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Issues in the Interpretation of 180-Day Exclusivity

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I. INTRODUCTION

Congress created 180-day exclusivity for generic drug applicants in the 1984 Hatch-Waxman amendments to the Federal Food, Drug, and Cosmetic Act (FDCA)¹ and amended it substantially in the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA).² The core concept of this exclusivity as it has been applied by FDA and the courts is that the first generic drug applicant to challenge an innovator's patent is entitled to six months of exclusivity against subsequent patent challengers for the same innovator drug. The 180-day exclusivity provision is governed by sections 505(j)(5)(B)(iv) and 505(j)(5)(D) of the FDCA, and it is intended to encourage generic applicants to challenge innovator patents. Although the basic idea is simple and the language enacted in 1984 was correspondingly brief, over the years the provision has given rise to a substantial number of interpretive disputes, both at the agency and in the courts. The courts are still grappling with interpretation of the 1984 provision, and it is already apparent that the amended language will trigger additional disputes.

An earlier article in this journal traced the history of the 180-day exclusivity provision from 1984 through its amendment in 2003 and court cases in 2004.³ This article updates the earlier piece through the end of 2006 but is arranged by issue rather than in a chronology. Part II presents the original and amended statutory language. For the most part, the amended language applies only to abbreviated new drug applications (ANDAs) filed after December 8, 2003, provided there was no paragraph IV certification to the reference drug prior to that date. We refer to these as "new ANDAs" and to all other ANDAs as "old ANDAs." Part III presents the interpretive issues that have been addressed by FDA and/or the courts and describes their resolution with respect to old ANDAs and, where different, new ANDAs.⁴

II. STATUTORY LANGUAGE AND EFFECTIVE DATES

A. *Original Statutory Language*

Between 1984 and 2003, section 505(j)(5)(B)(iv) of the FDCA provided that "[i]f the [abbreviated new drug] application contains a certification described in subclause

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¹ Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984).

² Pub. L. No. 108-173, 117 Stat. 2066 (2003).

³ Erika Lietzan, *A Brief History of 180-Day Exclusivity under the Hatch-Waxman Amendments*, 59 FOOD & DRUG L.J. 287 (2004). A subsequent update traced developments in 2004. Erika Lietzan, *2004 Update—180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act*, 59 FOOD & DRUG L.J. 459 (2004).

⁴ The earlier article identified the cases by party and roman numeral (e.g., Purepac I, Purepac II, Mylan I, Mylan II). The growing number of disputes involving the same companies has rendered this system unwieldy. Where shorthand is called for, we generally refer to the case by the active ingredient of the innovator's drug.

(IV) of paragraph (2)(A)(vii) [otherwise known as a “paragraph IV certification”] and is for a drug for which a previous application has been submitted under this subsection continuing [sic “containing”] such a certification, the application shall be made effective not earlier than one hundred and eighty days after—(I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or (II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed, whichever is earlier.”⁵ Put another way, the first⁶ generic applicant to file an ANDA containing a paragraph IV certification was to be awarded 180 days of marketing exclusivity, during which FDA could not approve a subsequent ANDA that challenged a patent for the same drug product. The 180 days was calculated from either the date of the first commercial marketing of the generic drug product by the first applicant or the date of a court decision declaring the patent invalid or not infringed, whichever was sooner.⁷

B. Amended Statutory Language

Section 505(j)(5)(B)(iv) now provides that “[i]f the [abbreviated new drug] application contains a certification described in paragraph (2)(A)(vii)(IV) [a paragraph IV certification] and is a drug for which a first applicant has submitted an application containing such a certification, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant.”⁸ In short, as before, the first generic applicant to file an ANDA⁹ containing a paragraph IV certification is awarded 180 days of marketing exclusivity, during which FDA may not approve a subsequently filed ANDA that challenged a patent for the same drug product. The exclusivity period is now calculated from the date of the first commercial marketing of the drug product (including the listed drug product) by a first applicant. A court decision does not by itself start the 180 days for new ANDAs.

In addition to making these seemingly modest changes to section 505(j)(5)(B)(iv), Congress added an elaborate provision governing a new statutory concept: forfeiture of 180-day exclusivity. Under section 505(j)(5)(D), the 180-day exclusivity period is forfeited by a first applicant if it fails to market the drug by the later of: 1) 75 days after the date on which approval of its application is effective, or 30 months after its application was submitted, whichever is earlier; or 2) 75 days after the date on which, as to each patent that is the subject of a paragraph IV certification by the first applicant (qualifying it for exclusivity), a court has found the patent invalid or not infringed, a court signs a settlement order or consent decree finding the patent invalid or not infringed, or the patent information is withdrawn by the holder of the approved NDA. The first applicant also forfeits the exclusivity period if any

⁵ 21 U.S.C. § 355(j)(5)(B)(iv) (1984) (amended 2003).

⁶ Although the statute refers to “previous” ANDAs, it has been interpreted over time to mean that only the first applicant is eligible.

⁷ Shortly after enactment of the 2003 amendments, Senator Hatch noted the “incongruity” of “awarding 180 days both for a successful invalidity challenge and a non-infringement action.” The latter, he noted, benefits only a specific party, the non-infringing generic manufacturer, rather than clearing the way for generic market entry in general. 149 CONG. REC. S 16104 (daily ed., Dec. 9, 2003) (Sen. Hatch).

⁸ 21 U.S.C. § 355(j)(5)(B)(iv) (2003).

⁹ As discussed below, there can be more than one “first applicant” eligible for 180-day exclusivity.

of the following occurs: 1) the first applicant withdraws its application or FDA considers it withdrawn because it did not meet the requirements for approval; 2) the first applicant amends or withdraws all of the paragraph IV certifications that qualified it for exclusivity; 3) the first applicant fails to obtain tentative approval of its application within 30 months after it was filed (unless the failure is caused by a change in or review of the requirements for approval of the application imposed after it was filed); 4) the first applicant enters into an agreement with another ANDA applicant, the NDA holder, or a patent holder, and the Federal Trade Commission (FTC) or a court has found that the agreement violates the antitrust laws; or 5) all of the patents as to which the first applicant filed a paragraph IV certification qualifying it for exclusivity have expired. Forfeiture events are determined individually for each first applicant. If all first applicants forfeit their 180-day exclusivity, any subsequent ANDA approval may be made effective immediately—that is, exclusivity does not “roll over” to a subsequent ANDA applicant.¹⁰

Congress also added definitions to the statute for “180-day exclusivity period,” “first applicant,” “substantially complete application,” and “tentative approval.” Some of these reflect new concepts. A “first applicant” is “an applicant that, on the first day on which a substantially complete application containing a [paragraph IV certification] is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a [paragraph IV certification] for the drug.” A “substantially complete application” means “an application under this subsection that on its face is sufficiently complete to permit a substantive review and contains all the information required by [section 505(j)(2)(A)].”¹¹

C. Effective Dates

With one exception, the amended rules apply only to ANDAs filed after December 8, 2003, and only if there was no paragraph IV certification to the listed drug prior to December 8.¹² The exception relates to the “court decision” trigger for exclusivity, described below in section III-E. Litigation even at the end of 2006 continues to revolve around the old rules.

III. INTERPRETIVE ISSUES

As noted above, the original statutory language was sparse. FDA proposed regulations in 1989 and finalized them in 1994. There has been substantial litigation over the provisions and regulations, which has led to further changes implemented by guidance and regulation. Although FDA proposed substantial changes to the regulations in 1999, the proposal was later withdrawn. Portions of it, however, continue to be agency policy.

We discuss below twelve interpretive issues that have been the subject of debate since enactment of 180-day exclusivity in 1984. The issues are arranged conceptually. We begin with issues relating to eligibility for exclusivity and timing and conclude with issues concerning enjoyment of the exclusivity, like transfer of it and “roll-over” to subsequent applicants. Most of the current debate relates to

¹⁰ 21 U.S.C. § 355(j)(5)(D).

¹¹ 21 U.S.C. § 355(j)(5)(B)(iv)(II).

¹² See Pub. L. No. 108-173 § 1102(b). See FDA, Draft Guidance for Industry, Listed Drugs, 30-Month Stays, and Approval of ANDAs and 505(b)(2) Applications Under Hatch-Waxman, as Amended by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (Oct. 2004).

whether exclusivity attaches to the listed patent or the reference product (see section III-B) and to the effect of changes in the status of the listed patent (e.g., expiry and delisting) (see sections III-F and III-G). A variety of other issues—such as whether the first applicant must be sued and prevail in patent litigation in order to receive exclusivity—were resolved long ago.

A. When Must an ANDA Applicant Send Notice of Paragraph IV Certification to Innovator To Earn 180-Day Exclusivity?

Old ANDAs: Exclusivity attaches to the first applicant to file a substantially complete ANDA with a paragraph IV certification. In the case of an amendment to an ANDA for a newly listed patent, if notice is provided after the certification is filed, in violation of the statute's notice provision, agency policy constructively moves the certification's filing date to the day on which the applicant mailed the notice. This policy was sustained as a reasonable exercise of agency discretion.

FDA published final regulations to implement the 180-day provision in October 1994.¹³ Section 314.107(c) stated that if an ANDA contained a paragraph IV certification and was for a generic copy of the same listed drug “for which one or more substantially complete abbreviated new drug applications were previously submitted” containing a paragraph IV certification, and “the applicant submitting the first application has successfully defended against a suit for patent infringement brought within 45 days of the patent owner’s receipt of notice,” then approval of the second ANDA would be made effective no sooner than the earlier of 1) the date the first applicant “first commences commercial marketing of its drug product,” or 2) the date “of a decision of the court holding the relevant patent invalid, unenforceable, or not infringed.”¹⁴ (The “successful defense” requirement is discussed in section III-C, below.) FDA stated that the “applicant submitting the first application” is the applicant that submits an application that both 1) is substantially complete, and 2) contains a paragraph IV certification, prior to the submission of any other application for the same listed drug that both is substantially complete and contains the same certification. In other words, the first applicant to satisfy both requirements would earn exclusivity. According to the regulation, a “substantially complete” application contains “the results of any required bioequivalence studies, or, if applicable, a request for a waiver of such studies.”¹⁵

¹³ 54 Fed. Reg. 28872 (July 10, 1989) (proposed rule); 59 Fed. Reg. 50338 (Oct. 3, 1994) (final rule).

¹⁴ The statute refers only to a decision holding the patent invalid or not infringed. FDA added “unenforceable.” See 59 Fed. Reg. at 50339 (“The agency, on its own initiative, has also amended [the proposed regulations] to include a reference to unenforceable patents. ... The alternative interpretation ... would be contrary to Congress’ obvious intent in allowing patent challenges under section 505 of the act and would lead to absurd results.”).

¹⁵ In the preamble to the proposed regulation, FDA had added that a “required bioequivalence study is one that meets any FDA guidance document or is otherwise reasonable in design and purports to show that the drug product for which the applicant seeks exclusivity is bioequivalent to the listed drug.” 54 Fed. Reg. at 28895. Rejecting concerns about so-called “file first fix later” practices on the part of generic manufacturers, however, FDA declined to establish criteria to determine whether changes to an ANDA have been so substantial that it can no longer be considered to have been the first filed. Instead, it would rely on its decision in 1992 to no longer accept ANDAs lacking complete bioequivalence study data (if such data are required for approval) and use a “case-by-case approach” to ANDA changes. 59 Fed. Reg. at 50354. FDA added, however that “[a] decision by the agency after receipt of an application that the bioequivalence information is inadequate for approval does not necessarily mean that the application was not substantially complete at the time of submission.” This effectively undermined the 1992 solution to what FDA itself referred to as a “significant and unwarranted expenditure of resources in reviewing applications that had little potential for approval.” *Id.*

Congress did not change the substance of this requirement in 2003. Under the amended statutory language, if an ANDA contains a paragraph IV certification and “is for a drug for which a first applicant has submitted an application containing such a certification” (i.e., is for a drug for which someone else submitted an ANDA earning it eligibility for exclusivity) the application “shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant.” The term “180-day exclusivity period” means “the 180-day period ending on the day before the date on which an application submitted by an applicant other than a first applicant could become effective under this clause.” As noted above, the term “first applicant” means “an applicant that, on the first day on which a substantially complete application containing a [paragraph IV] certification is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a [paragraph IV certification].”¹⁶ And, as noted earlier, a “substantially complete application” is “an application under this subsection that on its face is sufficiently complete to permit a substantive review and contains all the information required” under section 505(j)(2)(A) of the FDCA.

Because the statute requires the generic applicant to file a certification at FDA and provide notice of the certification to the patent owner and NDA holder, there is in fact a third eligibility requirement—the notice. FDA and the courts addressed the question of timing of this notice in two cases involving Purepac. The first was one of several court decisions in the dispute between Purepac and TorPharm over who would have 180-day exclusivity in marketing generic copies of Neurontin (gabapentin). This particular dispute involved a drug composition patent submitted by Warner-Lambert to FDA after both TorPharm and Purepac had filed their ANDAs. Both generic applicants amended their applications to include paragraph IV challenges to the patent in question. Purepac mailed its amended ANDA to FDA on May 25, 2000, and FDA received the amended ANDA on May 26. But Purepac waited until June 13 to send notice to the NDA holder. TorPharm, in contrast, mailed its amended ANDA and sent notice to the innovator on the same date, June 13. FDA received TorPharm’s amended ANDA on June 16 and deemed the new certification filed on that day. The agency concluded that the penalty for Purepac’s failure to provide notice simultaneously with its amended ANDA, as required by 21 U.S.C. § 355(j)(2)(B)(iii) and 21 C.F.R. § 314.95(d), should be postponement of the certification’s effective date—rather than nullification of the certification, as TorPharm had argued. Because Purepac still completed both tasks

¹⁶ The phrase “lawfully maintain” was added in the Conference Report. One cannot “lawfully maintain” a patent challenge if one loses the ensuing litigation. And the failure-to-market forfeiture event applies only to patents for which a paragraph IV certification has been lawfully maintained. Thus, if an ANDA applicant loses a patent challenge (for example, to a drug substance patent), that patent challenge no longer qualifies the applicant for exclusivity. The 75-day forfeiture clock would begin to run as soon as the eligible applicant prevails on a different patent. Put another way, if the ANDA applicant challenges a formulation patent but adds a frivolous challenge to a drug substance patent, prevails on the formulation patent and loses on the substance patent, then the 75-day clock begins to run. This precludes parking exclusivity by challenging two patents, knowing the challenger will lose on the patent that is not due to expire for some time. Now the generic applicant forfeits exclusivity, if it cannot market within 75 days of the appellate decision on a patent it successfully challenged. For a discussion of this issue, see *Eli Lilly, Hatch 180-Day Award Concerns May Slow Hatch-Waxman Deal*” www.OutsideHealthPolicy.com (Aug. 7, 2003); *CBO Says Generic Rx Language in Both Medicare Bills Could Delay Drug Competition*, HEALTH CARE DAILY (Sept. 2, 2003); Robert A. Armitage, Testimony on Behalf of Eli Lilly and Company Before the Committee on the Judiciary, United States Senate, on the “Greater Access to Affordable Pharmaceuticals Act” (Aug. 1, 2003).

before TorPharm did, FDA awarded Purepac exclusivity. The district court found this to be a reasonable exercise of the agency's discretion, and the D.C. Circuit affirmed on January 20, 2004.¹⁷

On October 29, 2003, Purepac filed suit against FDA concerning a different drug, challenging the agency's view that when an ANDA applicant submits an amendment to certify to a newly listed patent, the controlling date for exclusivity purposes is the date it sent notice to the patent holder and NDA holder. In July 2002, Purepac had filed an ANDA seeking to market a generic version of Glucophage XR (metformin hydrochloride extended release). On November 5, 2003, PTO issued a new patent claiming metformin hydrochloride. FDA listed the patent in the *Orange Book* on November 21. On November 5, and on every subsequent business day through November 25, Purepac submitted a paragraph IV certification to that patent. On November 27, Purepac sent notice of the paragraph IV certification to Bristol-Myers Squibb (BMS), the patent holder. BMS received that notice letter on December 3. IVAX filed an original ANDA after Purepac amended its ANDA, but before Purepac sent notice to BMS. IVAX included a paragraph IV certification to the second patent and notified BMS at that time. FDA awarded exclusivity to IVAX and not to Purepac, reasoning that the controlling dates for determination of first applicant status were Purepac's notice date (because Purepac was amending its ANDA) and IVAX's certification date (because IVAX was filing an original ANDA). FDA approved IVAX's product on October 28 and the company began shipping the product that same day. Purepac immediately obtained a restraining order (in a case often called Purepac II), and FDA suspended its approval of the IVAX product on October 30. The parties settled the lawsuit by agreeing to share profits during the exclusivity period, and the judge dismissed the case on November 26, 2003.¹⁸

In 2003, Congress amended the notice provision—not the 180-day exclusivity provision—to specify that a paragraph IV notice must be provided, in the case of an original ANDA, no later than 20 days after the date of the postmark on the notice from FDA that the ANDA has been filed.¹⁹ It did not change the statutory language stating that in the case of an ANDA amendment, notice must be provided when the generic applicant submits the amendment in question.²⁰ Both IVAX and Mylan contend, however, that Congress effectively directed FDA to apply the same rule to original and amended ANDAs—i.e., that it meant to overrule the FDA rule at issue in the metformin case.²¹

B. *What Are the Differences between Shared and Multiple Exclusivity?*

The related issues of “shared exclusivity” and “multiple exclusivity” arise in three situations: 1) multiple generic applicants submit ANDAs with paragraph IV

¹⁷ *Purepac Pharmaceutical Co. v. Thompson*, 354 F.3d 877 (D.C. Cir. 2004), *aff'g* *TorPharm, Inc. v. Thompson*, 260 F.Supp.2d 69 (D.D.C. 2003); *see also* *TorPharm Rebuffed on Bid to Overturn FDA Decision Awarding Exclusivity to Purepac*, BNA PHARMACEUTICAL LAW & INDUSTRY REPORT (Jan. 23, 2004); *Appeals Court Backs FDA: Purepac Gets Gabapentin 180-Day Award*, FDA WEEK (Jan. 23, 2004).

¹⁸ *See IVAX, Purepac Settle Metformin 180-Day Generic Drug Exclusivity Suit*, FDA WEEK (Dec. 5, 2003); *Glucophage XR Settlement: Purepac, IVAX Split Generic Profits for 180 Days*, HEALTH NEWS DAILY (Nov. 28, 2003).

¹⁹ 21 U.S.C. § 355(j)(2)(B)(ii)(II).

²⁰ *See* 21 U.S.C. § 355(j)(2)(B)(ii)(I).

²¹ *IVAX, Citizen Petition*, Docket No. 2004P-0520 (Nov. 19, 2004) (arguing that the notice date should control in both cases) (withdrawn); *Mylan Pharmaceuticals, Inc., Citizen Petition*, Docket No. 2006P-0245 (June 12, 2006) (same) (pending).

certifications to the same patent(s) on the same first day; 2) multiple ANDA applicants submit ANDAs with paragraph IV certifications for different dosage forms or strengths of the same innovator drug product; and 3) multiple ANDA applicants submit ANDAs with paragraph IV certifications to different listed patents for the same innovator drug product. Stakeholders use the phrases “shared exclusivity” and “multiple exclusivity” to mean different things. We use “shared exclusivity” to refer to the first situation described above, where two or more companies file first ANDAs on the same day, certifying to the same listed patent(s), and thus have the same claim to exclusivity to share.

If multiple applicants file substantially complete ANDAs with paragraph IV certifications on the same day as the first to do so, those applicants can share exclusivity. For old ANDAs, FDA developed this policy following invalidation of the successful defense requirement (see section III-C). For new ANDAs, it is required by the amended statutory language.

FDA interprets the rules governing old ANDAs as permitting “patent-by-patent” exclusivity, which can create multiple exclusivity periods for a product. Although the district court in D.C. is currently divided on the issue, the most recent decision found FDA’s interpretation to be permissible. In 2003, Congress provided that exclusivity should be “product-by-product,” rather than “patent-by-patent.”

Different Strengths. In a 1999 decision involving generic copies of Zantac, the D.C. Circuit resolved in the affirmative the question whether applicants who market different dosages of a drug are eligible for separate 180-day exclusivity periods.²² Among the ranitidine hydrochloride products sold by Glaxo as Zantac were 150 mg and 300 mg tablets, both prescription drug products intended for the treatment of ulcers, and 75 mg tablets, sold over the counter (OTC) for the treatment of heartburn. Genpharm was the first to file an ANDA for the 150 and 300 mg tablets, and its exclusivity ran in 1997. FDA had since approved additional ANDAs for those strengths. Novopharm was the first to file an ANDA with a paragraph IV certification for a 75 mg OTC product and claimed it was therefore eligible for 180-day exclusivity. Apotex sought immediate approval of its own 75 mg tablets, however, on the theory that FDA may not grant separate exclusivity periods for ANDA applications that concern patents listed with respect to previously approved drugs of different strengths. The district court disagreed, holding that permitting separate exclusivity periods for separate drug strengths is consistent with the statute, which requires that an ANDA must contain, among other things, “information to show that the route of administration, the dosage form, and the *strength of the new drug* are the same as those of the listed drug.”²³ (This holding is consistent with FDA’s practice of giving each strength a separate listing in the *Orange Book*.) For similar reasons, generic copies of tablet forms and capsule forms of the same drug are eligible for separate 180-day exclusivity periods.²⁴

Different Patents. While the appeal in Apotex’s ranitidine case was pending, FDA responded to two citizen petitions, stating that generic applicants who certify to different patents covering the same listed drug may hold exclusivity simultaneously.

²² Apotex v. Shalala, 53 F.Supp.2d 454 (D.D.C. 1999), *aff’d*, 1999 WL 956686 (D.C. Cir. 1999).

²³ *Id.* at 456 (emphasis added).

²⁴ See, e.g., Mylan Pharmaceuticals, Inc. v. Shalala, 81 F.Supp.2d at 30, 35 n.8 (D.D.C. 2000) (“The tablet and capsule forms of the drug, however, are distinct products for FDA purposes and are thus each eligible for their own exclusivity.”).

American Pharmaceutical Partners (APP) and Pharmachemie each had requested that FDA stay approval of any ANDA other than its own for a generic version of Platinol-AQ (cisplatin injection). Pharmachemie had filed the first substantially complete ANDA with a paragraph IV certification to one patent listed for the product. The patent holder did not file suit, and the patent expired. APP had filed the first substantially complete ANDA with a paragraph IV certification to a different patent listed for the product. Pharmachemie then did the same thing. BMS filed suit against both companies, and each argued that it had been the first to file a paragraph IV certification for the drug. FDA defined the controversy as "whether multiple ANDA applicants each can be eligible for 180-day exclusivity because each applicant was the first to file a paragraph IV certification as to a different patent for the listed drug."²⁵ The issue was new. A prior agency policy—just invalidated by a court—had held that a generic applicant must prevail in patent litigation in order to receive exclusivity (see discussion of the successful defense requirement in section III-C below). This FDA policy had effectively precluded more than one applicant from earning exclusivity. With the elimination of this rule, multiple eligible first applicants became a possibility. FDA concluded in the petition response that both applicants could be entitled to exclusivity. FDA stated that its regulations "direct that the inquiry is whether one or more substantially complete ANDAs were submitted that contained a certification that the same patent was invalid, not enforceable, or would not be infringed." Therefore, the agency wrote, "eligibility for exclusivity is to be determined on a patent-by-patent basis."²⁶ In this instance, however, FDA granted exclusivity only to APP. The agency reasoned that Pharmachemie's exclusivity had terminated automatically when the patent in question expired. (This theory was challenged in a citizen petition relating to Vasotec (enalapril), filed by TorPharm,²⁷ but the company withdrew the petition before FDA decided it.)

The agency indicated that it intended to revise its regulations in light of the court decision invalidating the successful defense requirement and to address the question of "multiple 180-day exclusivity periods."²⁸ Four days later, FDA published its proposal.²⁹ It made three relevant decisions. First, multiple applicants could share exclusivity: all ANDAs for a particular drug, with paragraph IV certifications, received on the same day would be eligible for exclusivity, so long as no ANDAs had been filed on a previous day.³⁰ Second, as the agency had decided in the Apotex ranitidine case, applicants would be eligible for a separate exclusivity period for each strength of the drug product that was a different listed drug.³¹ Third, exclusivity would be product-by-product. Specifically, "[i]f there are multiple patents for the listed drug, the applicant submitting the first paragraph IV certification to any listed patents will be the only ANDA applicant eligible for exclusivity for that drug."³² FDA withdrew the proposal in 2002.³³

The agency confirmed the first decision as agency policy, regardless of the withdrawal of the 1999 proposal, in a 2003 guidance document. In August 2000, Zenith

²⁵ See FDA, Response to APP and Pharmachemie Citizen Petitions, Docket No. 99P-1271 (Aug. 2, 1999) at 3.

²⁶ FDA, Response to APP and Pharmachemie Citizen Petitions, Docket No. 99P-1271 (Aug. 2, 1999) at 3.

²⁷ TorPharm, Citizen Petition, Docket No. 99P-5317 (Dec. 7, 1999).

²⁸ FDA, Response to APP and Pharmachemie Citizen Petitions, Docket No. 99P-1271 (Aug. 2, 1999), at 3.

²⁹ 64 Fed. Reg. 42873 (Aug. 6, 1999).

³⁰ *Id.* at 42876-42877.

³¹ *Id.* at 42881.

³² *Id.* at 42875.

³³ 67 Fed. Reg. 66593 (Nov. 1, 2002).

Goldline Pharmaceuticals petitioned FDA for a determination that “all [ANDAs] containing a paragraph IV certification delivered to FDA’s Office of Generic Drugs (OGD) on the same business day are submitted at the same time for 180-day exclusivity purposes,” each receiving 180 days of exclusivity without being subject to the other’s exclusivity.³⁴ In an accompanying petition, Zenith Goldline sought a stay of approval of a competitor’s ANDA for alendronate sodium tablets—marketed by the innovator as Fosamax—until its own ANDA received approval.³⁵ On May 13, 2003, Ranbaxy Laboratories submitted a citizen petition making the same request as Zenith Goldline had made, with respect to generic versions of Provigil (modafinil).³⁶

In July 2003, FDA issued a guidance document that permitted “shared exclusivity” in this situation and wrote both petitioners to explain that the guidance “essentially” granted their citizen petitions.³⁷ The agency explained that when, on the same day, more than one applicant submits an ANDA for the same drug containing a paragraph IV certification to a listed patent, and no such certification was submitted previously, all the applicants will share exclusivity. Exclusivity will be triggered for all first applicants for a specific listed patent when one of them begins to market its product (or on the date of any court decision finding that patent invalid, unenforceable, or not infringed, if earlier). The commercial marketing trigger would begin the 180-day period as to all listed patents; a relevant court decision would trigger it only as to patents addressed in the decision. This result is also required by the 2003 amendments to the statutory language, which precludes approval for 180 days after first commercial marketing by “any” first applicant, and which precludes rollover if “all first applicants” forfeit their exclusivity.³⁸

The question whether exclusivity is patent-by-patent where two patents are listed for the same listed drug and there is a separate first ANDA for each, not filed on the same day, has proven more controversial. TorPharm was the first applicant to file an ANDA for a generic version of Paxil (paroxetine hydrochloride). TorPharm was also the first to submit a paragraph IV certification challenging the only paroxetine patent listed at the time. On July 30, 2003, FDA approved TorPharm’s ANDA. On the same day, FDA determined that Alphapharm, which had an ANDA pending, would be entitled to share exclusivity with TorPharm because it was the first to file a paragraph IV certification to a later-listed paroxetine patent. Thus, Alphapharm’s product could be approved when its patent situation permitted. TorPharm launched its product on September 8, 2003, meaning that its 180-day exclusivity would therefore expire on March 6, 2004. TorPharm filed suit in November 2003, seeking a declaration that FDA’s shared exclusivity approach was unlawful and an order enjoining approval of any other ANDA for paroxetine until March 6, 2004. On January 2, the judge overturned FDA’s decision and permanently enjoined FDA from approving the Alphapharm ANDA (or any other ANDA for the same dosages of paroxetine

³⁴ Zenith Goldline Pharmaceuticals, Citizen Petition, Docket No. 00P-1445 (Aug. 8, 2000).

³⁵ Zenith Goldline Pharmaceuticals, Petition for Stay of Action, Docket No. 00P-1443 (Aug. 8, 2000).

³⁶ Ranbaxy Laboratories, Citizen Petition, Docket No. 03P-0217 (May 13, 2003).

³⁷ FDA, Guidance for Industry, 180-Day Exclusivity when Multiple ANDAs Are Submitted on the Same Day (July 2003); FDA, Letter to IVAX Pharmaceuticals, Docket No. 00P-1443 (July 31, 2003); FDA, Letter to IVAX Pharmaceuticals, Docket No. 00P-1445 (July 31, 2003); FDA, Letter to Venable, Baetjer, Howard & Civiletti, Docket No. 03P-02171 (July 31, 2003).

³⁸ See 21 U.S.C. § 355(j)(5)(B)(iv)((II)(bb)) (defining “first applicant” to mean “an applicant that, on the first day on which a substantially complete application containing a [paragraph IV certification] is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a [paragraph IV certification] for the drug.”); see also 149 CONG. REC. S15584 (daily ed., Nov. 25, 2003) (Senator Kennedy) (“and the exclusivity is available to more than one generic applicant, if they all challenge patents on the same day”); 21 U.S.C. § 355(j)(5)(D)(III) (if all first applicants forfeit exclusivity, “no applicant shall be eligible”).

hydrochloride) until expiration of TorPharm's exclusivity.³⁹ The Department of Justice appealed for FDA,⁴⁰ but the contested exclusivity period expired on March 6, 2004, and on December 17, 2004, the D.C. Circuit dismissed the appeal as moot.⁴¹

Although this district court's decision on paroxetine would appear to have settled the issue, another judge on the same court took the opposite view. This case, also, involved TorPharm—now known as Apotex—but a different drug, Neurontin (gabapentin). Purepac submitted an ANDA in March 1998 and was the first to submit a paragraph IV certification for a patent. Apotex submitted an ANDA in April 1998, including a paragraph IV certification to the same patent. While patent infringement litigation on that patent was pending against both applicants, Warner-Lambert listed another patent. Purepac and Apotex amended their ANDAs. Apotex prevailed in its litigation on the first patent, and Warner-Lambert did not appeal. This triggered Purepac's exclusivity on the first patent, which ran from October 2001 to April 2002. FDA then took the position that Purepac was entitled to exclusivity on the second patent (as the first filer on that patent) and that final approval of Apotex's ANDA was subject to the second exclusivity term. Apotex brought suit, taking issue with FDA's conclusion that Purepac had been the first filer on the second patent and that Apotex would have to await a relevant court decision on that patent or commercial marketing by Purepac. It also argued that the paroxetine decision means there can be only one exclusivity period per innovator product and that the exclusivity period in question had already run.⁴² It therefore challenged FDA's failure to grant final approval of its ANDA.⁴³ In a June 2004 ruling, the court denied Apotex's motion for a preliminary injunction and granted the government's motion to dismiss.⁴⁴ Although the written order is sparse, apparently the judge disagreed with the ruling in the paroxetine case, found the statute ambiguous, and concluded that the agency's patent-by-patent approach was reasonable. Two federal judges from the same district court, therefore, ruled differently on the validity of FDA's patent-by-patent approach.⁴⁵ The D.C. Circuit, however, concluded that *res judicata* barred Apotex from bringing suit and vacated the lower court's holding on the merits.⁴⁶

In a more recent case, a third judge in the same district addressed the issue and found FDA's patent-by-patent approach to be permissible. This case involves ANDAs for 40 mg versions of AstraZeneca's Prilosec (omeprazole). This com-

³⁹ See *TorPharm, Inc. v. FDA*, 2004 WL 64064 (D.D.C. Jan. 8, 2004) (written order memorializing oral order and judgment issued on January 2); *Court Overturns FDA Decision that TorPharm Must Share Paxil 180-Day Exclusivity*, INSIDE HEALTH POLICY (Jan. 5, 2004).

⁴⁰ *Apotex, Inc. v. FDA*, Case No. 04-5046 (D.C. Cir., Notice of Appeal filed Feb. 13, 2004).

⁴¹ *Apotex, Inc. v. FDA*, Case No. 04-5046 (D.C. Cir., Judgment, Dec. 17, 2004).

⁴² See *Appeals Court Backs FDA: Purepac Gets Gabapentin 180-day Award*, INSIDE WASHINGTON'S FDA WEEK, (Jan. 23, 2004), at 3.

⁴³ *Apotex, Inc. v. Food and Drug Administration*, 1:04-cv-00605-ESH (D.D.C. filed (Apr. 14, 2004)).

⁴⁴ *Apotex, Inc. v. Food and Drug Administration*, 1:04-cv-00605-ESH (D.D.C., Order, (June 3, 2004)); see *Court Split on FDA's Patent-by-Patent Approach to 180-Day Exclusivity*, INSIDE WASHINGTON'S FDA WEEK (June 11, 2004).

⁴⁵ See *Court Split on FDA's Patent-by-Patent Approach to 180-Day Exclusivity*, INSIDE WASHINGTON'S FDA WEEK (June 11, 2004).

⁴⁶ *Apotex v. FDA*, 393 F.3d 210 (D.C. Cir. 2004). The case giving rise to *res judicata* was *TorPharm, Inc. v. Thompson*, 260 F.Supp.2d 69 (D.D.C. 2003), discussed in section III-A above, which involved the same parties and the same ANDAs. That litigation related to FDA's decision to postpone the effective date of Purepac's certification to the second patent (rather than nullify it as TorPharm had argued). Although the causes of action were not the same, Apotex effectively accepted in the first case that exclusivity was patent-based and argued in the second case that it was not. See also *Appeals Court Says Apotex Cannot Relitigate Fight Over Gabapentin Exclusivity*, BNA INC. PHARMACEUTICAL LAW & INDUSTRY (Dec. 31, 2004).

plicated situation involves three dosage forms, ten listed patents, and four generic applicants.⁴⁷ FDA granted Andrx 180-day exclusivity on the basis that it was the first to file an ANDA for 40 mg omeprazole and to challenge the first six listed patents, only three of which were at issue in the exclusivity litigation. AstraZeneca brought suit against Andrx and other generic applicants for infringement of these three patents. Although the court found Andrx infringed two of the three patents at issue, it granted summary judgment in favor of other generic applicants on the third patent, holding it not infringed.⁴⁸ Accordingly, although FDA could not make approval of the Andrx ANDA effective until expiry of the two infringed patents (and a pediatric exclusivity period) in October 2007, the ruling on the third patent triggered its 180-day exclusivity term. In the meantime, Andrx was the first to challenge four other patents listed by AstraZeneca after the Andrx ANDA was submitted, earning it a second exclusivity period under FDA's patent-by-patent approach. Apotex has also filed an ANDA for the strength, and it included a paragraph IV certification to the two patents that Andrx was found to infringe. Apotex has received tentative approval, but because of the (second) 180-day term that Andrx will enjoy in 2007 (assuming FDA makes its ANDA approval effective then), the soonest Apotex may enter the market is April 2008. Apotex brought suit, challenging FDA's patent-by-patent approach. The district court found section 505(j)(5)(B)(iv) ambiguous with respect to how many exclusivity periods may arise in connection with a single drug product, and it found FDA's patent-based approach "not entirely irrational."⁴⁹ Under the highly deferential standard of *Chevron*,⁵⁰ therefore, the judge granted the agency's motion for summary judgment. Apotex appealed to the D.C. Circuit in February 2006, and the appeal was still pending when this article was drafted.

In 2003, Congress endorsed a product-by-product approach going forward, with one 180-day exclusivity period per product.⁵¹ If all first applicants forfeit exclusivity, approval of "any" application containing "a" paragraph IV certification may be made effective. Accordingly, the ruling in the Apotex omeprazole appeal could have limited application.

C. Must a Generic Applicant Have Been Sued and Must It Have Prevailed in That Patent Infringement Suit To Obtain the Benefit of 180-Day Exclusivity?

No to both. There is no suit or "successful defense" requirement. Another generic could be sued and prevail instead, triggering the exclusivity, or the case could be dismissed. For new ANDAs, Congress clarified that eligibility is based on being a first applicant, and the court decision trigger was removed.

⁴⁷ *Apotex v. FDA*, 414 F.Supp.2d 61 (D.D.C. 2006); see also *Federal Court Upholds FDA's Position on Patent-Based Exclusivity Periods*, BNA INC. PHARMACEUTICAL LAW & INDUSTRY (Feb. 17, 2006).

⁴⁸ See *In re Omeprazole Patent Litigation*, 222 F.Supp.2d 423 (S.D.N.Y. (2002)), *aff'd* 84 Fed. Appx. 76 (Fed. Cir. Dec. 11, 2003).

⁴⁹ 414 F.Supp. 2d at 74.

⁵⁰ *Chevron USA, Inc. v. Natural Resources Defense Council*, 467 U.S. 83 (1984).

⁵¹ 21 U.S.C. § 355 (j)(5)(D)(iii). See also 149 CONG. REC. S 15884 (daily ed., (Nov. 25, 2003)) (Senator Kennedy) ("The Hatch-Waxman provisions in this bill also make the exclusivity available only with respect to the patent or patents challenged on the first day generic applicants challenge brand drug patents, which makes the exclusivity a product-by-product exclusivity rather than a patent-by-patent exclusivity.")

When FDA initially proposed regulations to implement 180-day exclusivity, it stated that a generic applicant was entitled to exclusivity only when it has itself been sued for patent infringement and prevailed in that lawsuit. It stated that, to provide otherwise "would provide a windfall to an applicant who has not devoted the considerable time and money necessary for patent litigation."⁵²

After the FDA Commissioner signed the *Federal Register* notice of the proposed regulations, but before its publication in the *Federal Register*, a federal district court reached a contrary conclusion on the issue whether the generic applicant must have been sued, itself, by the patent holder. In this case, involving generic copies of In-deral (propranolol hydrochloride), the district court noted that the "alternatives are clear"—the "primary ANDA applicant can qualify for exclusivity beginning either on the date of a court decision invalidating a patent or holding that it is not infringed or on the date of first commercial marketing of the applicant's product."⁵³ "There is no ambiguity" in the statute, the court wrote, "that requires the Court or permits the FDA to read into it a requirement of a lawsuit which is simply not there."⁵⁴ The agency appealed the decision, however, and the case was dismissed as moot before FDA concluded the rulemaking.⁵⁵ In its final regulations, the agency stood by its earlier position. A generic applicant would be entitled to exclusivity only if it had successfully defended a patent infringement suit. Neither the court decision nor the commercial marketing trigger would apply, unless and until the first applicant won its patent infringement suit.⁵⁶ FDA believed that to provide otherwise would "create[] an incentive for frivolous claims of patent invalidity or noninfringement."⁵⁷

In January 1997, a federal district court invalidated the successful defense requirement. In December 1994, Mova filed an ANDA with a paragraph IV certification to market a generic version of Micronase (micronized glyburide), a diabetes drug marketed by Pharmacia. Pharmacia sued Mova for infringing its patent. In November 1995, while Mova was engaged in that litigation, Mylan filed an ANDA for the same product and eventually filed a paragraph IV certification. Pharmacia declined to sue, and FDA approved Mylan's application on December 19, 1996. FDA reasoned that Mova's exclusivity did not bar approval of the Mylan ANDA, because Mova had not yet successfully defended against Pharmacia's suit. Mova then brought suit to compel FDA to delay the effective date of its approval of Mylan's product until 180 days after the earlier of the date Mova won its lawsuit or the date it began to market its product. Mova challenged the successful defense regulation as contrary to the plain language of the statute. The district court found that Mova had a very high likelihood of success on the merits of its claim and granted a preliminary injunction.⁵⁸

In 1998, the D.C. Circuit affirmed that holding.⁵⁹ Although FDA argued that its successful defense requirement furthered the intent of Congress, the court disagreed.

⁵² 54 Fed. Reg. at 50352-50353.

⁵³ *Inwood Laboratories, Inc. v. Young*, 723 F.Supp. 1523, 1526 (D.D.C. 1989), vacated as moot, no. 89-5209 (D.C. Cir. Nov. 13, 1989).

⁵⁴ *Id.*

⁵⁵ Inwood asked the court of appeals to declare the case moot when six months had elapsed after the lower court enjoined FDA from approving another ANDA. See *Inwood Case May Not Set Precedent on Exclusivity*, WASHINGTON DRUG LETTER (Oct. 30, 1989), at 2.

⁵⁶ See *Mova Pharmaceutical Corp. v. Shalala*, 140 F.3d 1060, 1069-1070 (D.C. Cir. 1998) (discussing FDA's interpretation).

⁵⁷ 59 Fed. Reg. at 50353.

⁵⁸ *Mova Pharm. Corp. v. Shalala*, 955 F.Supp. 128 (D.D.C. 1997).

⁵⁹ *Mova Pharm. Corp. v. Shalala*, 140 F. 3d 1060 (D.C. Cir. 1998).

The successful defense requirement, the court wrote, is “gravely inconsistent with the text and structure of the statute.”⁶⁰ The D.C. Circuit explained, “[T]he commercial-marketing trigger seems intended to insure that, if a first ANDA applicant chooses to begin marketing its product before it has won its patent-infringement suit, the 180-day exclusivity period will begin to run immediately. Under the FDA’s regulation, however, the 180-day exclusivity period is only available to an applicant who has already ‘successfully defended against a suit for patent infringement.’”⁶¹ Its practical effect, the court wrote, is “to write the commercial-marketing trigger out of the statute.”⁶² The court recognized the issue, raised by Mylan, that the statutory scheme might penalize a meritorious second ANDA applicant.⁶³ Nevertheless, the court found that the successful defense requirement was too “blunt an instrument” to address that issue.⁶⁴ The regulation was, thus, invalid. The glyburide case (usually referred to as “Mova”) therefore established that the first generic applicant need not successfully defend a patent infringement suit in order to enjoy the benefit of 180-day exclusivity.⁶⁵

After the district court found FDA’s successful defense regulation invalid,⁶⁶ FDA decided to cease enforcing the regulation pending appeal. During the pendency of that appeal, the Fourth Circuit similarly invalidated the successful defense requirement in a case involving generic versions of Zantac.⁶⁷ There were two crystalline forms of ranitidine (Forms 1 and 2), and Form 2 was covered by a separate patent, the ’431 patent. In February 1991, Genpharm filed an ANDA for a generic Form 2 ranitidine product and included a paragraph IV certification to the ’431 patent. It was, therefore, the first to file. GlaxoWellcome (Glaxo) sued Genpharm for patent infringement and prevailed in 1995. In 1996, Genpharm filed another paragraph IV certification under the ANDA, alleging that it would market a Form 1 ranitidine product that did not infringe the ’431 patent. Glaxo again sued. In April 1994, in the interim between the two Genpharm paragraph IV certifications, Granutec filed an ANDA that included a paragraph IV certification also alleging that it would market a Form 1 product that did not infringe the ’431 patent. Glaxo brought suit, but Granutec prevailed. Glaxo and Granutec then entered into a licensing agreement for the final 15 days of the other patent, the ’658 patent,⁶⁸ and Granutec sought FDA approval of its ANDA beginning July 10, 1997. FDA refused, stating that Genpharm’s exclusivity had been triggered on March 3, 1997, when Glaxo’s right to appeal expired with respect to a “wholly unrelated” district court decision that Boehringer Ingelheim’s generic version of Form 1 ranitidine did not infringe

⁶⁰ *Id.* at 1069.

⁶¹ *Id.* at 1069-70.

⁶² *Id.* at 1069. The court reasoned that “if the first applicant begins marketing its product before it wins its infringement suit, the 180 days of exclusivity do not begin to run; other applicants remain eligible for FDA approval to begin marketing their products, at least up to the date that the first applicant wins the infringement action.” *Id.* at 1070.

⁶³ *Id.* at 1072.

⁶⁴ *Id.* at 1074.

⁶⁵ In *dictum*, the court also approved as “elegant and textually persuasive” an argument made by Teva (as *amicus curiae*) that the court decision trigger may be satisfied by any decision of a court holding the patent invalid or not infringed—including suits not brought by the patent holder, such as a declaratory judgment action by the second ANDA applicant. *Id.* at 1072-1073. The court noted, however, that it “seems odd to reward the first applicant if some later applicant was the party that actually prevailed in the patent-infringement litigation.” *Id.* at 1073.

⁶⁶ 955 F.Supp. 128 (D.D.C. 1997).

⁶⁷ *Granutec, Inc. v. Shalala*, 139 F.3d 889 (4th Cir. 1998) (unpublished).

⁶⁸ 139 F.3d 889, at *4.

Glaxo's '431 patent.⁶⁹ FDA concluded that because Genpharm had filed the first ANDA for generic ranitidine, and because FDA had suspended the successful defense requirement after the district court decision in *Mova*, Genpharm was entitled to exclusivity. (Genpharm did not, however, have final approval of its ANDA.). Granutec then brought suit, arguing that FDA's refusal to enforce the successful defense requirement was arbitrary and capricious. The district court agreed and issued an injunction requiring FDA to adhere to the successful defense requirement. This would effectively mean that no company would be entitled to exclusivity. The Fourth Circuit reversed, in an unpublished opinion, finding that the statute did not require a successful defense against a patent infringement suit. Genpharm was thus entitled to exclusivity.

Shortly after this decision and the *Mova* court of appeals decision invalidating the successful defense requirement, FDA published a guidance for industry.⁷⁰ This guidance detailed a new approach to 180-day exclusivity in light of the court decisions. FDA announced its intent to "formally" remove the successful defense requirement from the regulation and to issue new regulations.⁷¹ In the meantime, FDA stated, it would "regulate directly from the statute" and "make decisions on 180-day generic drug exclusivity on a case-by-case basis."⁷² The agency would inform the first applicant to submit a substantially complete abbreviated application with a paragraph IV certification that it was eligible for 180 days of exclusivity even though it had not been sued for patent infringement.⁷³ In November 1998, FDA published an interim rule, eliminating the successful defense requirement.⁷⁴

In December 1998, the D.C. Circuit confirmed that the first generic need not be sued for patent infringement to be eligible for exclusivity.⁷⁵ TorPharm was the first to file an ANDA for a generic version of Ticlid (ticlopidine hydrochloride). Its ANDA contained a paragraph IV certification. The patent owner did not file suit against TorPharm. FDA tentatively approved an ANDA filed by Purepac, but because the agency had not given final approval to TorPharm and there was not a qualifying court decision, TorPharm's exclusivity had not begin to run. Accordingly, FDA withheld final approval of Purepac's ANDA pending TorPharm's final approval, commercial marketing, and expiry of its 180-day exclusivity. Purepac sued FDA seeking an injunction claiming that TorPharm was not entitled to exclusivity because it had not been sued for infringement. The D.C. Circuit ultimately concluded that FDA's "revised system for granting exclusivity" was consistent with the statute and the *Mova* decision, noting that the statute does not on its face require the first applicant to be sued in order to benefit from market exclusivity.⁷⁶ Thus, FDA could withhold final approval of the Purepac ANDA until TorPharm had commercially marketed for 180 days.

If, however, a first applicant loses a patent infringement case, it must under FDA regulations amend its certification to a paragraph III certification, and it is no

⁶⁹ See *id.* at *5 (citing *Glaxo, Inc. v. Boehringer Ingelheim Corp.*, 954 F.Supp. 469 (D.Conn. 1996), judgment entered by 962 F.Supp. 295 (D.Conn. 1997), *aff'd*, No. 97-1283, 1997 WL 355339 (Fed. Cir. June 4, 1997)).

⁷⁰ See FDA, Guidance for Industry, 180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments to the FDCA (June 1998).

⁷¹ *Id.* at 4.

⁷² *Id.*

⁷³ *Id.* at 5.

⁷⁴ 63 Fed. Reg. 59710 (Nov. 5, 1998).

⁷⁵ *Purepac Pharm. Co. v. Friedman*, 162 F.3d 1201 (D.C. Cir. 1998).

⁷⁶ 162 F.3d at 1204.

longer eligible for exclusivity. This was confirmed in a 2000 case involving generic tamoxifen. The Southern District of New York had invalidated Imperial's patent, but that decision was subsequently appealed and vacated pursuant to a settlement agreement between Imperial and the generic manufacturer (Barr).⁷⁷ Also pursuant to the settlement, Barr amended its ANDA to change from a paragraph IV to a paragraph III certification.⁷⁸ Barr also obtained a license to market the product prior to patent expiry.⁷⁹ FDA declined to treat the New York decision as a "court decision" for purposes of exclusivity and instead agreed with Barr that its exclusivity was intact.⁸⁰ Mylan, a subsequent filer, sued FDA. The district court held that Barr had waived its eligibility for 180-day exclusivity, explaining that once a company changes its certification, the ANDA is no longer considered to have "contained" a paragraph IV certification.⁸¹ This meant Barr was no longer eligible for exclusivity, and because FDA took the position that there was no "rolling exclusivity" under the statute,⁸² the agency could approve Mylan's ANDA.

D. What Kind of Court Decision Triggers 180-Day Exclusivity?

The court decision trigger applicable to old ANDAs requires a decision of a court that on its face evidences a holding on the merits of patent non-infringement, invalidity, or unenforceability. In 2003, Congress eliminated the court decision trigger for exclusivity for new ANDAs (although it addressed it as a forfeiture event).

This issue was addressed in the context of two products several years apart. As noted above, TorPharm was the first to file an ANDA for ticlopidine hydrochloride, a generic version of Ticlid. On June 20, 1997, Teva Pharmaceuticals filed an ANDA for ticlopidine hydrochloride, and was not sued for patent infringement. Teva then sued the patent owner, Syntex, in the Central District of California for a declaratory judgment of non-infringement. After Syntex admitted that Teva's product did not infringe its patent, the California court dismissed the suit for lack of subject matter jurisdiction.⁸³ On October 29, 1998, FDA tentatively approved Teva's ANDA. FDA informed Teva, however, that because there was a prior ANDA applicant and neither commercial marketing nor a relevant court decision had occurred, Teva's application was ineligible for final approval. Teva argued to FDA, to no avail, that the California court's dismissal of its declaratory judgment suit against Syntex satisfied the "court decision" requirement, triggering the first filer's exclusivity. Teva then brought suit in federal district court in the District of Columbia, seeking to have its ANDA approved

⁷⁷ See *Mylan Pharmaceuticals v. Henney*, 94 F.Supp.2d 36 (D.D.C. 2000), *vacated and dismissed as moot*, 276 F.3d 627 (D.C. Cir. 2002).

⁷⁸ 94 F.Supp.2d at 41.

⁷⁹ *Id.*

⁸⁰ *Id.* at 42.

⁸¹ *Id.* at 56-57. On May 24, 2001, Gary Buehler, Acting Director of FDA's Office of Generic Drugs, confirmed FDA's view by telling the Senate Judiciary Committee that "[o]nly an application containing a paragraph IV certification may be eligible for exclusivity. If an applicant changes from a paragraph IV certification to a paragraph III certification, for example upon losing its patent infringement litigation, the ANDA will no longer be eligible for exclusivity." Competition in the Pharmaceutical Marketplace: Antitrust Implications of Patent Settlements: Hearing Before the Senate Committee on the Judiciary, 107th Cong. 12 (2001) (Statement of Gary Buehler, RPh).

⁸² 64 Fed. Reg. 42873 (Aug. 6, 1999). See the discussion below in section III-I.

⁸³ *Teva Pharmaceuticals, USA, Inc. v. FDA*, 182 F.3d 1003 (D.C. Cir. 1999) ("The California court dismissed the complaint for lack of subject-matter jurisdiction after finding, based on the patent holder's admission of non-infringement, that Teva lacked a reasonable apprehension of suit by the patent holder."). The California decision was not published.

effective 180 days after the California court dismissed the declaratory judgment suit. The district court upheld FDA's decision and denied injunctive relief.

The D.C. Circuit reversed, holding that FDA's unexplained refusal to recognize dismissal by the California court as the functional equivalent of a final decision of non-infringement was arbitrary.⁸⁴ The D.C. Circuit's discussion suggested several points. First, any court decision with "preclusive effect," even a dismissal of a declaratory judgment action for lack of subject matter jurisdiction, may trigger exclusivity. "A 'decision' can take several forms," the court wrote "including final judgment after a full trial, summary judgment or partial summary judgment, or even dismissal for failure to state a cause of action."⁸⁵ Second, although the statute provides that exclusivity dates to a decision that the patent is invalid or not infringed, FDA's regulations have since 1994 said, "invalid, unenforceable, or not infringed." The D.C. Circuit rejected the argument that estoppel (in the case at hand) should be treated differently from unenforceability (in the regulation), invalidity, and non-infringement.⁸⁶ Third, the court decision that triggers exclusivity need not involve the first generic. It may, instead, involve the patent holder and another ANDA applicant. Thus, if the pioneer has sued subsequent ANDA filers for patent infringement on the same drug, a decision of a district court finding the patent invalid, not infringed, or unenforceable in any of those cases will trigger exclusivity.⁸⁷

A decision from the court of appeals in 2006 has prompted FDA to re-evaluate the court decision trigger. On December 20, 2000, Teva filed the first ANDA to market generic copies of Pravachol (pravastatin sodium) in 10, 20, and 40 mg tablets. Teva included a paragraph III certification on the product patent (the patent on the molecule itself) and paragraph IV certifications as to certain other listed patents. Bristol-Myers did not sue Teva or any of the other generic drug manufacturers that filed applications with paragraph IV certifications. Teva's ANDA was tentatively approved (pending expiry of the product patent) in May 2002. One of the other generic applicants, Apotex, sued Bristol-Myers in October 2003, seeking a declaratory judgment that the patents in question were invalid or not infringed by Apotex. In July 2004, the court entered a "stipulation and order," signed by both parties, stating that Bristol-Myers had "no intention to bring suit against Apotex for infringement." Apotex then returned to FDA, asking that it find this to be a "court decision" that triggered Teva's exclusivity. FDA agreed, apparently concluding that the decision in the Teva ticlopidine case meant any dismissal of a declaratory judgment case triggers exclusivity. This meant Teva's exclusivity would run before the patent expired for which Teva had submitted a Paragraph III certification, so Teva brought suit.

⁸⁴ *Teva Pharmaceuticals, USA, Inc. v. FDA*, 182 F.3d 1003 (D.C. Cir. 1999).

⁸⁵ *Id.* at 1007-1008.

⁸⁶ *Id.* at 1009.

⁸⁷ Following this decision, FDA provided a rationale for refusing to recognize dismissal of Teva's declaratory judgment action as a triggering court decision. In essence, FDA explained, generic applicants seeking to avail themselves of the court decision trigger must submit a copy of the court decision in question. The agency will not review any additional papers from the underlying litigation. The reason for Teva's dismissal "was not evident from the face of the court order, the court did not issue a memorandum opinion explaining the basis for the order," and requiring staff in the Office of Generic Drugs to delve beyond these documents would "place an unbearable burden" on the office. On remand, the district court rejected FDA's explanation, noting—among other things—that "this is not a case where a great deal of sophisticated legal analysis is required." In addition, the court noted, FDA had not met the challenge of squaring its approach to the California dismissal with its handling of the Boehringer decision (a partial summary judgment on the basis of an admission of non-infringement) that triggered the exclusivity at issue in the *Granutech* case. FDA's claim that the California decision was not a "holding" failed, for example, because the term is open to interpretation. *Teva Pharmaceuticals USA, Inc. v. United States Food & Drug Administration*, 1999 WL 1042743 (D.D.C. Aug. 19, 1999), *aff'd* 254 F.3d 316 (D.C. Cir. 2000).

In March 2006, the D.C. Circuit rejected FDA's reading of the Teva ticlopidine decision. In the ticlopidine case, it explained, "the court stated the statute could be interpreted to include dismissals of declaratory judgment actions as triggering events," but "it left the final decision to FDA."⁸⁸ In short, the court only found the trigger ambiguous. The agency "mistakenly thought itself bound," which "renders its decision arbitrary and capricious."⁸⁹ Thus, "[w]hile the statute may preclude treating voluntary dismissals ... as triggering events, we express no opinion on the matter." Instead, it is "up to the agency to ... make a reasonable policy choice," and "FDA has not yet done so."⁹⁰ The agency responded to this court decision in an April 11 letter to Apotex and the other generic applicants, stating that "FDA interprets the court decision trigger provision to require a decision of a court that on its face evidences a holding on the merits of patent non-infringement, invalidity, or unenforceability."⁹¹ In the case at hand, therefore, Teva's exclusivity period had not been triggered by the July 2004 dismissal of the Apotex litigation. Following another rush of litigation by Apotex (a request for injunction and then appeal to the D.C. Circuit), FDA granted Teva final approval on April 24.⁹²

In 2003, Congress eliminated the court decision trigger for 180-day exclusivity. For new ANDAs, exclusivity begins with the first commercial marketing of the drug product by a first applicant. Although Congress eliminated the court decision trigger for beginning the period of exclusivity, it established a new court decision trigger for forfeiture of exclusivity.⁹³ The legislative history contains a reference to the Teva ticlopidine case,⁹⁴ but FDA's subsequently adopted April 2006 policy presumably applies.

E. *What Level of Court Decision Triggers 180-Day Exclusivity?*

This is the sole topic on which the 2003 legislation is retroactive. For old ANDAs, exclusivity begins when a decision is rendered by "the court from which no appeal (other than a petition of the Supreme Court for a writ of certiorari) has been or can

⁸⁸ Teva v. FDA, 441 F.3d 1, 3 (D.C. Cir. 2006).

⁸⁹ *Id.* at 6.

⁹⁰ *Id.*

⁹¹ FDA, Letter to Pravastatin ANDA Applicant (Apr. 11, 2006), available at www.fda.gov/cder/ogd/announce/Pravastatin-180Day-amend.pdf; see also *FDA Narrows Interpretation of Exclusivity Court Decision Triggers*, [THE PINK SHEET] (Apr. 17, 2006).

⁹² *FDA Approves Teva's Generic Pravastatin, As Court Denies Apotex Emergency Relief*, BNA, INC. PHARMACEUTICAL LAW & INDUSTRY (Apr. 28, 2006). Apotex Inc. v. FDA, D.D.C., No. 06-00627 (April 19, 2006) (denying motions for temporary restraining order and preliminary injunction); Apotex Inc. v. FDA, D.C. Cir., No. 06-5105 (April 20, 2006) (granting emergency motion for injunctive relief—issuing administrative injunction—pending further order of the court); D.C. Cir., No. 06-5105 (April 24, 2006) (dissolving administrative injunction and denying motion for injunctive relief pending appeal).

⁹³ Put simply, once the first generic obtains final approval of its ANDA, its exclusivity does not begin to run until it commercially markets, and—unless another forfeiture provision applies—that exclusivity is not forfeited until 75 days after a court decision on every patent qualifying it for exclusivity. Shortly after passage of the 2003 amendments, Senator Hatch pointed out that if the court decision in question involves a different ANDA applicant—*i.e.*, if the second applicant, not the first, successfully challenged the innovator's patents—the first generic is still entitled to exclusivity, and, indeed, could launch on the 74th day after the court decision, thereby effectively blocking the second applicant for 254 days. In his view, at least in the winter of 2003, this inappropriately penalizes the successful patent challenger. 149 CONG. REC. S 16104 (daily ed., Dec. 9, 2003) (Sen. Hatch).

⁹⁴ See 149 CONG. REC. S 15885 (daily ed., Nov. 25, 2003) (Sen. Kennedy) ("We do intend that a court decision like the one in the D.C. Circuit's 1999 decision in *Teva v. Shalala*—a decision dismissing a declaratory judgment action for lack of subject matter jurisdiction because the patent owner has represented that the patent is not infringed—will count as a court decision under the new 'failure to market' provision.").

be taken." There is no court decision trigger for exclusivity for new ANDAs, but a similar rule applies to a forfeiture event.

In the preamble to its final 1994 regulations, FDA stated that the court decision activating the court decision trigger "must be a final decision from which no appeal can be or has been taken."⁹⁵ A federal district court disagreed in January 2000.⁹⁶ In a case involving generic copies of Hytrin (terazosin hydrochloride)—often referred to as Mylan I—a federal district court rejected FDA's position that the triggering event is "either the date that a district court decision is affirmed by the Federal Circuit, or the date on which the time for filing an appeal has lapsed."⁹⁷ In other words, the court held that "decision of a court" includes "the decision of a United States district court regardless of whether that decision is appealed."⁹⁸ The rule that resulted, therefore, was that the first generic's 180-day exclusivity period began to run on the date of a district court decision finding invalidity, unenforceability, or non-infringement.

In March 2000, FDA issued a guidance document responding to this court decision.⁹⁹ The agency stated that it would interpret the term "court" to mean "the first court that renders a decision finding the patent at issue invalid, unenforceable, or not infringed."¹⁰⁰ It would apply this to both 30-month stays and 180-day exclusivity. Thus, if a district court rendered such a decision, the 30-month stay would end for that ANDA as of the date the district court entered its decision, and 180-day exclusivity for the first filer would also begin to run on that date (unless it had begun already with commercial marketing). Neither a stay nor a reversal of this decision would lead to revocation of approval of that ANDA or the first filer's 180-day exclusivity. If a district court found patent infringement, however, and that ruling was reversed by the Federal Circuit, that generic's ANDA would be approved and the 180-day exclusivity would start "on the date the district court issues a judgment that the patent is invalid, unenforceable, or not infringed pursuant to a mandate issued by a court of appeals."¹⁰¹ FDA agreed that this could compromise companies that had developed marketing strategies in reliance on the old definition of court decision. It could put them in the position of exposing themselves to damages if they market (to take advantage of the 180-day period) but lose in the appeal of the patent case. The new definition of court would therefore apply only to ANDAs filed after March 30, 2000.¹⁰² In July 2000, FDA published interim regulations amending the definition of "court decision" as detailed in the March 2000 guidance and consistent with the terazosin decision.¹⁰³

Congress reversed the rule in 2003, however, and this is the sole topic on which the 2003 legislation is retroactive. Exclusivity for old ANDAs begins when a decision is rendered by "the court from which no appeal (other than a petition of the Supreme Court for a writ of certiorari) has been or can be taken."¹⁰⁴ There is

⁹⁵ 59 Fed. Reg. at 50354.

⁹⁶ Mylan Pharmaceuticals, Inc. v. Shalala, 81 F.Supp.2d 30 (D.D.C. 2000).

⁹⁷ *Id.* at 41-42.

⁹⁸ *Id.* at 47.

⁹⁹ FDA, Guidance for Industry, Court Decisions, ANDA Approvals, and 180-Day Exclusivity Under the Hatch-Waxman Amendments to the FDCA (Mar. 2000).

¹⁰⁰ *Id.* at 4.

¹⁰¹ *Id.*

¹⁰² *Id.*

¹⁰³ 65 Fed. Reg. 43233 (July 13, 2000).

¹⁰⁴ Pub. L. No. 108-173 § 1101(b)(3). By way of contrast, when it amended the statute in 2003 Congress provided that 30-month stays for new ANDAs would end with a district court decision. Thus, under the MMA district court decisions will end 30-month stays but not trigger the running of the 180 days. If the 30-month stay ends, however, and FDA approves the ANDA, any commercial marketing under the ANDA will trigger 180-day exclusivity for old ANDAs or new ANDAs.

no court decision trigger for exclusivity for new ANDAs. And the court decision trigger for forfeiture of exclusivity is unambiguous: the period is forfeited if the applicant fails to market 75 days after, as to each patent at issue, “a court enters a final decision from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the patent is invalid or not infringed” (unless 75 days have not elapsed since the ANDA approval was effective and 30 months have not elapsed since the ANDA was submitted).

F. *What Is the Effect of Patent Expiry once a Paragraph IV Certification Has Been Submitted?*

If a patent expires before the first generic applicant has final approval of its ANDA, the applicant must amend its certification from a paragraph IV to a paragraph II and will no longer be entitled to 180 days of exclusivity when finally approved.

On October 14, 2003, a federal district court in New Jersey found that Dr. Reddy’s Laboratories was not entitled to share Andrx’s 180-day exclusivity for generic copies of Prilosec (omeprazole).¹⁰⁵ Although Andrx was the first to file a paragraph IV certification to the 40 mg version on ten of the eleven patents listed by AstraZeneca, Dr. Reddy’s was the first to file a paragraph IV for the 40 mg version on the other patent.¹⁰⁶ (Andrx filed a paragraph III.) The patent expired after both ANDAs were tentatively approved, but before either was finally approved. FDA concluded that Dr. Reddy’s lost its eligibility for exclusivity when the patent expired, on the theory that the company was required at that time to amend its ANDA to convert the paragraph IV certification to a paragraph II certification.¹⁰⁷ Dr. Reddy’s sued FDA in the District of New Jersey. The court noted that the agency had set forth its interpretation of the statute at least twice prior to its decision on Dr. Reddy’s application.¹⁰⁸ Dr. Reddy’s argued that FDA may not require generic applicants to amend their certifications prior to final ANDA approval, and that an ANDA is eligible for exclusivity if it contains the appropriate paragraph IV certification at the time of filing. The court found the statute ambiguous on both points, however, and upheld the agency’s decision.¹⁰⁹

For new ANDAs, the first applicant forfeits exclusivity if all of the patents as to which it filed a paragraph IV certification qualifying it for exclusivity have expired.¹¹⁰

G. *What Is the Effect of Delisting Patent once Paragraph IV Certification Has Been Submitted?*

With respect to old ANDAs, generally speaking, if a patent is removed from the Orange Book, FDA requires ANDA sponsors to delete their paragraph IV certifications.

¹⁰⁵ Dr. Reddy’s Laboratories, Inc. v. Thompson, 302 F.Supp.2d 340 (D.N.J. 2003).

¹⁰⁶ *Id.* at 345.

¹⁰⁷ See 21 C.F.R. § 314.94(a)(12)(viii)(C).

¹⁰⁸ *Id.* at 351, citing 59 Fed. Reg. 50338, 50348 (Oct. 3, 1994) (“a patent is deemed to be relevant until the end of the term of the patent or applicable 180-day period, whichever occurs first”) and FDA, Response to APP and Pharmachemie Citizen Petitions, 99P-1271 (Aug. 2, 1999). The court characterized the latter as stating that, “because exclusivity cannot extend beyond the expiration of a patent, an ANDA applicant who is first to file a paragraph IV certification on a patent loses its eligibility based upon that patent when the patent expires before either of the triggering events occurs.”

¹⁰⁹ *Id.* at 354-355.

¹¹⁰ 21 U.S.C. § 355(j)(5)(D)(i)(VI).

FDA's policy creating an exception if a first ANDA applicant were sued by the patent owner was recently found to be inconsistent with the statute.

Earlier we discussed litigation involving Purepac and TorPharm over generic copies of Neurontin (gabapentin), including a case where FDA decided the penalty for Purepac's failure to provide notice simultaneously with its paragraph IV certification was postponement of the certification's effective date. Also at issue in the case was a patent that had been listed in the *Orange Book* and then, after litigation, deemed by FDA to be ineligible for listing.¹¹¹ The patent in question claimed a method of use of Neurontin in the treatment of neurodegenerative diseases for which the innovator drug was not approved, and for which the ANDA applicants therefore could not seek approval.¹¹² In another lawsuit, a district court determined that Purepac's "section viii" statement as to this patent was appropriate.¹¹³ TorPharm had, however, submitted a paragraph IV certification on the patent. Under agency regulations, when a patent has been the "subject of a lawsuit" based on a paragraph IV certification, it may be delisted only if no ANDA applicant is entitled to exclusivity on the patent.¹¹⁴ Under well-established agency policy, however, where a section viii statement is proper, a paragraph IV certification is not. In the gabapentin situation, FDA determined that—in light of the ruling that Purepac's section viii statement was appropriate—TorPharm's paragraph IV certification was improper. This eliminated TorPharm's eligibility for exclusivity. FDA also removed the patent from the *Orange Book*, on the ground that it claimed a use the agency had not approved. No company was therefore entitled to exclusivity on the patent. The district court found this decision to be reasonable, and the D.C. Circuit affirmed.¹¹⁵

As noted, when FDA delists a patent, any applicant with a pending ANDA who has made a certification with respect to that patent must amend its certification.¹¹⁶ Agency regulations, however, create an exception if the first applicant (as to that patent) has been sued.¹¹⁷ In this situation, FDA policy was not to delist the patent. A court of appeals recently invalidated this regulation. IVAX sought approval of generic 5 mg, 10 mg, 20 mg, and 40 mg versions of Merck's Zocor (simvastatin). IVAX was the first generic applicant to challenge two patents claiming approved methods of use. The patents in question apparently claimed compounds related to simvastatin, rather than simvastatin itself.¹¹⁸ Following submission of the IVAX

¹¹¹ *Purepac Pharmaceutical Co. v. Thompson*, 2004 WL 76594 (D.C.Cir. Jan. 20, 2004), *aff'g* *TorPharm, Inc. v. Thompson*, 260 F.Supp.2d 69 (D.D.C. 2003); *see also TorPharm Rebuffed on Bid to Overturn FDA Decision Awarding Exclusivity to Purepac*, BNA PHARMACEUTICAL LAW & INDUSTRY REPORT (Jan. 23, 2004); *Appeals Court Backs FDA: Purepac Gets Gabapentin 180-Day Award*, FDA WEEK (Jan. 23, 2004).

¹¹² FDA clarified in its 2003 regulations that only patents claiming approved uses could be listed. This is confirmed in the 2003 amendments, which authorize a counterclaim to an infringement case on the grounds that a listed method of use patent does not claim an approved use of the product.

¹¹³ *Purepac Pharmaceutical Co. v. Thompson*, 238 F.Supp. 2d 191 (D.D.C. 2002). A section viii statement states that the patent in question has been listed but does not claim a use for which the ANDA applicant seeks approval. 21 U.S.C. § 355(j)(2)(A)(viii). Because it is not a paragraph IV certification, it does not entitle the innovator to notice, and it does not entitle the ANDA applicant to exclusivity.

¹¹⁴ 21 C.F.R. § 314.94(a)(12)(viii)(B).

¹¹⁵ *Purepac Pharmaceutical Co. v. Thompson*, 2004 WL 76594 (D.C.Cir. Jan. 20, 2004), *aff'g* *TorPharm, Inc. v. Thompson*, 260 F.Supp.2d 69 (D.D.C. 2003).

¹¹⁶ 21 C.F.R. § 314.94(a)(12)(viii)(B).

¹¹⁷ *Id.*

¹¹⁸ The FTC characterized the substance as "related to" simvastatin. Federal Trade Commission, Response to Citizen Petition by IVAX Pharmaceuticals, Inc., Docket No. 2005P-0008 (April 5, 2005), at 4. Ranbaxy characterized the compounds as "related compounds of simvastatin" that it believed to be "present in Zocor" and that were "a byproduct of Merck's manufacture of simvastatin." Ranbaxy Laboratories Limited, Citizen Petition, Docket No. 2005P-0046 (Feb. 1, 2005), at 2.

ANDA, FDA amended its regulations to state that listed drug substance patents must claim the active ingredient of an approved drug product, rather than a metabolite or an intermediate.¹¹⁹ At Merck's request, and following several additional letters to the agency (from private law firms, presumably representing generic company interests) stating that the patents should not be listed, the agency removed the patents from the *Orange Book*. This had the effect of permitting subsequent ANDA applicants to omit certifications relating to the patents. IVAX petitioned the agency to reinstate the patents and not approve subsequent ANDAs until its 180 days of exclusivity had concluded.¹²⁰ Ranbaxy filed a citizen petition with respect to 80 mg simvastatin and raised the same issue with respect to the same two delisted patents.¹²¹ Teva opposed the petitions, arguing that, "incorrectly listed patents cannot support exclusivity."¹²²

In a 20-page letter, FDA denied both petitions, stating that it does "not interpret the statute to require that an ANDA applicant who has submitted the first paragraph IV certification to a patent always remain eligible for 180-day exclusivity as to that patent even if the NDA holder has asked that the patent be delisted."¹²³ Instead, FDA noted, it is "consistent with the language and purposes of the statute generally to delist a patent when the NDA holder requests that we do so" and to therefore "remove the basis for exclusivity as to that patent." There is "one limited exception" (to this "ministerial" role) in the regulations, pursuant to which FDA maintains the listing of a patent where the paragraph IV challenge of the first ANDA applicant has resulted in litigation. This ensures that victory in the patent litigation, which would result in delisting of the patent, will not also result in loss of exclusivity. Merck had not sued either IVAX or Ranbaxy, however, so this limited exception did not apply. The patents were delisted, and FDA concluded that neither generic manufacturer was entitled to exclusivity with respect to the patents.¹²⁴

In litigation that followed, however, both the district court and the D.C. Circuit found that FDA should not have delisted the patents. The district court noted that section 505(j)(5)(B)(iv) is "clear and unambiguous" in providing that the first generic applicant may qualify for exclusivity "in one of two ways"¹²⁵—i.e., a court decision or commercial marketing. Further, "[o]f the two methods Congress has provided by which the first ANDA applicant's 180-day period of exclusivity is triggered, one requires litigation and one does not."¹²⁶ The issue, according to the court, was whether FDA could "effectively restrict the reward to only a sued ANDA holder, by delisting a patent after the ANDA holder successfully avoided suit."¹²⁷ It noted that the delisting practice "as applied here effectively eliminated Congress's 'first commercial marketing' trigger, in violation of the clear command of Congress."¹²⁸ Although FDA may adopt a delisting practice, it cannot favor "one of two equal statutory provisions over the other."¹²⁹ The agency relisted the

¹¹⁹ 68 Fed. Reg. 36676 (June 18, 2003).

¹²⁰ IVAX Pharmaceuticals, Inc., Citizen Petition, Docket No. 2005P-0008 (Jan. 5, 2005).

¹²¹ Ranbaxy Laboratories Limited, Citizen Petition, Docket No. 2005P-0046 (Feb. 1, 2005).

¹²² Teva, Response, Docket No. 2005P-0046 (June 8, 2005), at 2.

¹²³ FDA, Response, Docket Nos. 2005P-0008 and 2005P-0046 (Oct. 24, 2005).

¹²⁴ *Id.* at 2.

¹²⁵ *Ranbaxy v. Leavitt*, 2006 WL 1147797 (D.D.C. (April 30, 2006)), at 7; see also *Ivax, Ranbaxy Score Win on Generic Zocor As Court Reverses FDA on Exclusivity Issue*, BNA, INC. PHARMACEUTICAL LAW & INDUSTRY (May 5, 2006).

¹²⁶ *Id.*

¹²⁷ *Id.* at 8.

¹²⁸ *Id.*

¹²⁹ *Id.*

patents in June 2006, and in November the Court of Appeals affirmed the lower court's decision.¹³⁰

For new ANDAs, the MMA contains a forfeiture provision based on withdrawal of patent listings. Specifically, if 75 days have elapsed since approval of the first applicant's ANDA was made effective (or 30 months have elapsed since the first applicant's ANDA was submitted), then if the last of the patents qualifying it for exclusivity is delisted, the first applicant will forfeit exclusivity if it fails to market within 75 days.¹³¹

H. Are 180-day Exclusivity Rights Waivable and/or Transferable?

FDA developed a policy that the first generic may relinquish its exclusivity altogether at any time and may waive its 180-day exclusivity rights in favor of another specific generic applicant after exclusivity is triggered. Congress did not address this issue in 2003, and presumably this continues to be agency policy.

In a 1997 case relating to generic copies of Zantac (ranitidine hydrochloride), a federal district court rejected a motion for a temporary restraining order, after FDA approved an ANDA filed by a second applicant who had purchased 180-day exclusivity from the first applicant.¹³² The court noted that the Hatch-Waxman amendments are silent on the question of transferability of 180-day exclusivity, and FDA pointed to other instances where the agency had approved waivers and transfers with respect to five-year and three-year exclusivity under the Hatch-Waxman amendments.¹³³ The court concluded that FDA's interpretation of the statute was not based on an impermissible construction of the statute, was neither arbitrary nor capricious, and was not an abuse of discretion.¹³⁴ It therefore denied emergency relief.

FDA restated its position that 180-day exclusivity rights are transferable in proposed regulations published in 1999,¹³⁵ and it has continued to approve ANDAs filed by applicants who have acquired the exclusivity rights of the first to file.¹³⁶

¹³⁰ *Ranbaxy v. Leavitt*, No. 06-5154 (D.C. Cir. Nov. 14, 2006); *see also FDA Loses in Court on Delisting Patents*, DICKINSON'S FDA WEBVIEW (Nov. 14, 2006). While the appeal was pending, Sandoz, which also sought to market generic simvastatin, separately challenged FDA's relisting of the patents in the *Orange Book* and its requirement that all pending ANDAs be updated with either a paragraph III certification or a paragraph IV certification to each patent. The district court denied its motion for a preliminary injunction, and the court of appeals summarily affirmed. *See Sandoz v. Food and Drug Administration*, 439 F.Supp.2d 26 (D.D.C. 2006), *aff'd* 2006 WL 2591087 (D.C. Cir. 2006) (unpublished). The district court noted that "FDA's refusal to give final approval to Sandoz's simvastatin application until Ivax and Ranbaxy have exhausted their 180 days of exclusivity is not a discretionary act to be reviewed again, but was compelled by [the] decision in *Ranbaxy*." *Id.* at 30. It also rejected the only new argument made by Sandoz—that it was not required to update its ANDA with respect to the relisted patents—as inconsistent with the plain language of the statute and regulations. *Id.* at 31.

¹³¹ 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(CC).

¹³² *Boehringer Ingelheim Corp. v. Shalala*, 993 F.Supp.1 (D.D.C. 1997).

¹³³ 993 F.Supp. at 2.

¹³⁴ *Id.*

¹³⁵ 64 Fed. Reg. 42873, 42881 (Aug. 6, 1999).

¹³⁶ *See Generic Drug Entry Prior to Patent Expiration: An FTC Study* (July 2002), at 36 ("For 6 out of 68 drug products in which there was more than one generic applicant, the first and second generic applicant entered into agreements related to generic market entry. In 4 of these agreements, one of the main provisions specified which generic applicant had or retained rights to the 180-day exclusivity."); *id.* ("In 1 agreement, the first generic applicant relinquished its rights to 180-day exclusivity for a \$35 million license and royalty payment based on the second generic applicant's sales for a period of 7 years.").

The court that decided the terazosin case (Mylan I) in 2000 also confirmed that exclusivity may be transferred separately from the ANDA, writing that “[e]xclusivity periods are a transferable commodity which can be waived in favor of another generic manufacturer for a substantial price.”¹³⁷

FDA addressed transfer in the regulations it proposed in 1999.¹³⁸ Under one part of this proposal, once a subsequent generic received tentative approval for its generic drug from FDA (such that the exclusivity was the only obstacle it faced for final approval), a triggering period would begin to run.¹³⁹ Within 180 days, one of the two triggering events—a favorable court decision regarding the patent or commercial marketing by the first applicant—would need to occur, or the first generic would lose its exclusivity.¹⁴⁰ After a triggering event, the first generic would have been permitted to transfer its rights to another company.¹⁴¹ FDA noted that transfer can be particularly useful when a subsequent generic wins its patent suit with the pioneer before the first generic’s suit goes to trial.¹⁴² Prior to the triggering event, however, the first generic would not have been permitted to transfer its exclusivity rights. It could relinquish its rights—waive its exclusivity entirely—permitting FDA to approve all subsequent ANDAs, but it could not waive its rights in favor of a particular generic manufacturer (i.e., sell its rights).

Although FDA withdrew its proposed regulations in 2002, in 2004 the agency made it clear that it would continue to require a triggering event to distinguish between relinquishment and selective waiver of exclusivity. On May 11, 2004, Pfizer submitted a citizen petition to FDA asking the agency to “acknowledge” that 180-day exclusivity cannot lawfully be waived or transferred.¹⁴³ Pfizer argued, among other things, that the plain language of the statute does not permit waiver or transfer, and that permitting exclusivity to be fully alienable encourages ANDA applicants to file weak applications simply to vest a lucrative asset. On July 2, 2004, the agency denied that citizen petition.¹⁴⁴ FDA rejected the textual argument on the ground that section 505(j)(5)(B)(iv) is ambiguous and can reasonably be interpreted to permit waiver. Further, the agency added, the statute confers a private benefit to specific entities, and in such situations judicial precedent supports inferring that the agency may allow an alternative course of action more favorable to the beneficiary. Finally, the agency noted, allowing generic applicants to waive their exclusivity promotes competition by enabling other generic applicants to market their products sooner. FDA’s response makes it clear that the agency continues to require a triggering event in order to distinguish between relinquishment and selective waiver. “As to potential ‘gaming,’ if the first applicant could selectively waive [transfer] its exclusivity at any time,” FDA wrote, the agency “could reasonably expect the development of a ‘market’ for 180-day exclusivity, with a resulting increase in ANDA’s submitted solely to claim exclusivity.” FDA concluded, however, “that by permitting selective waiver [transfer] only once the exclusivity is triggered, it can prevent ‘gaming’ of exclusivity, avoid unnecessary exclusivity disputes, and still maintain exclusivity as an adequate incentive and reward.”¹⁴⁵

¹³⁷ *Id.* at 42.

¹³⁸ 64 Fed. Reg. 42873 (Aug. 6, 1999).

¹³⁹ *Id.* at 42878.

¹⁴⁰ *Id.*

¹⁴¹ *Id.* at 42881.

¹⁴² *Id.*

¹⁴³ Pfizer, Inc., Citizen Petition, 2004P-0227 (May 11, 2004).

¹⁴⁴ FDA, Response to Pfizer Citizen Petition, 2004P-0227 (July 2, 2004).

¹⁴⁵ *Id.* at n. 5.

I. *Does 180-day Exclusivity "Roll Over" to Second ANDA Applicant in the Event the First Applicant Does Not Perfect Its Rights?*

No. In FDA's August 1999 draft regulations, the agency confirmed its view that exclusivity would not roll over to a second applicant, even if the first applicant withdrew its ANDA. Although these regulations were not finalized, this has been FDA's policy since the proposal issued. The amended legislation requires this result as well.

Prior to 1999, there were no cases or official FDA pronouncements on the question whether exclusivity might "roll over" to a second applicant, although the agency did note in 1994 that if the first applicant was "not actively pursuing approval" of its ANDA, FDA would make approval of subsequent ANDAs immediately effective.¹⁴⁶ It did not address the question whether the next applicant would receive exclusivity. Five years later, it addressed the issue. FDA's August 1999 proposed regulations stated that, in order to be entitled to 180-day exclusivity, an ANDA applicant must be the first to file a substantially complete ANDA with a paragraph IV certification.¹⁴⁷ An ANDA was not substantially complete if FDA determined that the required bioequivalence data failed to meet FDA standards. If FDA found the bioequivalence studies to be deficient, that applicant would lose its exclusivity, and no other applicant would be granted exclusivity. FDA noted that, as this suggests, there would be no "rolling exclusivity."¹⁴⁸ Thus, for example, if the first generic withdrew its application, no subsequent applicant would be granted exclusivity. If the first generic did not perfect its right to the 180-day period (for example, if it lost the patent infringement case), exclusivity would not roll over to the next-filed ANDA.

The 2003 legislation requires the same result for new ANDAs: if all first applicants forfeit exclusivity, "no applicant shall be eligible."¹⁴⁹

J. *Will Marketing by First Generic of Pioneer's Product under Private Generic Label Satisfy Commercial Marketing Trigger?*

FDA decided that private label sales could constitute commercial marketing in 2001, and this was upheld by a federal court in West Virginia. Congress confirmed this in 2003 for new ANDAs with the addition of the words "including the commercial marketing of the listed drug" in the sentence describing the commercial marketing trigger.

In a case involving generic copies of Procardia XL (nifedipine), a district court in West Virginia upheld FDA's determination that a generic manufacturer begins commercial marketing and thereby starts the 180-day clock even when it sells a private label version of the innovator's product, rather than the product that is the subject of its ANDA.¹⁵⁰ In April 1997, Mylan submitted an ANDA with a paragraph IV certification to the 30 mg dosage. It was, therefore, the first generic. The pioneer, Pfizer, sued Mylan, for infringement, and the parties settled in February 2000. Although the settlement terms were not made public or given to the court, the court stated that Pfizer apparently licensed Mylan to sell a private label

¹⁴⁶ 59 Fed. Reg. at 50367-50368.

¹⁴⁷ 64 Fed. Reg. 42873 (Aug. 6, 1999).

¹⁴⁸ *Id.* at 42873.

¹⁴⁹ 21 U.S.C. § 355(j)(5)(D)(III).

¹⁵⁰ Mylan Pharmaceuticals, Inc. v. Thompson, 207 F.Supp.2d 476 (N.D. W.Va. 2001).

version of its own 30 mg, 60 mg, and 90 mg nifedipine products. Pfizer may also have permitted Mylan to market its own 30 mg product under its own ANDA, but Mylan never did so. Mylan claimed the settlement allowed it to maintain its paragraph IV certification, and it never amended the paragraph IV certification to a paragraph III. After the settlement, Biovail, a generic manufacturer aspiring to market nifedipine, attempted without success to persuade Mylan to waive its 180-day exclusivity. When this failed, Teva (its licensee) submitted a citizen petition to FDA asking the agency to find either a) the Mylan ANDA was not eligible for exclusivity, or b) any exclusivity had expired. FDA responded in February 2001, agreeing on both grounds. The agency reasoned, first, that the settlement effectively turned Mylan's paragraph IV certification into a paragraph III certification, and second, that the private label sales constituted commercial marketing and triggered exclusivity. Because the 180 days had expired, FDA approved Biovail's ANDA. Mylan brought suit.

In the decision that resulted, the district court found that FDA had been unreasonable on the first issue and reasonable on the second. The court was not prepared to allow FDA unilaterally to deem the paragraph IV certification to be a paragraph III certification, particularly since Mylan had not amended the certification in its ANDA. But it upheld FDA's determination that the private label sales were commercial marketing, and thus the 180-day period had expired.

The 2003 amendments were consistent with this decision. Congress provided that if an ANDA contains a paragraph IV certification and "is for a drug for which a first applicant has submitted an application containing such a certification" (i.e., is for a drug for which someone else submitted an ANDA earning it exclusivity) the application "shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant."¹⁵¹

K. Does an ANDA Applicant's 180-Day Exclusivity Preclude an Innovator from Distributing an "Authorized Generic" Version of its Drug?

No. The statute does not prohibit the holder of an approved NDA from marketing an authorized generic during the exclusivity period.

In a citizen petition filed in February 2004, Mylan Pharmaceuticals argued that authorized generics are "generic" drugs and, therefore, subject to (may not be marketed during) the exclusivity period awarded to the first generic applicant.¹⁵² The company also argued that the "emerging trend" of marketing authorized generics "will negatively affect the incentive given to generic manufacturers to challenge drug patents."¹⁵³ Teva Pharmaceuticals submitted a similar citizen petition in June 2004, regarding an authorized generic of Pfizer's Accupril (quinapril hydrochloride).¹⁵⁴ On July 2, FDA denied both petitions.¹⁵⁵ Among other things, the agency wrote that, "FDA does not regulate drug prices and has no legal basis on which to prevent an

¹⁵¹ 21 U.S.C. § 355(j)(5)(B)(iv)(I).

¹⁵² Mylan Pharmaceuticals, Inc., Citizen Petition, 2004P-0075 (Feb. 17, 2004).

¹⁵³ *Id.* at 2.

¹⁵⁴ Teva Pharmaceuticals USA, Inc., Citizen Petition, 2004P-0261 (June 9, 2004).

¹⁵⁵ FDA, Response to Teva and Mylan Citizen Petitions, 2004P-0075 and 2004P-0261 (July 2, 2004).

innovator company from marketing its approved NDA product at a price that is competitive with that charged by a first generic applicant to the market.”¹⁵⁶

Teva filed suit against FDA seeking review of FDA's denial of its citizen petition. It later amended its complaint to name Pfizer and its subsidiary Greenstone as defendants, seeking to enjoin the launch of a generic version of Pfizer's Neurontin (gabapentin) by Greenstone. In an oral ruling following launch by Greenstone, the court denied Teva's motion for a temporary restraining order. The district court granted summary judgment for FDA and Pfizer in December 2004,¹⁵⁷ and the D.C. Circuit affirmed in June 2005, noting that the statute “clearly does not prohibit the holder of an approved NDA from marketing, during the 180-day exclusivity period, its own ‘brand-generic’ version of its drug.”¹⁵⁸

Mylan also brought suit, with the same result. The Mylan case involved a generic version of Procter & Gamble's Macrobid (nitrofurantoin), which is used to treat urinary tract infections. FDA approved Mylan's application on March 22, 2004, and the company began to market the product on March 23. On the same day, Watson Pharmaceuticals began to sell an authorized generic under a license from Procter & Gamble. Mylan had filed its citizen petition (discussed above) in anticipation of this authorized generic, and once FDA denied the citizen petition, the company filed suit against the agency in the Northern District of West Virginia.¹⁵⁹ Later the same month, shortly after oral argument, it withdrew the suit.¹⁶⁰ Three months later, it filed the suit again, and in September 2005, the district court dismissed Mylan's complaint for failure to state a claim. The Fourth Circuit affirmed in July 2006 that FDA lacks the power to prohibit the marketing of authorized generics during the 180-day exclusivity period.¹⁶¹

¹⁵⁶ *Id.* at 2.

¹⁵⁷ *Teva Pharms. Indus. v. Crawford*, 355 F.Supp.2d 111 (D.D.C. 2004).

¹⁵⁸ *Teva Pharm. Indus. v. Crawford*, 410 F.3d 41 (D.C. Cir. 2005).

¹⁵⁹ *Mylan Pharmaceuticals, Inc. v. Food and Drug Administration*, Case No. 1:04cv174 (N.D. W.Va., filed Aug. 4, 2004).

¹⁶⁰ Notice of Voluntary Dismissal without Prejudice, *Mylan Pharmaceuticals, Inc. v. Food and Drug Administration*, Case No. 1:04cv174 (N.D. W.Va., Aug. 30, 2004). Trade press reported that “[t]he judge seemed to indicate that Mylan might not be able to get FDA to act under the FDC Act because the law is silent on the issue.” *Mylan Drops Authorized Generics Suit Against FDA*, INSIDE WASHINGTON'S FDA WEEK, (Sept. 3, 2004), at 2.

¹⁶¹ *Mylan v. FDA*, 454 F.3d 270 (4th Cir. 2006). See *Mylan Loses Fight Against Agency: Court Says Authorized Generics Policy Legal*, BNA INC. PHARMACEUTICAL LAW & INDUSTRY (July 14, 2006). Legislation was, however, introduced in both houses during the 109th Congress apparently intending to prohibit the practice. See S. 3695 (109th Cong.); H.R. 5993 (109th Cong.). The Senate bill was referred to the Committee on Health, Education, Labor and Pensions. The House bill was referred to the House Committee on Energy and Commerce Subcommittee on Health. Neither bill passed out of Committee before the end of the Congress. Congress also included a provision in the Deficit Reduction Act of 2005 requiring that, after Jan. 1, 2007, average manufacturer price (AMP) and best price include all drugs marketed under a single NDA. Deficit Reduction Act of 2005, Pub. L. No. 109-171. And at the request of Senators Grassley, Leahy, and Rockefeller, the FTC is examining the competitive effect of authorized generics. See Congressional Research Service Report for Congress, *Authorized Generic Pharmaceuticals: Effects on Innovation* (Aug. 8, 2006) (CRS Report), at 16; see also *Grassley, Other Senators Want FTC Study on Market Effects of “Authorized Generics,”* BNA INC. PHARMACEUTICAL LAW & INDUSTRY (May 20, 2005). This report should be released in 2007. FTC Press Release, “FTC Proposes Study of Competitive Impacts of Authorized Generic Drugs” (March 29, 2006) (“With OMB approval, the Commission will likely issue the orders later this year, and prepare a final report in 2007.”); see also CRS Report, *supra*, at 16; 71 Fed. Reg. 16779 (Apr. 4, 2006). The HHS Office of Inspector General (OIG) also recently announced a study of the impact of authorized generics on Medicaid drug pricing and rebates. See CRS Report, at 16.

L. Do 180-Day Exclusivity and Pediatric Exclusivity Run Concurrently or Consecutively?

If a pioneer earns six months of pediatric exclusivity, the first generic applicant's ANDA is approved effective the first day after conclusion of that exclusivity, and the 180 days begin to run at that point. The terms are consecutive.

In May 2001, FDA sought public comment on whether pediatric exclusivity for an innovator runs concurrently or consecutively with 180-day exclusivity for the first generic.¹⁶² The agency evidently believed that the two exclusivity provisions run concurrently.¹⁶³ At least one generic manufacturer challenged this assertion. Barr was the first generic for Lilly's Prozac. A district court found infringement, but the Federal Circuit reversed and held the second of two challenged patents invalid, while upholding the first.¹⁶⁴ The upheld patent was not set to expire until February 2001, followed by an additional six months of pediatric exclusivity. Had the appellate court ordered the district court to enter a judgment of invalidity on the second patent in September 2000, Barr's exclusivity would have started to run and would have expired before Lilly's pediatric exclusivity was due to expire. Barr prepared to challenge FDA's interpretation, but it turned out never to be necessary. The timing of the Federal Circuit's denial of a petition for rehearing and the district court's resulting judgment of invalidity (triggering Barr's 180 days) was such that pediatric exclusivity had already expired.

The issue was resolved by Congress, however, in the Best Pharmaceuticals for Children Act (BPCA).¹⁶⁵ In this legislation, Congress added section 505A(k) to the FDCA, which states that 180-day exclusivity does not begin until an innovator's pediatric exclusivity has expired. This ensures that generic drug manufacturers entitled to 180-day exclusivity do not lose a portion of that exclusivity due to the overlap with the innovator's pediatric exclusivity.¹⁶⁶

IV. CONCLUSION

It is impossible to predict all of the interpretive issues that will arise with respect to the 2003 exclusivity provisions. One would expect that issues would arise as FDA interprets the amendments. It would appear likely because of their complexity that the forfeiture provisions will be a focus of considerable litigation. To date, however, no exclusivity terms have been forfeited even though the provisions could apply to some products, especially given that it has been well over 30 months since passage of the 2003 amendments. Citizen petitions filed at the agency since 2003 continue for the most part to invoke the old rules, although—as discussed earlier—two petitions have argued that Congress meant to overrule the FDA policy at issue in the metformin case (*see* section III-A, above) and that under the amended rules, therefore, the date notice of a paragraph IV certification is provided to the innovator controls for exclusivity purposes, whether the paragraph IV certification is included in an original ANDA or added as an amendment to a pending ANDA.¹⁶⁷

¹⁶² 66 Fed. Reg. 27983 (May 21, 2001).

¹⁶³ *See* [THE PINK SHEET] (Mar. 12, 2001), at 3.

¹⁶⁴ *Eli Lilly & Co. v. Barr Laboratories Inc.*, 222 F.3d 973 (Fed. Cir. 2000).

¹⁶⁵ Pub. L. No. 107-109, 115 Stat. 1408 (2002).

¹⁶⁶ Pediatric exclusivity is due for reauthorization in 2007.

¹⁶⁷ *See* Mylan Pharmaceuticals, Inc., Citizen Petition, Docket No. 2006P-0245 (June 12, 2006) (pending); IVAX, Citizen Petition, Docket No. 2004P-0520 (Nov. 19, 2004) (withdrawn).

