daunting rule-of-reason analysis by creating bright-line tests.[222] In a recent class action suit, a district judge interpreted *Actavis* as imposing a rigid three-part test, and provided no analysis of the competitive effects of the settlement in question.[223] Similarly, another district court reduced its rule-of-reason analysis to the consideration of just "three primary factors."[224] The rationale behind creating such bright-line rules is to lend predictability to courts and

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[221] *Id.* at 2234–37.

[222] Jeffrey I. Shinder & Ankur Kapoor, *Are Bright-Line Rules the Right Prescription for Reverse-Payment Cases?*, ANTITRUST TODAY (Mar. 5, 2014), http://www.antitrusttoday.com/2014/03/05/are-bright-line-rules-the-right-prescription-for-reverse-payment-cases.

[223] *In re* Lamictal Direct Purchaser Antitrust Litig., 18 F. Supp. 3d 560, 564 (D.N.J. 2014) ("In Step One, a district court must ask, is there a reverse payment? . . . In Step Two, a district court must ask, is that reverse payment large and unjustified? . . . Step Three is the rule of reason); *see also* Richard Ripley & Sarah Hasford, *Antitrust: Scrutiny of Reverse Payment Settlements*, HAYNES BOONE (2014), http://www.haynesboone.com/files/Publication/1554b320-f61e-4884-8529-8ebdc7c44bd6/Presentation/PublicationAttachment/90244baf-0223-475c-9cb0-4e8e26c56173/Antitrust-Scrutiny-of-Reverse-Payment-Settlements.pdf.

[224] *In re* Nexium (Esomeprazole) Antitrust Litig., 968 F. Supp. 2d 367, 387 (D. Mass. 2013) ("Judges engaging in 'rule-of-reason' analysis are directed to consider three primary factors: (1) whether the alleged agreement involved the exercise of power in a relevant economic market, (2) whether this exercise had anticompetitive consequences, and (3) whether those detriments outweighed efficiencies or other economic benefits.").

pharmaceutical companies.[225] However, judicial convenience should not trump justice—it cannot justify letting the court impose antitrust liability on an innocent party.[226] Rigid application of bright-line rules inevitably leads to undesirable results, either punishing meritorious settlements or giving pharmaceutical patent holders a roadmap on how to exclude competition without impinging on antitrust law.[227] Importantly, *Actavis* rejected the FTC's bright-line "quick-look" rule that would give a rebuttable presumption of anticompetitive effect to reverse payments greater than the patentee's anticipated costs of continued litigation.[228] When crafting a framework for the analysis of reverse-payment settlements, lower courts should therefore avoid bright-line rules.

Perhaps the most divisive issue faced by lower courts is whether *Actavis* applies to non-monetary settlements.[229] Resolution of this issue will therefore be a critical step in

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[225] Shinder et al., *supra* note 222.

[226] *Id.*

[227] *Id.*

[228] *Id.* ("In directing application of a full rule-of-reason analysis, which requires courts to balance the anticompetitive and procompetitive effects of the settlement, the Supreme Court made clear that courts should not apply bright-line rules in evaluating these settlements.").

[229] Cases that have interpreted *Actavis* as requiring cash payments include *In re* Lamictal Direct Purchaser Antitrust Litigation, 18 F. Supp. 3d 560 (D.N.J. 2014) and *In re* Loestrin 24 Fe Antitrust Litig., 45 F. Supp. 3d 180 (D.R.I. 2014). Cases that have interpreted *Actavis* as not requiring cash payments include *In re* Nexium (Esomeprazole) Antitrust Litig., 968 F. Supp. 2d 367 (D. Mass. 2013), *In re* Lipitor Antitrust Litig., MDL No. 2332, 2013 WL 4780496 (D.N.J. Sept. 12, 2014), and *In re* Niaspan Antitrust Litig., 42 F. Supp. 3d 735 (E.D. Pa. 2014). Note that, as of the date of writing, none of the circuit courts has yet issued an opinion interpreting *Actavis*, although *In re Lamictal* was argued at the Third Circuit in November 2014. *In re* Aggrenox Antitrust Litig., No. 3:14-md-2516 (SRU), 2015 WL 1311352 (D. Conn. Mar. 23, 2015).

establishing a coherent framework for evaluating settlements between brand-name and generic manufacturers post-*Actavis*. Because the *Actavis* decision only explicitly discussed monetary payments, many pharmaceutical companies have responded by entering into settlements that exchange services rather than money.[230] The theory is that these agreements, while still technically "reverse-payment settlements," are not as anticompetitive as the monetary payments at issue in *Actavis*.[231] However, non-monetary reverse-payment settlements may still sometimes violate antitrust laws under *Actavis*.[232] In one post-*Actavis* case, a district judge ruled that a non-monetary settlement could convey sufficient value to the generic manufacturer so as to constitute a "payment."[233] This means that the *Actavis* holding may extend to non-monetary payments that provide any value to the generic challenger since these could be considered unreasonably anticompetitive.[234] Plaintiffs' attorneys argue that to rule otherwise would prioritize form over function, especially when services are used as a mere substitute for financial compensation.[235] In structuring the rule of reason post-*Actavis*, lower courts should therefore extend antitrust scrutiny to non-monetary settlements.

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[230] For example, pioneers are now more likely to offer cross-licensing deals or marketing services in exchange for generics' delayed market entry. *See* Daryl Lim, *Reverse Payments: Life After* Actavis, 45 INT'L REV. INT. PROP. & COMPETITION 1 (2013).
[231] Botti et al., *supra* note 131.
[232] *Id.*
[233] *Id.*
[234] *Id.*
[235] Richard Ripley & Sarah Hasford, *Antitrust: Scrutiny of Reverse Payment Settlements*, HAYNES BOONE (2014), http://www.haynesboone.com/files/Publication/1554b320-f61e-4884-8529-8ebdc7c44bd6/Presentation/PublicationAttachment/90244baf-0223-475c-9cb0-4e8e26c56173/Antitrust-Scrutiny-of-Reverse-Payment-Settlements.pdf.

While applying the rule-of-reason under *Actavis* has proven challenging, it is certainly not an insurmountable task. Over time, district courts should identify particular characteristics of reverse-payment settlements that are *per se* illegal, and only proceed with the rule-of-reason analysis if the agreement does not have those characteristics.[236] This does not amount to a bright-line rule, but is rather a time-saving method of filtering out the most blatantly anticompetitive settlements at the outset. The rule-of-reason standard requires the court to consider the "totality of the circumstances," and does not provide for any easy shortcuts.[237] Rather, lower courts must slowly develop a clear, comprehensive framework on a case-by-case basis.[238] Once a coherent system for analysis is in place, pioneers will have more guidance on how to form legal reverse-payment settlements and, in turn, will be able to effectively manage risk via settlement.

VI. CONCLUSION

The *Actavis* Court declined to find reverse-payment settlements presumptively illegal, as argued for by the FTC, but also declined to uphold prior appellate court cases that found such settlements to be effectively *per se* legal under the antitrust laws. Instead, the majority ruled that reverse-payment settlements violate the antitrust laws when their anticompetitive effects outweigh their procompetitive effects, which must be evaluated using a vague rule-of-reason analysis.[239] In his dissent, Chief Justice Roberts expressed

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[236] Krueger, *supra* note 219, at 116.
[237] Shinder et al., *supra* note 222.
[238] *Id.*
[239] FTC v. Actavis, Inc., 133 S. Ct. 2223, 2236 (2013).

concern that the decision may have the unintended anticompetitive effect of discouraging generics from challenging pioneers' patents in the first place.[240] Our analysis shows that these fears are misplaced, as the number of Paragraph IV challenges post-*Actavis* has actually increased.[241] However, *Actavis* has raised the specter of antitrust liability for all settlements between pioneers and generics, and unfairly shifted the burden of proving their settlements are reasonable to pioneers, thereby undercutting their ability to manage risk through settlement. To ensure that pioneers' incentive to innovate is not harmed, Congress should require the FTC to prove the invalidity of the underlying patent before bringing an antitrust action challenging a settlement. Further, the FDA should adopt more transparent disclosure policies, Congress should amend the Hatch-Waxman Act to include a "rolling exclusivity" procedure, and courts should adopt a more coherent framework for evaluating reverse-payment settlements.

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[240] *Id.* at 2247 (Roberts, C.J., dissenting).
[241] *See* Appendix 1.

VII. APPENDIX

Appendix 1: First-Filer Paragraph IV Challenges: Before Versus After *Actavis*

	Interval 1	Interval 2	Interval 3	Interval 4	Interval 5
Number of First-Filer Paragraph IV Challenges	91	81	55	54	65

FTC v. Actavis decision (June 17, 2013)

KEY
Interval 1 = June 17, 2009 – June 16, 2010
Interval 2 = June 17, 2010 – June 16, 2011
Interval 3 = June 17, 2011 – June 16, 2012
Interval 4 = June 17, 2012 – June 16, 2013
Interval 5 = June 17, 2013 – June 16, 2014

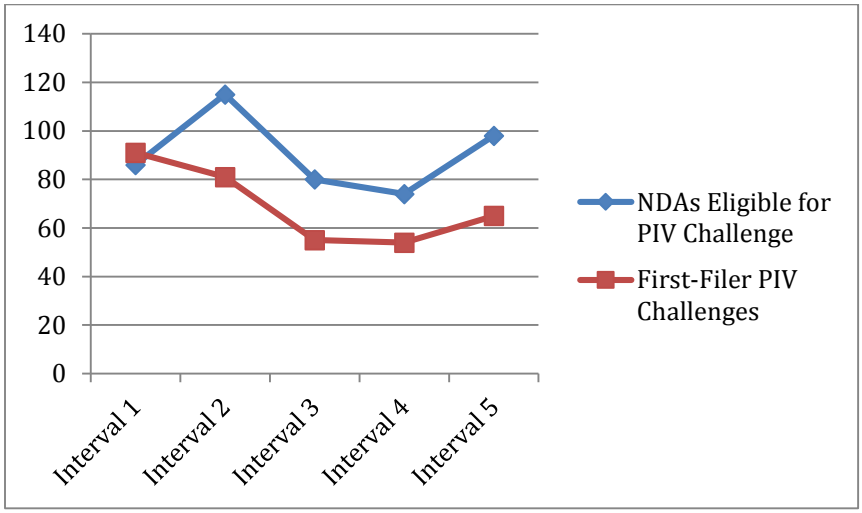
Appendix 2: New Drugs Eligible for Paragraph IV Challenge: Before versus After *Actavis*

	Interval -3	Interval -2	Interval -1	Interval 0	Interval 1
Number of NDAs Approved	86	115	80	74	98

New drugs eligible for Paragraph IV challenge during Interval 5 from Appendix 1 (after *Actavis*)

KEY
Interval -3 = June 17, 2005 – June 16, 2006
Interval -2 = June 17, 2006 – June 16, 2007
Interval -1 = June 17, 2007 – June 16, 2008
Interval 0 = June 17, 2008 – June 16, 2009
Interval 1 = June 17, 2009 – June 16, 2010

Appendix 3: First-Filer Paragraph IV Challenges versus NDAs Eligible for Paragraph IV Challenge



Appendix 4: First-Filer Paragraph IV Challenges Filed Between 6/17/2009 and 6/16/2010 (Interval 1)

DRUG NAME	DOSAGE FORM	STRENGTH	RLD	DATE OF SUBMISSION
Tramadol Hydrochloride	Extended-release Tablets	100 mg, 200 mg and 300 mg	Ryzolt	6/18/2009
Caspofungin Acetate	For Injection	50 mg/vial and 70 mg/vial	Cancidas	6/26/2009
Tobramycin	Inhalation Solution	300 mg/5 mL	Tobi	6/29/2009
Diclofenac Sodium and Misoprostol*	Delayed-release Tablets	50 mg/0.2 mg	Arthrotec	6/29/2009
Olopatadine Hydrochloride	Nasal Spray	0.665 mg/ Spray	Patanase	6/29/2009
Docetaxel	Injection	40 mg/mL, 0.5 mL and 2 mL vials	Taxotere	6/30/2009
Colesevelam Hydrochloride	Tablets	625 mg	Welchol	7/1/2009
Vardenafil Hydrochloride	Tablets	5 mg and 10 mg	Levitra	7/10/2009
Ropinirole Hydrochloride	Extended-release Tablets	6 mg	Requip XL	7/14/2009
Atazanavir Sulfate	Capsules	300 mg	Reyataz	7/20/2009
Epinephrine	Injection (Auto-injector)	0.15 mg/0.3 mL and 0.3 mg/0.3 mL	Epipen and Epipen Jr.	7/20/2009
Ramelteon	Tablets	8 mg	Rozerem	7/22/2009

Armodafinil	Tablets	50 mg, 150 mg and 250 mg	Nuvigil	7/24/2009
Ezetimibe and Simvastatin	Tablets	10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg and 10 mg/80 mg	Vytorin	7/27/2009
Metformin Hydrochloride	Extended-release Tablets	500 mg and 1000 mg	Glumetza	7/27/2009
Ketoconazole	Foam	2%	Extina	7/30/2009
Levofloxacin	Oral Solution	25 mg/mL	Levaquin	7/30/2009
Morphine Sulfate*	Extended-release Capsules	45 mg and 75 mg	Avinza	7/30/2009
Linezolid	Oral Suspension	100 mg/5 mL	Zyvox	8/3/2009
Cisatracurium Besylate (preserve free)	Injection	2 mg/mL, 5 mL vial and 10 mg/mL, 20 mL vial	Nimbex	8/4/2009
Mometasone Furoate	Nasal Spray	50 mcg/ Spray	Nasonex	8/7/2009
Cisatracurium Besylate (multi-dose)	Injection	2 mg/mL, 10 mL vial	Nimbex	8/12/2009
Sibutramine Hydrochloride	Capsules	10 mg and 15 mg	Meridia	8/14/2009

Glycopyrrolate	Tablets	1 mg	Robinul	8/14/2009
Bivalirudin	For Injection	250 mg/vial	Angiomax	9/1/2009
Fenofibrate Choline	Delayed-release Capsules	135 mg	Trilipix	9/1/2009
Linezolid	Injection	2 mg/mL, 300 mL bag	Zyvox	9/1/2009
Fenofibrate Choline	Delayed-release Capsules	45 mg	Trilipix	9/2/2009
Armodafinil	Tablets	200 mg	Nuvigil	9/3/2009
Vardenafil Hydrochloride	Tablets	2.5 mg	Levitra	9/4/2009
Armodafinil	Tablets	100 mg	Nuvigil	9/8/2009
Amlodipine, Hydrochlorothiazide and Valsartan!	Tablets	5 mg/12.5 mg/160 mg, 5 mg/25 mg/160 mg, 10 mg/25 mg/160 mg and 10 mg/25 mg/320 mg	Exforge HCT	9/14/2009
Adapalene	Topical Gel	0.30%	Differin	9/15/2009
Amlodipine Besylate and Atorvastatin Calcium	Tablets	2.5 mg/10 mg, 2.5 mg/20 mg and 10 mg/40 mg	Caduet	9/17/2009

Niacin and Simvastatin	Extended-release Tablets	1000 mg/20 mg	Simcor	9/17/2009
Bupropion Hydrobromide	Extended-release Tablets	348 mg	Aplenzin	9/24/2009
Bupropion Hydrobromide	Extended-release Tablets	174 mg	Aplenzin	9/28/2009
Arformoterol Tartrate	Inhalation Solution	Eq. 0.015 mg base/2 mL	Brovana	10/1/2009
Fulvestrant	Injection	50 mg/mL, 2.5 mL and 5 mL syringe	Faslodex	10/1/2009
Tadalafil	Tablets	20 mg	Adcirca	10/15/2009
Ciprofloxacin	Oral Suspension	250 mg/5 mL and 500 mg/ 5 mL	Cipro	10/16/2009
Atovaquone	Oral Suspension	750 mg/5 mL	Mepron	10/20/2009
Amlodipine, Hydrochlorothiazide and Valsartan!	Tablets	10 mg/12.5 mg/160 mg	Exforge HCT	10/22/2009
Lidocaine	Topical Patch	5%	Lidoderm	11/13/2009
Levonorgestrel; Ethinyl Estradiol; Ethinyl Estradiol	Tablets	0.1 mg/0.02 mg and 0.01 mg	LoSeasonique	11/16/2009
Dextroamphetamine saccharate; Amphetamine aspartate; Dextroamphetamine Sulfate; Amphetamine Sulfate	Tablets	5 mg, 10 mg, 20 mg, 30 mg	Adderall	11/18/2009

Lovastatin and Niacin	Extended-release Tablets	40 mg/1000 mg	Advicor	11/19/2009
Minocycline Hydrochloride	Extended-release Tablet	65 mg and 115 mg	Solodyn	11/19/2009
Esomeprazole Sodium	For Injection	20 mg/vial and 40 mg/vial	Nexium IV	11/23/2009
Calcipotriene	Topical Cream	0.005%	Dovonex	12/2/2009
Mesalamine	Delayed-release Tablets	1.2 g	Lialda	12/16/2009
Diclofenac Sodium	Topical Gel	3%	Solaraze	12/16/2009
Meloxicam	Oral Suspension	7.5 mg/5 mL	Mobic	12/17/2009
Sirolimus	Tablets	1 mg and 2 mg	Rapamune	12/17/2009
Lamotrigine	Orally Disintegrating Tablets	25 mg, 50 mg, 100 mg, and 200 mg	Lamictal ODT	12/21/2009
Pioglitazone Hydrochloride and Glimepiride	Tablets	30 mg/2 mg and 30 mg/4 mg	Duetact	12/22/2009
Butoconazole Nitrate	Vaginal Cream	2%	Gynazole-1	12/23/2009
Bupropion Hydrobromide	Extended-release Tablets	522 mg	Aplenzin	12/24/2009
Guanfacine Hydrochloride	Extended-release Tablets	1 mg, 2 mg, 3 mg and 4 mg	Intuniv	12/29/2009
Linezolid	Injection	2 mg/mL, 100 mL bag	Zyvox	12/29/2009

Sevelamer Carbonate	Powder for Oral Suspension	0.8 g/packet and 2.4 g/packet	Renvela	12/30/2009
Fexofenadine Hydrochloride	Oral Suspension	30 mg/5 mL	Allegra	1/25/2010
Sunitinib Malate	Capsules	12.5 mg, 25 mg, 37.5 mg and 50 mg	Sutent	1/26/2010
Tenofovir Disoproxil Fumarate	Tablets	300 mg	Viread	1/26/2010
Doxercalciferol	Capsules	1 mcg	Hectorol	2/12/2010
Niacin and Simvastatin	Extended-release Tablets	500 mg/20 mg	Simcor	2/12/2010
Atazanavir Sulfate	Capsules	200 mg	Reyataz	2/16/2010
Niacin and Simvastatin	Extended-release Tablets	750 mg/20 mg	Simcor	2/17/2010
Clobetasol Propionate	Emulsion Foam	0.05%	Olux-E	2/25/2010
Fenofibrate	Tablets	40 mg and 120 mg	Fenoglide	3/17/2010
Atazanavir Sulfate	Capsules	100 mg and 150 mg	Reyataz	3/19/2010
Eletriptan Hydrobromide	Tablets	20 mg and 40 mg	Relpax	3/29/2010
Calcipotriene and Betamethasone Dipropionate	Ointment	0.005%/0.064 %	Taclonex	3/31/2010
Colesevelam Hydrochloride	Powder for Oral Suspension	1.875 g/Packet and 3.75	Welchol	4/9/2010
Methylphenidate Hydrochloride	Oral Solution	5 mg/5 mL and 10 mg/5 mL	Methylin	4/13/2010

Omeprazole and Sodium Bicarbonate	Capsules	20 mg/1100 mg	Zegerid OTC	4/20/2010
Estradiol	Transdermal System	0.025 mg/day, 0.0375 mg/day, 0.05 mg/days, 0.075 mg/day and 0.1 mg/day	Vivelle Dot	4/27/2010
Zolpidem Tartrate	Sublingual Tablets	5 mg and 10 mg	Edluar	4/29/2010
Bimatoprost	Topical Solution	0.03%	Latisse	5/3/2010
Morphine Sulfate and Naltrexone Hydrochloride	Extended-release Capsules	100 mg/4 mg	Embeda	5/3/2010
Eprosartan Mesylate	Tablets	400 mg and 600 mg	Teveten	5/10/2010
Varenicline Tartrate	Tablets	0.5 mg and 1 mg	Chantix	5/10/2010
Ranolazine	Extended-release	500 mg and 1000 mg	Renexa	5/17/2010
Rasagiline Mesylate	Tablets	0.5 mg and 1 mg	Azilect	5/17/2010
Pregablin	Oral Solution	20 mg/mL	Lyrica	5/19/2010
Morphine Sulfate and Naltrexone Hydrochloride	Extended-release Capsules	60 mg/2.4 mg	Embeda	5/25/2010
Morphine Sulfate and Naltrexone Hydrochloride	Extended-release Capsules	30 mg/1.2 mg, 50 mg/2 mg and 80 mg/3.2 mg	Embeda	5/28/2010
Budesonide	Inhalation Suspension	1 mg/2 mL	Pulmicort Respules	5/28/2010

Pramipexole Dihydrochloride	Extended-release Tablets	0.375 mg, 0.75 mg, 1.5 mg, 3 mg and 4.5 mg	Mirapex ER	6/1/2010
Adefovir Dipivoxil	Tablets	10 mg	Hepsera	6/8/2010
Entecavir	Tablets	0.5 mg and 1 mg	Baraclude	6/14/2010

Appendix 5: First-Filer Paragraph IV Challenges Filed Between 6/17/2010 and 6/16/2011 (Interval 2)

DRUG NAME	DOSAGE FORM	STRENGTH	RLD	DATE OF SUBMISSION
Darunavir Ethanolate	Tablets	75 mg, 150 mg, 300 mg, 400 mg and 600 mg	Prezista	6/23/2010
Dasatinib	Tablets	20 mg, 50 mg, 70 mg and 100 mg	Sprycel	6/28/2010
Hydrocortisone Butyrate	Cream	0.10%	Locoid Lipocream	6/28/2010
Donepezil Hydrochloride	Orally Disintegrating Tablets	5 mg and 10 mg	Aricept ODT	6/30/2010
Sodium Oxybate	Oral Solution	500 mg/mL	Xyrem	7/8/2010
Tretinoin	Gel	0.1%	Retin-A Micro	7/8/2010
Lenalidomide	Capsules	25 mg	Revlimid	7/12/2010
Prednisolone Sodium Phosphate	Orally Disintegrating Tablets	10 mg, 15 mg and 30 mg	Orapred	7/22/2010
Polyethylene Glycol 3350, Sodium Chloride, Sodium Bicarbonate, Potassium Chloride and Bisacodyl	For Oral Solution and Delayed-release Tablet	210 g, 5.6 g, 0.74 g, 2.86 g and 5 mg (1 Tablet Regimen)	Halflytely and Bisacodyl	7/30/2010

Hydromorphone Hydrochloride	Extended-release Tablets	16 mg	Exlago	8/2/2010
Metoclopramide Hydrochloride	Orally Disintegrating Tablets	5 mg and 10 mg	Metozolv ODT	8/24/2010
Dexlansoprazole	Delayed-release Capsules	60 mg	Dexilant	8/25/2010
Sirolimus	Tablets	0.5 mg	Rapamune	8/25/2010
Lenalidomide	Capsules	5 mg, 10 mg and 15 mg	Revlimid	8/30/2010
Hydromorphone Hydrochloride	Extended-release Tablets	8 mg and 12 mg	Exlago	9/2/2010
Orlistat	Capsules	60 mg	Alli	9/8/2010
Tacrolimus	Ointment	0.10%	Protopic	9/9/2010
Atovaquone and Proguanil Hydrochloride	Tablets	62.5 mg/25 mg	Malarone	9/14/2010
Doxepin Hydrochloride	Tablets	3 mg and 6 mg	Silenor	9/16/2010
Ibupofen Lysine	Injection	10 mg/mL, 2 mL vials	Neoprofen	10/1/2010
Oxycodone Hydrochloride	Extended-release Tablets	40 mg	Oxycontin (NDA 022272)	10/4/2010
Voriconazole	Oral Suspension	40 mg/mL	Vfend	10/8/2010
Glycopyrrolate	Tablets	2 mg	Robinul Forte	10/12/2010

Oxycodone Hydrochloride	Extended-release Tablets	30 mg, 60 mg and 80 mg	Oxycontin (NDA 022272)	10/18/2010
Sitagliptin Phosphate	Tablets	25 mg, 50 mg and 100 mg	Januvia	10/18/2010
Sitagliptin Phosphate and Metformin Hydrochloride	Tablets	50 mg/500 mg and 50 mg/1000 mg	Janumet	10/18/2010
Trazodone Hydrochloride	Extended-release Tablets	150 mg and 300 mg	Oleptro	10/18/2010
Estradiol Valerate and Dienogest	Tablets	3 mg;2 mg/2 mg;2 mg/3 mg and 1 mg	Natazia	10/22/2010
Oxycodone Hydrochloride	Extended-release Tablets	10 mg	Oxycontin (NDA 022272)	10/25/2010
Dutasteride and Tamsulosin Hydrochloride	Capsules	0.5 mg/0.4 mg	Jalyn	10/26/2010
Minocycline Hydrochloride	Extended-release Tablet	80 mg	Solodyn	10/27/2010
Oxycodone Hydrochloride	Extended-release Tablets	15 mg	Oxycontin (NDA 022272)	10/28/2010
Oxycodone Hydrochloride	Extended-release Tablets	20 mg	Oxycontin (NDA 022272)	10/29/2010
Naproxen and Esomeprazole Magnesium	Delayed-release Tablets	375 mg/20 mg and 500 mg/20 mg	Vimovo	11/5/2010
Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate	Oral Solution	17.5 g/3.13 g/1.6 g	Suprep Bowel Prep Kit	11/8/2010
Oseltamivir Phosphate	Capsules	75 mg	Tamiflu	11/15/2010
Tacrolimus	Ointment	0.03%	Protopic	11/22/2010

Dexlansoprazole	Delayed-release Capsules	30 mg	Dexilant	11/30/2010
Desonide	Gel	0.05%	Desonate	12/1/2010
Alosetron Hydrochloride	Tablets	0.5 mg and 1 mg	Lotronex	12/2/2010
Minocycline Hydrochloride	Extended-release Tablet	55 mg	Solodyn	12/2/2010
Gatifloxacin	Ophthalmic Solution	0.5 %	Zymaxid	12/7/2010
Minocycline Hydrochloride	Extended-release Tablet	105 mg	Solodyn	12/13/2010
Dexmethylphenidate Hydrochloride	Extended-release Capsules	30 mg	Focalin XR	12/15/2010
Clindamycin Phosphate and Tretinoin	Gel	1.2%/0.025%	Ziana	12/17/2010
Dexmethylphenidate Hydrochloride	Extended-release Capsules	40 mg	Focalin XR	12/20/2010
Tretinoin	Gel	0.04%	Retin-A Micro	12/20/2010
Ritonavir	Tablets	100 mg	Norvir	12/21/2010
Levetiracetam	Extended-release Tablets	500 mg and 750 mg	Keppra XR	1/7/2011
Levetiracetam	Extended-release Tablets	1000 mg	Keppra XR	1/7/2011
Venlafaxine Hydrochloride	Extended-release Tablets	225 mg	Venlafaxine Hydrochloride	1/10/2011
Diclofenac Potassium	Oral Solution (Sachet)	50 mg	Cambia	1/24/2011

Niacin and Simvastatin	Extended-release Tablets	1000 mg/40 mg	Simcor	2/4/2011
Niacin and Simvastatin	Extended-release Tablets	500 mg/40 mg	Simcor	2/9/2011
Lisdexamfetamine Dimesylate	Capsules	20 mg, 30 mg, 40 mg, 50 mg, 60 mg and 70 mg	Vyvanse	2/23/2011
Hydromorphone Hydrochloride	Oral Solution	5 mg/5mL	Dilaudid	2/25/2011
Posaconazole	Oral Suspension	40 mg/mL	Noxafil	2/28/2011
Azithromycin	Ophthalmic Solution	1%	Azasite	3/3/2011
Clonidine Hydrochloride	Extended-release Tablets	0.1 mg and 0.2 mg	Jenloga	3/4/2011
Clonidine Hydrochloride	Extended-release Tablets	0.1 mg and 0.2 mg	Kapvay	3/4/2011
Dextromethorphan Hydrobromide and Quinidine Sulfate	Capsules	20 mg/10 mg	Nuedexta	3/7/2011
Frovatriptan Succinate	Tablets	2.5 mg	Frova	3/9/2011
Lapatinib Ditosylate	Tablets	250 mg	Tykerb	3/14/2011
Malathion	Topical Lotion	0.50%	Ovide	3/16/2011
Valganciclovir Hydrochloride	Oral Solution	50 mg/mL	Valcyte	3/21/2011
Abacavir Sulfate, Lamivudine and Zidovudine	Tablets	300 mg/150 mg	Trizivir	3/22/2011

Mycophenolic Mofetil	For Oral Suspension	200 mg/mL	Cellcept	3/25/2011
Bimatoprost	Ophthalmic Solution	0.01%	Lumigan	4/5/2011
Acetaminophen	Injection	1000 mg/100 mL (10 mg/mL)	Ofirmev	4/7/2011
Clozapine	Orally Disintegrating Tablets	150 mg	Fazaclo	4/8/2011
Methylphenidate	Transdermal System	10 mg/9 hrs, 15 mg/9 hrs, 20 mg/9 hrs and 30 mg/9 hrs	Daytrana	4/13/2011
Clozapine	Orally Disintegrating Tablets	200 mg	Fazaclo	4/18/2011
Megestrol Acetate	Oral Suspension	125 mg/mL	Megace ES	4/27/2011
Rivastigmine	Transdermal System Extended-release	4.6 mg/24 hr and 9.5 mg/24 hr	Exelon	4/27/2011
Norethindrone Acetate and Ethinyl Estradiol / Ethinyl Estradiol and Ferrous Fumarate	Tablets	1 mg/0.01 mg, 0.01 mg and 75 mg	Lo Loestrin Fe	4/29/2011
Tranexamic Acid	Tablets	650 mg	Lysteda	5/24/2011
Temsirolimus	Injection	25 mg/mL, 1.8 mL vial	Torisel	5/25/2011
Palonosetron Hydrochloride	Injection	0.05 mg/mL, 1.5 mL and 5 mL	Aloxi	5/27/2011
Bexarotene	Capsules	75 mg	Targretin	6/6/2011
Risedronate Sodium	Delayed-release Tablets	35 mg	Atelvia	6/9/2011

Appendix 6: First-Filer Paragraph IV Challenges Filed Between 6/17/2011 and 6/16/2012 (Interval 3)

DRUG NAME	DOSAGE FORM	STRENGTH	RLD	DATE OF SUBMISSION
Azithromycin	For Injection	500 mg/vial	Zithromax	6/17/2011
Dasatinib	Tablets	80 mg and 140 mg	Sprycel	6/17/2011
Hydromorphone Hydrochloride	Injection	2 mg/mL	Dilaudid	6/22/2011
Mesalamine	Delayed-release Tablets	800 mg	Asacol HD	7/13/2011
Fluticasone Furoate	Nasal Spray	27.5 mcg	Veramyst	7/15/2011
Pramipexole Dihydrochloride	Extended-release Tablets	2.25 mg and 3.75 mg	Mirapex ER	7/26/2011
Fluorouracil	Cream	0.5%	Carac	7/29/2011
Oseltamivir Phosphate	Capsules	30 mg and 45 mg	Tamiflu	8/2/2011
Norethindrone and Ethinyl Estradiol and Ferrous Fumarate	Chewable Tablets	0.8 mg/0.025 mg and 75 mg	Generess Fe	8/5/2011
Maraviroc	Tablets	150 mg and 300 mg	Selzentry	8/8/2011
Ketorolac Tromethamine	Opthalmic Solution	0.45%	Acuvail	8/24/2011

Pioglitazone Hydrochloride and Metformin	Extended-release Tablets	15 mg/1000 mg and 30 mg/1000 mg	Actoplus Met XR	9/23/2011
Dexmethylphenidate	Extended-release Capsules	35 mg	Focalin XR	9/29/2011
Dexmethylphenidate	Extended-release Capsules	25 mg	Focalin XR	9/30/2011
Doripenem	Injection	250 mg/vial and 500 mg/vial	Doribax	10/12/2011
Raltegravir	Tablets	400 mg	Isentress	10/12/2011
Levoleucovorin Calcium	Injection	10 mg/mL, 17.5 mL vial and 25 mL vial	Fusilev	10/26/2011
Deferasirox	Tablets	125 mg, 250 mg, and 500	Exjade	10/28/2011
Gabapentin	Tablets	300 mg and 600 mg	Gralise	10/31/2011
Hydromophone Hydrochloride	Injection	10 mg/mL	Dilaudid-HP	11/4/2011
Lamivudine	Oral Solution	10 mg/mL	Epivir	11/22/2011
Treprostinil Sodium	Injection	10 mg/mL, 20 mL vial	Remodulin	12/2/2011
Ibuprofen and Famotidine	Tablets	800 mg/26.6 mg	Duexis	12/6/2011
Piperacillin Sodium and Tazobactam Sodium	For Injection	12 g/1.5 g per vial (pharmacy bulk)	Zosyn	12/6/2011
Azelastine Hydrochloride	Nasal Spray	205.5 mcg/spray	Astepro	12/15/2011

Argatroban in Sodium Chloride	Injection	1 mg/mL, 50 mL vials	Argatroban	12/16/2011
Nebivolol Hydrochloride	Tablets	2.5 mg, 5 mg, 10 mg, and 20 mg	Bystolic	12/19/2011
Vardenafil Hydrochloride	Orally Disintegrating Tablets	10 mg	Staxyn	12/22/2011
Colchicine	Tablets	0.6 mg	Colcrys	12/23/2011
Doxercalciferol*	Injection	2 mcg/mL, 1 mL in 2 mL vial	Hectorol	12/28/2011
Adapalene and Benzoyl Peroxide	Gel	0.1%/2.5%	Epiduo	12/30/2011
Fosamprenavir Calcium	Tablets	700 mg	Lexiva	1/18/2012
Fosaprepitant Dimeglumine	Injection	115 mg/vial	Emend	1/25/2012
Fosaprepitant Dimeglumine	Injection	150 mg/vial	Emend	1/25/2012
Zoledronic Acid	Injection	4 mg/100 mL, 100 mL vial	Zometa	1/31/2012
Oxycodone Hydrochloride	Tablets	5 mg and 7.5 mg	Oxecta	2/7/2012
Ciclesonide	Nasal Spray	50 mcg	Omnaris	2/13/2012
Clofarabine	Injection	1 mg/mL, 20 mL vial	Clolar	2/23/2012
Levalbuterol Tartrate	Inhalation Aerosol	0.045 mg/actuation	Xopenex	2/27/2012
Desvenlafaxine Succinate	Extended-release Tablets	50 mg and 100 mg	Pristiq	2/29/2012

Moxifloxacin Hydrochloride	Ophthalmic Solution	0.5%	Moxeza	2/29/2012
Ketorolac Tromethamine	Nasal Spray	15.75 mg/spray	Sprix	3/12/2012
Sitagliptin Phosphate and Metformin Hydrochloride	Extended-release Tablets	50 mg/500 mg and 50 mg/1000 mg	Janumet XR	3/16/2012
Oxymorphone Hydrochloride	Extended-release Tablets	7.5 mg, 10 mg, and 15 mg	Opana ER (NDA 201655)	3/23/2012
Oxymorphone Hydrochloride	Extended-release Tablets	5 mg	Opana ER (NDA 201655)	3/26/2012
Ganirelix Acetate	Injection	250 mcg/0.5 mL, 1 mL PFS	Ganirelix Acetate	3/30/2012
Mesalamine	Extended-release Capsules	0.375 g	Apriso	4/3/2012
Oxymorphone Hydrochloride	Extended-release Tablets	20 mg, 30 mg, 40 mg	Opana ER (NDA 201655)	4/3/2012
Acetylcysteine	Injection	200 mg/mL, 30 mL vials	Acetadote	4/4/2012
Testosterone	Gel	1.62%	Androgel	4/6/2012
Regadenoson	Injection	0.08 mg/mL, 5 mL vial	Lexiscan	4/10/2012
Zolpidem Tartrate	Sublingual Tablets	1.75 mg and 3.5 mg	Intermezzo	4/10/2012

Ixabepilon	Injection	15 mg/vial and 45 mg/vial, single-use vials	Ixempra Kit	4/16/2012
Nitroglycerin	Sublingual Spray	400 mcg/spray, 4.9 g and 12 g bottles	Nitrolingual Pumpspray	4/17/2012
Duloxetine Hydrochloride	Delayed-release Capsules	40 mg	Cymbalta	5/10/2012
Tenofovir Disoproxil Fumarate	Tablets	150 mg, 200 mg, and 250 mg	Viread	5/17/2012
Albuterol Sulfate	Inhalation Aerosol	0.09 mg base per actuation	Pro-Air HFA	5/18/2012

Appendix 7: First-Filer Paragraph IV Challenges Filed Between 6/17/2012 and 6/16/2013 (Interval 4)

DRUG NAME	DOSAGE FORM	STRENGTH	RLD	DATE OF SUBMISSION
Sitagliptin Phosphate and Simvastatin	Tablets	100 mg/10 mg and 100 mg/40	Juvisync	6/19/2012
Glycopyrrolate	Oral Solution	1 mg/5 mL	Cuvposa	6/20/2012
Sitagliptin Phosphate and Simvastatin	Tablets	100 mg/20 mg	Juvisync	6/25/2012
Pemetrexed Disodium	For Injection	1000 mg/vial	Alimta	6/27/2012
Diclofenac Sodium	Topical Solution	1.5%	Pennsaid	7/11/2012
Azelaic Acid	Gel	15%	Finacea	7/27/2012
Imiquimod	Cream	3.75%	Zyclara	8/8/2012
Testosterone	Gel	10 mg/actuation	Fortesta	8/14/2012
Lubiprostone	Capsules	8 mcg and 24 mcg	Amitiza	8/20/2012
Drospirenone and Ethinyl Estradiol and Levomefolate Calcium and Levomefolate Calcium	Tablets	3 mg/0.03 mg/0.451 mg and 0.451 mg	Safyral	9/28/2012
Silodosin	Capsules	4	Rapaflo	10/9/2012

Buprenorphine Hydrochloride and Naloxone Hydrochloride	Sublingual Film	2 mg/0.5 mg and 8 mg/2 mg	Suboxone	10/15/2012
Phentermine Hydrochloride	Orally Disintegrating Tablets	15 mg and 30 mg	Suprenza	10/19/2012
Timolol Maleate	Ophthalmic Solution	0.5%	Istalol	10/19/2012
Sitagliptin Phosphate and Metformin Hydrochloride	Extended-release Tablets	100 mg/1000 mg	Janumet XR	10/22/2012
Lacosamide	Oral Solution	10 mg/mL	Vimpat	10/29/2012
Lacosamide	Tablets	50 mg, 100 mg, 150 mg, and 200 mg	Vimpat	10/29/2012
Fesoterodine Fumarate	Extended-release Tablets	4 mg and 8 mg	Toviaz	10/31/2012
Ritonavir	Capsules	100 mg	Norvir	10/31/2012
Sitagliptin Phosphate and Simvastatin	Tablets	50 mg/10 mg, 50 mg/20 mg, and 50 mg/40	Juvisync	11/6/2012
Drospirenone and Ethinyl Estradiol and Levomefolate Calcium and Levomefolate Calcium	Tablets	3 mg/0.02 mg/0.451 mg and 0.451 mg	Beyaz	11/13/2012
Diclofenac Potassium	Capsules	25 mg	Zipsor	11/14/2012
Rufinamide	Tablets	100 mg, 200 mg and 400 mg	Banzel	11/14/2012

Tapentadol Hydrochloride	Tablets	50 mg, 75 mg, and 100 mg	Nucynta	11/20/2012
Tapentadol Hydrochloride	Extended-release Tablets	50 mg, 100 mg, 150 mg, 200 mg, and 250 mg	Nucynta ER	11/20/2012
Prednisone	Delayed-release Tablets	1 mg, 2 mg, and 5 mg	Rayos	11/26/2012
Treprostinil Sodium	Injection	1 mg/mL, 2.5 mg/mL, and 5 mg/mL, 20 mL vial	Remodulin	12/7/2012
Plerixafor	Injection	24 mg/1.2 mL vials (20 mg/mL)	Mozobil	12/17/2012
Clindamycin Phosphate and Benzoyl Peroxide	Gel	1.2%/2.5%	Acanya	12/20/2012
Ertapenem	Injection	1 g/vial	Invanz	12/21/2012
Busulfan	Injection	6 mg/mL	Busulfex	12/26/2012
Isotretinoin	Capsules	30 mg and 40 mg	Absorica	12/31/2012
Estradiol	Vaginal Tablets	10 mcg	Vagifem	1/2/2013
Isotretinoin	Capsules	20 mg	Absorica	1/7/2013
Nicardipine Hydrochloride	Injection	0.1 mg/mL, 200 mL and 0.2mg/mL, 200 mL	Cardene in 0.86% Sodium Chloride in plastic container and Cardene 0.83%	1/9/2013

Milnacipran Hydrochloride	Tablets	12.5 mg, 25 mg, 50 mg, and 100 mg	Savella	1/14/2013
Icosapent Ethyl	Capsules	1 g	Vascepa	1/15/2013
Rivastigmine	Transdermal System Extended-release	13.3 mg/24 hr	Exelon	1/22/2013
Nicotine Polacrilex	Gum	2 mg	Nicorette	1/22/2013
Nicotine Polacrilex	Gum	4 mg	Nicorette	1/22/2013
Testosterone	Topical Solution	30 mg/1.5 mL	Axiron	1/29/2013
Febuxostat	Tablets	40 mg and 80 mg	Uloric	2/13/2013
Bupropion Hydrochloride	Extended-release Tablets	450 mg	Forfivo XL	2/28/2013
Oxcarbazepine	Extended-release Tablets	600 mg	Oxtellar XR	3/20/2013
Phentermine Hydrochloride	Orally Disintegrating Tablets	37.5 mg	Suprenza	3/22/2013
Oxcarbazepine	Extended-release Tablets	150 mg and 300 mg	Oxtellar XR	4/12/2013
Itraconazole	Oral Solution	10 mg/mL	Sporanox	5/3/2013
Iloperidone	Tablets	1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg, & 12 mg	Fanapt	5/6/2013
Darunavir Ethanolate	Tablets	800 mg	Prezista	5/14/2013

Buprenorphine Hydrochloride and Naloxone Hydrochloride	Sublingual Film	4 mg/1 mg	Suboxone	5/14/2013
Mesalamine	Suppository	1000 mg	Canasa	5/24/2013
Bendamustine Hydrochloride	Injection	25 mg/vial and 100 mg/vial	Treanda	6/4/2013
Buprenorphine	Transdermal System	5 mcg/hr, 10 mcg/hr, and 20 mcg/hr	Butrans	6/6/2013
Memantine Hydrochloride	Extended-release Capsules	7 mg, 14 mg, 21 mg, and 28 mg	Namenda XR	6/10/2013

Appendix 8: First-Filer Paragraph IV Challenges Filed Between 6/17/2013 and 6/16/2014 (Interval 5)

DRUG NAME	DOSAGE FORM	STRENGTH	RLD	DATE OF SUBMISSION	APPROVAL DATE OF CHALLENGED
Ethinyl Estradiol and Etonogestrel	Vaginal Ring	0.015 mg/24 hour and 0.12 mg/24 hour	Nuvaring	6/17/2013	10/3/2001
Isotretinoin	Capsules	10 mg	Absorica	6/19/2013	5/25/2012
Testosterone	Gel	1.62% (1.25 g and 2.5 g packets)	Androgel	6/19/2013	4/29/2011
Busulfan	Injection	6 mg/mL	Busulfex	6/20/2013	2/4/1999
Ertapenem	Injection	1 g/vial	Invanz	6/20/2013	11/21/2001
Nicardipine Hydrochloride	Injection	0.1 mg/mL, 200 mL and 0.2mg/mL, 200 mL	Cardene in 0.86% Sodium Chloride in plastic container and Cardene 0.83%	6/20/2013	1/30/1992
Nevirapine	Extended-release Tablets	400 mg	Viramune XR	6/21/2013	3/25/2011
Dronedarone Hydrochloride	Tablets	400 mg	Multaq	7/1/2013	7/1/2009

Donepezil Hydrochloride	Tablets	23 mg	Aricept	7/9/2013	7/23/2010
Prasugrel Hydrochloride	Tablets	5 mg and 10 mg	Effient	7/10/2013	7/10/2009
Levonorgestrel; Ethinyl Estradiol;Ethinyl Estradiol	Tablets	0.15 mg/0.02 mg, 0.15 mg/0.025 mg, 0.15 mg/0.03 mg and 0.01 mg	Quartette	7/10/2013	3/28/2013
Phentermine Hydrochloride and Topiramate	Extended-release Capsules	3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg	Qsymia	7/18/2013	7/17/2012
Bromfenac Sodium	Ophthalmic Solution	0.07%	Prolensa	7/26/2013	4/5/2013
Saxagliptin Hydrochloride	Tablets	2.5 mg and 5 mg	Onglyza	7/31/2013	7/31/2009
Saxagliptin Hydrochloride and Metformin Hydrochloride	Extended-release Tablets	5 mg/500 mg, 2.5 mg/1000 mg, and 5 mg/1000 mg	Kombiglyze XR	7/31/2013	11/5/2010
Doxylamine Succinate and Pyridoxine Hydrochloride	Delayed-release Tablets	10 mg/10 mg	Diclegis	8/1/2013	4/8/2013
Methylphenidate Hydrochloride	Extended-release Oral Suspension	5 mg/mL	Quillivant XR	8/2/2013	9/27/2012

Hydromorphone Hydrochloride	Tablets	2 mg, 4 mg, and 8 mg	Dilaudid	8/5/2013	1/11/1984
Pitavastatin Calcium	Tablets	1 mg, 2 mg, and 4 mg	Livalo	8/5/2013	8/3/2009
Asenapine Maleate	Sublingual Tablets	5 mg and 10 mg	Saphris	8/13/2013	8/13/2009
Bepotastine Besilate	Ophthalmic Solution	1.5%	Bepreve	9/9/2013	9/8/2009
Tolvaptan	Tablets	15 mg and 30 mg	Samsca	9/23/2013	5/19/2009
Pralatrexate	Injection	20 mg/mL and 40 mg/2 mL	Folotyn	9/24/2013	9/24/2009
Tacrolimus	Extended-release Capsules	0.5 mg, 1 mg, and 5 mg	Astagraf XL	9/24/2013	7/19/2013
Everolimus	Tablets	0.25 mg, 0.5 mg, and 0.75 mg	Zortress	9/30/2013	4/20/2010
Buprenorphine Hydrochloride and Naloxone Hydrochloride Dihydrate	Sublingual Tablets	1.4 mg/0.36 mg and 5.7 mg/1.4 mg	Zubsolv	10/22/2013	7/3/2013
Balsalazide Disodium	Tablets	1.1 g	Giazo	11/5/2013	2/3/2012
Romidepsin	Injection	10 mg/vial	Istodax	11/5/2013	11/5/2009
Zolmitriptan	Nasal Spray	5 mg/spray	Zomig	11/14/2013	9/16/2013
Glycerol Phenylbutyrate	Oral Liquid	1.1 g/mL	Ravicti	11/19/2013	2/1/2013

Rotigotine	Extended-release Transdermal Film	1 mg/24 hr, 2 mg/24 hr, 3 mg/24 hr, 4 mg/24 hr, 6 mg/24 hr, and 8 mg/24 hr	Neupro	11/26/2013	5/9/2007
Calcium Acetate	Oral Solution	667 mg/5 mL	Phoslyra	12/5/2013	4/18/2011
Aliskiren Hemifumarate	Tablets	150 mg and 300 mg	Tekturna	12/13/2013	3/5/2007
Desoximetasone	Topical Spray	0.25%	Topicort	12/18/2013	4/11/2013
Levoleucovorin Calcium	Injection	50 mg/vial	Fusilev	12/19/2013	3/7/2008
Tapentadol	Oral Solution	20 mg/mL	Nucynta	12/20/2013	10/15/2012
Dexmedetomidine	Injection	4 mcg/mL, 50 mL and 100 mL vials	Precedex	12/26/2013	12/17/1999
Eltrombopag Olamine	Tablets	50 mg and 75 mg	Promacta	1/7/2014	11/20/2008; 9/8/2009
Dalfampridine	Extended-release Tablets	10 mg	Ampyra	1/22/2014	1/22/2010
Imatinib Mesylate	Capsules	400 mg	Gleevec	1/24/2014	4/18/2003
Esmolol Hydrochloride	Injection	10 mg/mL, 250 mL infusion bags and 20 mg/mL, 100 mL	Brevibloc	1/31/2014	2/16/2001
Thalidomide	Capsules	150 mg	Thalomid	2/3/2014	1/10/2007

Eltrombopag Olamine	Tablets	12.5 mg and 25 mg	Promacta	2/4/2014	11/20/2008; 10/20/2011
Moxifloxacin Hydrochloride	Injection	1.6 mg/mL	Avelox in Sodium Chloride 0.8% in plastic container	2/7/2014	11/30/2001
Lamotrigine	Extended-release Tablets	25 mg, 50 mg, 100 mg, 200 mg, 250 mg, and 300 mg	Lamictal XR	2/12/2014	8/24/1998
Glatiramer Acetate	Injection	40 mg/mL, 1 mL pre-filled syringe	Copaxone	2/26/2014	1/28/2014
Hydrocodone Bitartrate	Extended-release Capsules	10 mg, 15 mg, 20 mg, 30 mg, 40 mg, and 50 mg	Zohydro ER	2/26/2014	10/25/2013
Sorafenib Tosylate	Tablets	200 mg	Nexavar	2/28/2014	12/20/2005
Aliskiren and Hydrochlorothiazide Hemifumarate	Tablets	150 mg/12.5 mg, 150 mg/25 mg, 300 mg/12.5 mg, 300 mg/25 mg	Tekturna HCT	3/7/2014	1/18/2008
Topiramate	Extended-release Capsules	200 mg	Trokendi XR	4/3/2014	8/16/2013
Paroxetine	Capsules	7.5 mg	Brisdelle	4/7/2014	6/28/2013

Esomeprazole Magnesium	Delayed-release Capsules	20 mg	Nexium (OTC)	4/24/2014	2/20/2001
Dofetilide	Capsules	0.125 mg, 0.25 mg, and 0.5 mg	Tikosyn	5/1/2014	10/1/1999
Topiramate	Extended-release Capsules	25 mg, 50 mg, and 100 mg	Trokendi XR	5/12/2014	8/16/2013
Unoprostone Isopropyl	Ophthalmic Solution	0.15%	Rescula	5/12/2014	8/3/2000
Ribavirin	For Inhalation Solution	6 gm/vial	Virazole	5/22/2014	12/31/1985
Carbamazepine	Extended-release Capsules	100 mg	Equetro	5/23/2014	12/10/2004
Nicotine	Transdermal System	7 mg/24 hrs, 14 mg/24 hrs, and 21 mg/24 hrs	Nicoderm CQ	5/30/2014	5/2/1997
Sapropterin Dihydrochloride	Tablets	100 mg	Kuvan	5/30/2014	12/13/2007
Diclofenac Sodium	Topical Solution	2.0%	Pennsaid	6/3/2014	1/16/2014
Exenatide	Injection	250 mg/mL, 1.2 mL and 2.4 mL prefilled syringe	Byetta	6/11/2014	4/28/2005
Testosterone Undecanoate	Injection	250 mg/mL	Aveed	6/11/2014	3/4/2014

Azelastine Hydrochloride and Fluticasone Propionate	Nasal Spray	137 mcg/50 mcg per spray	Dymista	6/13/2014	5/1/2012
Rufinamide	Oral Suspension	40 mg/mL	Banzel	6/16/2014	3/3/2011
Micafungin Sodium	For Injection	50 mg/vial and 100 mg/vial	Mycamine	6/16/2014	3/16/2005

*ANDA withdrawn[242]

[242] Note that withdrawn ANDAs were included in this study, because the study is assessing the incentive of generics to file Paragraph IV challenges in the first place, and thus is only concerned with ANDAs that are filed—even if the ANDA is never approved or if it is later withdrawn.