UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

APOTEX INC., **Plaintiff,** **v.** **FOOD AND DRUG ADMINISTRATION, et al.,** **Defendants.**	**Civil Action No. 05-0125 (JDB)**

MEMORANDUM OPINION

Plaintiff Apotex, Inc. ("Apotex") brings this action against the Food and Drug Administration ("FDA"), Secretary of Health and Human Services Michael O. Leavitt, and Acting FDA Commissioner Lester M. Crawford, challenging FDA's decision to deny immediate approval to Apotex for a generic version of the drug omeprazole as arbitrary and capricious under the Administrative Procedure Act ("APA"), 5 U.S.C. § 706(2). In essence, the parties disagree regarding the proper interpretation of 21 U.S.C. § 355(j)(5)(B)(iv) (2000),[1] the same statutory provision at issue in Teva Pharms. USA, Inc. v. FDA, 398 F. Supp. 2d 176 (D.D.C. 2005), and several other recent cases in this district and the D.C. Circuit.

[1]Although the relevant statute was amended in 2003 by the Medicare Prescription Drug, Improvement and Modernization Act of 2003 ("MMA"), the pre-amendment version applies to this case. Hence, all statutory citations to the Hatch-Waxman Act and the Food, Drug, and Cosmetic Act ("FDCA") in this opinion refer to the pre-amendment version of the statute.

BACKGROUND

1. Statutory and Regulatory Framework

In order to market an original pharmaceutical product, a company must file a New Drug Application ("NDA") with the FDA, providing technical information regarding the pharmaceutical's composition, clinical trial results as to safety and effectiveness, the method of manufacture, and proposed labeling for the pharmaceutical's use. See 21 U.S.C. § 355(b)(1). The FDA must approve the NDA, and the applicant must also submit information concerning patents that "claim[] the drug . . . or which claim[] a method of using such drug . . . ." 21 U.S.C. §§ 355(b)(1), (c)(2). The FDA then "lists" this information, once approved, in a publication called "Approved Drug Products With Therapeutic Equivalence Evaluations" (also known as "the Orange Book"). See 21 U.S.C. § 355(c)(2); 21 C.F.R. § 314.53(a).

The Drug Price Competition and Patent Term Restoration Act of 1984, codified at 21 U.S.C. § 355 and 35 U.S.C. §§ 156, 271, 282, governs the marketing of generic versions of pharmaceuticals that are covered by pre-existing NDAs. See 21 U.S.C. § 355(j). The generic pharmaceutical company must submit an Abbreviated New Drug Application ("ANDA"), which is a truncated version of the original NDA, enabling the generic applicant to avoid the considerable expense of repeating the detailed clinical studies originally conducted in connection with the NDA. See Dr. Reddy's Labs., Inc. v. Thompson, 302 F. Supp. 2d 340, 343 (D. N.J. 2003). The ANDA-applicant must establish that its generic product is bioequivalent to the NDA-product, and must ordinarily show that the ANDA-product has the same active ingredient, dosage form and strength, method of administration, and labeling as the NDA-product. 21 U.S.C. § 355(j)(2)(A). In addition, the ANDA must include one of four certifications as to each patent

that is listed in the Orange Book in connection with the NDA-product. See 21 U.S.C. § 355(j)(2)(A)(vii). The four available certifications state that: (1) there is no patent information; (2) the listed patent has expired; (3) the ANDA-applicant will not market its generic drug until the listed patent expires ("paragraph III certification"); or (4) the listed patent is invalid and/or will not be infringed by the ANDA-drug ("paragraph IV certification"). See 21 U.S.C. § 355(j)(2)(A)(vii)(I)-(IV).

An ANDA-applicant seeking to market its drug before the NDA-drug's patent has expired must make a paragraph IV certification with respect to the "listed patents" (i.e., the patents that are listed in the Orange Book when the ANDA is filed), as well as those that are placed in the Orange Book subsequently (i.e., "later-listed patents"), and must further advise the NDA-holder of the legal and factual grounds for the certifications. See 21 U.S.C. § 355(j)(2)(B). Under the law, as soon as an ANDA-applicant makes a paragraph IV certification as to a patent that claims the NDA-drug, the ANDA-applicant has infringed that patent, and the NDA-holder may immediately sue the ANDA-applicant for infringement. See 35 U.S.C. § 271(e)(2)(A). If the NDA-holder files the infringement suit within forty-five days of the date on which it received notice of the paragraph IV certification, then any approval of the ANDA is automatically stayed for thirty months thereafter. 21 U.S.C. § 355(j)(5)(B)(iii). The thirty-month stay will not apply, however, if a final court decision is rendered earlier in the patent case, or if the presiding court orders otherwise. 21 U.S.C. § 355(j)(5)(B)(iii).

As an incentive for generic pharmaceutical companies to further the statutory purpose of helping the public gain access to lower-cost drug products more expeditiously, Hatch-Waxman grants a 180-day period of generic marketing exclusivity to a "previous" ANDA-applicant that

has filed a paragraph IV certification. See 21 U.S.C. § 355 (j)(5)(B)(iv). Each strength and dosage form of a particular generic drug is a separate drug product for which an ANDA applicant can potentially qualify for generic exclusivity. During this 180-day exclusivity period, no other generic competition is permitted. Id. The 180-day period is triggered by the earlier of either: (1) "the date on which the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application"; or (2) "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." See 21 U.S.C. § 355(j)(5)(B)(iv). The latter triggering-event is referred to as the "court-decision trigger."

The present litigation concerns whether a 180-day exclusivity period is awarded to each ANDA-applicant who is the first to make a paragraph IV certification as to a listed patent ("patent-based" exclusivity), or rather only to the single ANDA-applicant who is the first to make a paragraph IV certification as to any listed patent on the drug ("drug-product based" exclusivity).[2] The patent-based interpretation allows for multiple exclusivity periods that may be conferred in connection with a single drug product. The drug-product based interpretation, on the other hand, permits only one exclusivity period to arise in relation to a particular drug product. Hence, the FDA (which has adopted the patent-based approach) submits that an exclusivity period attaches to each individual patent, but Apotex (as a proponent of the drug-product based approach) contends that a single exclusivity period attaches to the drug product as a whole.

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[2]The "drug-product based" approach has also been referred to as the "first-filer" approach. See, e.g., Apotex, Inc. v. FDA, 393 F.3d 210, 211 (D.C. Cir. 2004).

2. Factual Background

Apotex, formerly known as TorPharm, Inc., is a generic pharmaceutical manufacturer organized under the corporate laws of Canada. Pl.'s Statement of Undisputed Material Facts at 1 ¶ 1 ("Pl.'s Stmt."). AstraZeneca LP ("AstraZeneca") initially held seven patents in connection with its approved NDA for Prilosec®, the branded version of the generic drug omeprazole, which is most commonly prescribed to treat gastroesophageal reflux disease. Compl. at 8 ¶¶ 25-26; see Pl.'s Stmt. at 2 ¶ 6. Six of the seven originally-listed Prilosec® patents are relevant to this litigation: Nos. 4,636,499 ("'499 patent"); 4,786,505 ("'505 patent"); 4,853,230 ("'230 patent"); 5,093,342 ("'342 patent"); 5,629,305 ("'305 patent"); and 5,599,794 ("'794 patent"). Pl.'s Stmt. at 2-3 ¶ 8. AstraZeneca's approved NDA covers 10 mg, 20 mg, and 40 mg capsule dosages. Compl. at 8 ¶ 25. The present litigation concerns the 40 mg dosage.

On March 17, 1998, Andrx Pharmaceuticals, Inc. ("Andrx"), submitted an ANDA seeking to market 10 mg and 20 mg generic dosages. Compl. at 9 ¶ 27. More than six months later, on September 28, 1998, Andrx amended its ANDA to include the 40 mg dosage. Id. When Andrx amended its ANDA, it also submitted paragraph IV certifications as to AstraZeneca's six listed patents. Id. Andrx was the first to file an ANDA containing paragraph IV certifications regarding the 40 mg product. Id. at ¶ 28. In connection with the September 28, 1998 paragraph IV certifications for the 40 mg product, FDA granted Andrx a 180-day exclusivity period under Hatch-Waxman. See id.

Following Andrx's September 28, 1998 amendment to its ANDA, AstraZeneca listed four additional patents in connection with Prilosec®: U.S. Patent Nos. 6,147,103 ("'103 patent"); 6,150,380 ("'380 patent"); 6,166,213 ("'213 patent"); and 6,191,148 ("'148 patent"). Compl. at 12

¶ 37. In the spring of 2001, Andrx amended its ANDA a second time, so as to include paragraph IV certifications with respect to the later-listed '103, '380, '213 and '148 patents. Id.; Admin. Rec. Exh. 51; see also Admin. Rec. Exh. 50 at 2; Admin. Rec. Exh. 62 at 1. FDA then granted Andrx a 180-day period of generic exclusivity in connection with the paragraph IV certifications as to these later-listed patents. Compl. at 12 ¶ 37. On or about December 23, 1998, Andrx withdrew its paragraph IV certifications as to the '342, '305 and '794 patents (three of the relevant group of six originally-listed patents). Id. at ¶ 29. Once withdrawn, those patents could no longer serve as the basis for exclusivity, see Dr. Reddy's Labs., 302 F. Supp. 2d at 360-66, and exclusivity could only be predicated upon the remaining paragraph IV certifications as to the '499, '505, and '230 patents (from the originally-listed group).

In February of 1999, another generic pharmaceutical company, Dr. Reddy's Laboratories, Inc. ("DRL"), filed an ANDA seeking to market the 40 mg dosage, simultaneously making paragraph IV certifications as to all of AstraZeneca's listed patents. See Pl.'s Mot. Summ. J. Exh. 3 at ¶¶ 23-25; Pl.'s Mot. Summ. J. Exh. 4 at ¶¶ 23-25; see also Admin. Rec. Tab 68 at 1. AstraZeneca then sued Andrx, DRL,[3] and a third ANDA-applicant by the name of Genpharm in the United States District Court for the Southern District of New York for infringement of the '499, '505 and '230 patents. That court ultimately granted summary judgment in favor of Genpharm and DRL as to the '499 patent, holding it not infringed. See Admin. Rec. Tab 34 at Exh. F, Exh. G. Final judgment of infringement against Andrx with respect to several claims of the '505 and '230 patents was entered on October 30, 2002. See Admin Rec. Tab 34 at Exh. F;

[3]The suit actually named Cheminor Drugs Ltd., which later merged with DRL. See Compl. at 10 ¶ 30; Pl.'s Mot. Summ. J. Exh. 5.

see also In re Omeprazole Patent Litig., 222 F. Supp. 2d 423, 433, 541-47 (S.D.N.Y. 2002); Compl. at 10 ¶ 31. The court also enjoined Andrx from selling generic omeprazole capsules in any strength until the expiration of the '505 and '230 patents -- and the subsequent pediatric exclusivity period held by AstraZeneca[4] -- on October 20, 2007. See Admin. Rec. Tab 34 at Exh. F. Furthermore, the effective date of approval for Andrx's ANDA was delayed at least until that date. See id. The judgment of infringement against Andrx was affirmed on December 11, 2003. See In re Omeprazole Patent Litig., 84 Fed. Appx. 76, 83, 2003 U.S. App. LEXIS 24899, at *17 (Fed. Cir. Dec. 11, 2003).

On December 5, 2000, Apotex submitted an ANDA for omeprazole products in 10 mg, 20 mg and 40 mg strengths. Compl. at 11 ¶ 35. The ANDA contained paragraph IV certifications as to the '505 and '230 patents. Id. AstraZeneca then sued Apotex for infringement as to those patents, and that litigation currently remains pending without a court decision. Id. The FDA granted tentative approval to Apotex for its 40 mg product on October 6, 2003, but delayed final approval on the grounds that Andrx's 180-day exclusivity period had not yet expired. Id. at ¶ 36. Apotex's ability to obtain final approval from the FDA and to market its 40 mg product, then, is blocked by the FDA's decision to grant a second 180-day exclusivity period to Andrx, which was conferred in connection with Andrx's ANDA for AstraZeneca's later-listed patents. See id. at ¶¶ 37-41. As a result, the soonest that Apotex can hope to market its generic product is April of 2008 -- not earlier than 180 days following the expiration of the '505 and '230

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[4]Pediatric exclusivity is provided for by 21 U.S.C. § 355a, which confers an additional six-month period of exclusive marketing and sales upon the patent-holder following the expiration of a drug patent for which the patent-holder has conducted satisfactory pediatric testing. See Mylan Labs., Inc. v. Thompson, 389 F. 3d 1272, 1275 (D.C. Cir. 2004).

patents (and AstraZeneca's period of pediatric exclusivity) on October 20, 2007.

3. Applicable Legal Standards

Under the APA, a court may vacate the FDA's decision if it is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with the law." 5 U.S.C. § 706(2)(A). Agency actions are entitled to much deference under this narrow standard of review. See Citizens to Preserve Overton Park, Inc. v. Volpe, 401 U.S. 402, 416 (1971). The reviewing court is not permitted to substitute its judgment for that of the agency. See id. That is, it is not enough for the agency decision to be incorrect -- as long as the agency decision has some rational basis, the court is bound to uphold it. See id. The court may only review the agency action to determine "whether the decision was based on a consideration of the relevant factors and whether there has been a clear error of judgment." Id.

The familiar framework of Chevron USA, Inc. v. Natural Resources Defense Council, 467 U.S. 837 (1984), applies in this case. At step one of Chevron, the Court first must inquire whether the statute "speaks clearly 'to the precise question at issue.'" Chevron, 467 U.S. at 842-43. If so, then the analysis proceeds no further -- the Court must "give effect to the unambiguously expressed intent of Congress." Id.; see also Robinson v. Shell Oil Co., 519 U.S. 337, 340 (1997) (if text is plain and unambiguous, then the analysis ends there). If, however, the statute is not clear in relation to the specific issue before the Court, then under Chevron step two, the Court must consider whether the FDA's interpretation is supported by a "permissible construction" of the statute. Chevron, 467 U.S. at 843. But the Court will only reach the second inquiry under Chevron if it determines that the statute is "silent or ambiguous with respect to the specific issue" presented. Id. The "[e]xistence of ambiguity is not enough per se to warrant

deference to the agency's interpretation. The ambiguity must be such as to make it appear that Congress either explicitly or implicitly delegated authority to cure that ambiguity." Am. Bar Ass'n v. FTC, 430 F.3d 457, 469 (D.C. Cir. 2005); see also Michigan v. EPA, 268 F.3d 1075, 1082 (D.C. Cir. 2001). Hence, under the Chevron step two deferential analysis, if the statute is "ambiguous in such a way as to make the [FDA's] decision worthy of deference," then this Court should "uphold the [FDA's] interpretation of the ambiguous statute as long as that interpretation is 'permissible,' that is, if it is 'reasonable.'" Am. Bar Ass'n, 430 F.3d at 468 (quoting Chevron, 467 U.S. at 843, 845).

Because the FDA is interpreting its own statute here, the appropriate degree of deference will be determined based upon the circumstances surrounding that interpretation. See United States v. Mead, 533 U.S. 218, 227-31 (2001). An agency will receive utmost deference if "it appears that Congress delegated authority to the agency generally to make rules carrying the force of law, and that the agency interpretation claiming deference was promulgated in the exercise of that authority." Mead, 533 U.S. at 226-27. The FDCA, pursuant to 21 U.S.C. § 371(a), grants explicit authority to the FDA "to promulgate regulations for the efficient enforcement of" the statute. Similarly, the Hatch-Waxman Amendments permit the FDA to promulgate regulations that are "necessary for the administration" of those amendments. See 21 U.S.C. § 355 note, Pub. L. No. 98-417, 105, 98 Stat. 1585, 1597 (1984).

ANALYSIS

I. Chevron Step One: Does the Language of § 355(j)(5)(B)(iv) Clearly Address the Issue?

Under Chevron's familiar framework, the plain language of Hatch-Waxman is the starting

point for the Court's analysis. See Am. Bar Ass'n, 430 F.3d at 467 (citing Group Life & Health Ins. Co. v. Royal Drug Co., 440 U.S. 205, 210 (1979)); see also Barnhart v. Sigmon Coal Co., 534 U.S. 438, 450 (2002). "In determining whether a statutory provision speaks directly to the question before [it, a court must] consider it in context." Holly Sugar Corp. v. Johanns, No. 05-5067, slip op. at 5 (D.C. Cir. Feb. 7, 2006) (citing FDA v. Brown & Williamson Tobacco Corp., 529 U.S. 120, 132-33 (2000)). Section 355(j)(5)(B)(iv) provides:

> If the application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) and is for a drug for which a previous application has been submitted under this subsection [containing][5] such a certification, the application shall be made effective not earlier than one hundred and eighty days after --
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> (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
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> (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.

The provision thus cross-references the requirement for an ANDA set out in § 355(j)(2)(A)(vii)(IV):

> a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (I) or which claims a use for such listed drug for which the applicant is seeking approval under this

[5]The statute actually uses the word "continuing," but courts have concluded that this is a typographical error and the proper word is "containing." See, e.g., Purepac Pharm. Co. v. Friedman, 162 F.3d 1201, 1203 n.3 (D.C. Cir. 1998); Mova Pharm. Corp. v. Shalala, 140 F.3d 1060, 1063 n.3 (D.C. Cir. 1998); Dr. Reddy's Labs., 302 F. Supp. 2d at 351 n.4. This, in itself, reflects some lack of clarity in the language.

> subsection and for which information is required to be filed under subsection (b) or (c) of this section-
>
> (I) that such patent information has not been filed,
> (II) that such patent has expired,
> (III) of the date on which such patent will expire, or
> (IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted.

Apotex argues that the statute is drug-product specific, conferring a single 180-day exclusivity period in connection with the drug product upon the first ANDA applicant to make a paragraph IV certification as to any patent that is listed for that drug product. FDA, on the other hand, contends that a separate 180-day exclusivity entitlement arises in connection with each patent that is listed for the drug product and as to which an ANDA applicant is the first to file a paragraph IV certification. Hence, under FDA's view, distinct 180-day exclusivity entitlements may be awarded to multiple ANDA-applicants, or even to a single ANDA-applicant.

This issue has not yet been resolved by the courts. When describing the effect of § 355(j)(5)(B)(iv), some courts have assumed that the text of the provision only allows for a single 180-day exclusivity entitlement. See, e.g., Teva Pharms. v. Pfizer, Inc., 395 F.3d 1324, 1328 (Fed. Cir. 2005) (stating that "[t]he first ANDA applicant to file a paragraph IV certification enjoys a 180-day period of generic marketing exclusivity"). But those courts were not squarely confronted with the issue. Two members of this District Court have specifically considered whether § 355(j)(5)(B)(iv) is ambiguous, and have reached opposite conclusions. Compare Torpharm, Inc. v. FDA, Civil Action No. 03-2401 (D.D.C. Jan. 8, 2004) (order) (Roberts, J.) (finding that the statutory language is clear that only one exclusivity period is allowed), vacated on other grounds sub nom. Apotex, Inc. v. FDA, 115 Fed. Appx. 93, 2003 WL 2931131 (D.C.

Cir. Dec. 17, 2004), with Apotex, Inc. v. FDA, Civil Action No. 04-0605, 2004 WL 3088676 (D.D.C. Jun. 3, 2004) (Huvelle, J.) (finding that the statutory language is silent or ambiguous on the issue), vacated on other grounds, 393 F.3d 210 (D.C. Cir. 2004), and Ivax Pharms., Inc. v. FDA, Civil Action No. 04-1603 (D.D.C. Sep. 17, 2004) (memorandum and opinion) (Huvelle, J.) (same). This Court now concludes that the language of § 355(j)(5)(B)(iv) is silent regarding the issue of how many exclusivity periods may arise in connection with a single drug product. Moreover, because of that silence, the provision lends itself to multiple interpretations, and hence is ambiguous under Chevron step one.

By its terms, the relevant statutory provision (§ 355(j)(5)(B)(iv)) actually addresses "subsequent" ANDAs -- that is, the language affirmatively speaks of an ANDA that is not the first ANDA to be submitted in connection with a particular drug product. The provision delays approval for the subsequent ANDA until at least 180 days following either of the triggering events enumerated in clauses (I) and (II) -- the commercial-marketing and court-decision triggers. The 180-day exclusivity period, then, is conferred upon the previous ANDA-applicant only by negative implication -- the plain language of the statute never affirmatively mentions an exclusivity period, and it is silent regarding the issue of how many exclusivity periods may arise in connection with the drug. There is certainly no requirement in the words of § 355(j)(5)(B)(iv) that the paragraph IV certification in the previous ANDA must concern the same patent as the paragraph IV certification in the subsequent ANDA, but there is also no language to establish that they need not match. At step one of Chevron, the Court may only ascertain whether the language of § 355(j)(5)(B)(iv) clearly forecloses the FDA's patent-based approach. The Court cannot say that it does -- because the statutory language mentions neither approach, it is silent on

the subject.

Clarity of the statutory text on this issue cannot be drawn from surrounding language because various parts of the provision are themselves subject to different interpretations. To begin with, § 355(j)(5)(B)(iv) requires that both the "previous" and "subsequent" ANDAs each contain a certification pursuant to § 355(j)(2)(A)(vii)(IV). The required certification, in turn, is a statement that a patent claimed by the drug-product is either invalid or will not be infringed by the new drug that the ANDA-applicant seeks to market. See § 355(j)(2)(A)(vii)(IV). Section 355(j)(5)(B)(iv) uses the term "such a certification" with reference to the paragraph IV certification contained in the previous ANDA. That language may be interpreted generically to mean "such a certification [under paragraph IV as to any patent]," or, alternatively, it may be interpreted, in a more particularized fashion, to mean "such a [paragraph IV] certification." The more particularized interpretation supports the view that the paragraph IV certifications in the "previous" and "subsequent" ANDAs must match -- that is, that they must relate to the exact same patent. The more generic interpretation, however, supports the view that the paragraph IV certifications need not match; as long as both the previous and subsequent ANDAs contain a paragraph IV certification, nothing more is required, even if the paragraph IV certifications concern different patents. Hence, the ambiguity of this language, coupled with statutory silence as to the number of exclusivity periods, leaves the statute ambiguous on that point as well.

Another source of ambiguity in § 355(j)(5)(B)(iv) derives from Congress's use of the word "previous" in reference to the earlier ANDA application that is eligible for an award of exclusivity. "Previous" is not always synonymous with the word "first"; it may refer to any of several, rather than just to the first of several. For example, assume that Company A is the first

to submit an ANDA as to Drug X, with Company B submitting the second ANDA and Company C submitting the third. Each company's ANDA contains a proper paragraph IV certification, and Company A gives notice to the Secretary that it began commercial marketing of the generic version of Drug X pursuant to its ANDA on March 3. With respect to Company C, then, approval of its ANDA is delayed for 180 days following March 3. But the statute does not, by its terms, prevent Company B from giving notice that it intends to market a generic version of Drug X pursuant to its ANDA on April 1: the ANDAs of both Company A and Company B are "previous" to the ANDA of Company C, and the language of the statute does not specifically brand Company A as the only ANDA that, by virtue of its status as the first ANDA for Drug X, can be considered "previous."

Certainly, it is not the case that "previous" may never mean "first." "First" is subsumed within the concept of "previous": by its very nature, the "first" ANDA application is "previous" to a "subsequent" ANDA application. It may very well be, then, that as used in the statute, the first ANDA application is "the previous" application, and all later applications are "subsequent" ANDAs (as Apotex submits). But this language is susceptible to multiple interpretations, and the statutory silence on the issue of the number of possible exclusivity periods thus cannot be clarified through reference to the term "previous." At step one of Chevron, the Court "must assume 'that the legislative purpose is expressed by the ordinary meaning of the words used.'" Cal. Indep. Operator Sys. v. FERC, 372 F.3d 395, 400 (D.C. Cir. 2005) (citing Sec. Indus. Ass'n v. Bd. of Governors, 468 U.S. 137, 149 (1984)). The ordinary definitions of "previous," taken together with the context in which the word is used in the statute, simply do not foreclose the FDA's argument on this point.

It is also significant that § 355(j)(2)(A)(vii) uses particularized language such as "each patent" and "such patent." The parties agree that because § 355(j)(5)(B)(iv) cross-references § 355(j)(2)(A)(vii)(IV), the provisions must be read together. Their disagreement centers on the result of that synthesis. Again, the Court concludes that there are two ways to interpret the cross-reference based upon the structure of the statutory language, and this language cannot therefore create clarity out of the statutory silence. Apotex submits that the provisions address different stages of the ANDA process, and the mere fact that § 355(j)(2)(A)(vii) may be patent-specific does not necessarily mean that § 355(j)(5)(B)(iv) is also patent-specific. Although there is some force to this view, it cannot be said that this is the only reasonable way to interpret the statute. Section 355(j)(5)(B)(iv) certainly seems to incorporate only the language of § 355(j)(2)(A)(vii)(IV), not the language of § 355(j)(2)(A)(vii) as a whole. But under such a literal construction, § 355(j)(5)(B)(iv) would then begin: "[i]f the application contains a certification [that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug that is the subject of the ANDA] . . . . " The result would be that § 355(j)(5)(B)(iv) would be rendered nonsensical because at this point it has not yet referenced a specific patent; hence, there is no patent to which the "such patent" language could relate.

There is an alternative approach, however. The "such patent" language in paragraph IV may reasonably be viewed as referring back to the patent addressed by the introductory language of § 355(j)(2)(A)(vii). In this way, the patent-specific nature of § 355(j)(2)(A)(vii) may reasonably be imputed to § 355(j)(5)(B)(iv) through the cross-reference. Simply put, then, there are two ways to view the cross-reference: either (1) it incorporates the language of paragraph IV only, or (2) by virtue of the "such patent" language in paragraph IV, it also incorporates the "each

patent" language in the introductory paragraph of § 355(j)(2)(A)(vii). In the Court's view, the cross-reference probably was meant only to establish that a certification under paragraph IV, rather than any of the other three certifications, is what causes the exclusivity entitlement to arise. But because it is possible to read the language and structure of the statute to support two different interpretations, the Court cannot be certain. Hence, again, under the strict mandate of Chevron step one, the intent of Congress is not unambiguously expressed.

The language of the court-decision trigger clause in § 355(j)(5)(B)(iv)(II) further highlights the statute's ambiguity on the issue presently before the Court. This clause triggers the 180-day exclusivity clock only if the relevant court decision relates to the same patent that is the subject of the paragraph IV certification. A structural argument can be made that, in order to avoid interpreting § 355(j)(5)(B)(iv) in a way that is internally inconsistent, the remainder of the provision must also be patent-specific. The Court disagrees with this argument -- the court-decision trigger language seems to identify the time that the 180-day exclusivity period begins; it does not, as FDA appears to suggest, necessarily define what causes that exclusivity entitlement to arise. The Court can conceive of no reason why, for example, the court-decision trigger clause could not be patent-specific even though the remainder of § 355(j)(5)(B)(iv) is drug-product-specific, particularly because the language of the court-decision trigger clause is very clearly patent-specific (in stark contrast to the rest of § 355(j)(5)(B)(iv)). There is simply nothing in the court-decision trigger clause to suggest that multiple 180-day exclusivity periods attach to a single drug-product on a patent-by-patent basis. But there is also nothing in that clause to foreclose the possibility of multiple exclusivity periods, and if one reads the language of the court-decision trigger clause in pari materia with the language of the introductory paragraph of §

355(j)(5)(B)(iv), it is evident that there is more than one way to interpret the statutory text. Of course, the Court's sentiments regarding which of the possible interpretations is the better or more likely approach is irrelevant under the legal calculus of Chevron step one. It is enough that the provision is subject to more than one interpretation on the issue of the permissible number of exclusivity periods.

Finally, the language of § 355(j)(5)(B)(iv) is unclear as to which patent the referenced court decision must concern. An example is illustrative. Assume that Company A submitted the first ANDA for Drug X, making a paragraph IV certification as to Patent 1. Company B subsequently submits its own ANDA for Drug X, making a paragraph IV certification as to Patent 2. If there is then a court decision holding Patent 2 invalid or not infringed as described in § 355(j)(5)(B)(iv), is the exclusivity period that Company A holds based upon its certification as to Patent 1 triggered by the court decision concerning Patent 2? Or would the exclusivity period only be triggered by a court decision finding Patent 1 invalid or not infringed? Certainly, § 355(j)(5)(B)(iv) does not clearly resolve this question. But such a conundrum highlights the ambiguity that is, unfortunately, characteristic of the statutory text, and forecloses Apotex's argument that the statutory language is plain or clear. The statute simply does not lend itself clearly to either approach urged by the parties here, and "'the text and reasonable inferences from it [do not] give a clear answer against'" the FDA. Cal. Indep. Sys. Operator Corp., 372 F.3d at 402 (quoting Brown v. Gardner, 513 U.S. 115, 120 (1994)). Because the statute is silent or ambiguous on the relevant issue, the Court simply cannot conclude that there is a "clear[,] textually[-]grounded conclusion in [Apotex's] favor that is fatal to the remaining principal arguments advanced against it." Id. at 401 (quoting Brown, 513 U.S. at 120). Accordingly, the

Court will now proceed to step two of the Chevron analysis.

II. Chevron Step Two: Is the FDA's Patent-Based Approach a Permissible Construction of § 355(j)(5)(B)(iv)?

At the second step of Chevron, the Court must determine whether the agency's patent-based approach is "based on a permissible construction of the statute," Chevron, 467 U.S. at 843 -- that is, is it one of the possible interpretations reasonably supported by the language and structure of the statute? For many of the reasons already discussed, the Court concludes that the FDA's patent-based approach is a permissible construction of § 355(j)(5)(B)(iv). As indicated above, the statute is silent regarding how many exclusivity periods may arise in connection with a single drug product. The language of the statute -- as well as its structure -- can support both the drug-product specific approach urged by Apotex and the patent-specific approach taken by the FDA. Because the FDA's approach is one of two permissible ways to interpret the language of the statute, the Court must conclude that the patent-based approach is a reasonable construction of the statutory provision.

But the Court's analysis does not end there. Chevron step two also considers whether the agency's approach is reasonable in practice. See Associated Gas Distribs. v. FERC, 899 F.2d 1250, 1261-63 (D.C. Cir. 1990) (finding the FERC's interpretation of the Natural Gas Policy Act unreasonable at Chevron step two because it was contrary to the statute's language and legislative history, did not further the statute's policies, and essentially had the "potential wholly to undermine" the statutory regime); cf. Teva Pharms., USA, Inc. v. FDA, 182 F.3d 1003, 1011 (D.C. Cir. 1999) (stating that the FDA must interpret the court-decision trigger clause of Hatch-Waxman in a manner that "avoid[s] absurd results and further[s] the statute's purpose"). An

approach that is practically infeasible may thus prove not to be a permissible construction of the statute. Each party contends that the approach urged by the other is unreasonable or absurd in practice. The Court concludes that both approaches are imperfect, and that even if the approach urged by Apotex is less imperfect, that would not provide a sufficient basis to render the FDA's approach impermissible under Chevron step two.

Apotex contends that the FDA's patent-based approach creates several serious practical absurdities that directly negate the purpose of the statute. Most significantly, the patent-based approach, Apotex maintains, results in "exclusivity stand-offs," during which two ANDA-applicants that were the first to file paragraph IV certifications as to different patents for the same drug product are each granted a distinct 180-day exclusivity period. Neither applicant can utilize its exclusivity period, however, because it is blocked from doing so by the exclusivity period that is held by the other applicant. This result is, Apotex argues, plainly contrary to the purpose of Hatch-Waxman. The problem is not ameliorated, in Apotex's view, by the FDA's formulation of a "shared exclusivity" rule as an exception (under certain circumstances) to the patent-based approach, because the very fact that the patent-based approach causes such absurdities suggests that the statute does not contemplate a patent-based approach. Apotex also submits that the patent-based approach confers significant power upon the NDA-holder because it allows the NDA-holder to control whether multiple exclusivity periods will be awarded and provides an incentive for the NDA-holder not to list all of its patents initially. See Pl.'s Mot. Summ. J. Exh. 6 at 56.

The FDA responds by noting that the drug-product approach suffers from its own theoretical conundrums. For example, according to the FDA, if different ANDA applicants were

to submit paragraph IV certifications as to distinct patents for the same drug-product on the same day, it is unclear to whom the 180-day exclusivity period would be awarded under the drug-product approach. This problem is indeed a real one, but in the end, the parties offer no reason why the FDA's shared exclusivity rule could not be used to address such situations. If the FDA can adopt an extra-statutory exception to the patent-based approach in order to avoid the incongruous result of an exclusivity stand-off, then it can certainly do so in order to remedy a statutory complication that is simple to solve, and is just as possible under the FDA's patent-based approach as it is under the drug-product approach.

The FDA also characterizes the drug-product approach as "bad policy," arguing that it vests all exclusivity in the first ANDA-applicant to make a paragraph IV certification. According to the FDA, the result is to remove the incentive promptly to challenge later-listed patents. When Congress amended Hatch-Waxman through the MMA to adopt the drug-product approach, the FDA submits, certain changes were made in order to preserve this incentive in the absence of the patent-based approach.[6] However, the Court concludes that ultimately FDA's argument is a red

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[6]FDA has also argued that because Congress adopted a drug-product approach when it amended Hatch-Waxman through the MMA in 2003, the previous statutory regime must have been patent-specific. The Court is not so persuaded, and its ultimate conclusion is not based upon this argument. The MMA could as easily reflect a reaffirmation and clarification of, rather than an abrupt change in, the existing law. That is, the amendments may have "restructured" the FDA's interpretation of the statute, not the statute itself. See 149 Cong. Rec. S 15882 (remarks of Senator Kennedy) (Tues. Nov. 25, 2003) (stating that the MMA will "restructure[] how the 180-day generic exclusivity provisions work"). Hence, the MMA may be the product of Congress' realization that the FDA had incorrectly interpreted Hatch-Waxman, and may evidence congressional desire to bring the FDA's administration of the law into conformity with the drug-product interpretation originally intended. See, e.g., Pl.'s Mot. Summ. J. Exh. 6 at 58; Pl.'s Mot. Summ. J. Exh. 10 at 11. In any event, attempting to decipher the intent of a previous Congress is a difficult and delicate exercise, with little certainty and a generous margin for error, particularly where the legislative history for both the original statute and the subsequent amendment is inconclusive.

herring. The statute already requires ANDA applicants to certify to the originally-listed patents as well as to any later-listed patents; an ANDA applicant cannot obtain final FDA approval unless it has certified "with respect to each patent which claims the listed drug." See 21 U.S.C. § 355(j)(2)(A)(vii). Hence, the contention that there must be some further incentive to certify to later-listed patents ultimately carries little weight.

Finally, the FDA argues that even the drug-product approach is actually premised upon a patent-specific interpretation of the statute. For example, imagine that Company A is the first to make a paragraph IV certification to Patent X, which is claimed by a particular drug product. There is no approved ANDA for Patent X, however, when the NDA-holder sues Company A for infringement of Patent X. If the court rules in favor of Company A, then there is a court-decision trigger under § 355(j)(5)(B)(iv)(II) based upon Patent X. But because there is no approved ANDA for the drug product, the 180-day exclusivity entitlement will expire without ever having been used -- no company may market a drug product before the expiration of a patent that is claimed for that product unless the ANDA has been approved. The only alternative to a wasted exclusivity period would be for an exclusivity entitlement to arise in connection with another patent for that drug product. Likewise, if Patent A expires before any ANDA for that drug product has been approved, then either no ANDA would be eligible for exclusivity at all or a subsequent certification as to another patent would have to provide the basis for exclusivity. See Def.'s Mem. Opp'n at 27. The FDA's arguments on this point certainly highlight a theoretical complexity of the drug-product approach. Again, however, the problem might be addressed through the development of a special rule or exception (a course of conduct that certainly is not unusual for the FDA).

When the flaws in each approach are balanced, then, it may well be that the drug-product approach advocated by Apotex is the more reasonable approach. The drug-product approach is less counterintuitive than the patent-based approach, and its theoretical difficulties are somewhat less daunting. But because the drug-product approach has its own practical difficulties, and because the FDA's patent-based approach may be reasonably derived from the language and structure of the statute, the Chevron step two analysis leads the Court to conclude that the patent-based approach is a permissible construction of the statute, and hence FDA's choice of that approach is reasonable and entitled to deference. The Court is not permitted to substitute its judgment for that of the agency. Am. Bar Ass'n, 430 F.3d at 468. Under Chevron's highly deferential standard, it matters not which is the better or even the correct approach, as long as the FDA's approach is not entirely irrational. See id. at 468. This is particularly so in an administrative context that, like the one currently before the Court, is admittedly fraught with complications and conflicts. The FDA has been given substantial delegated authority over a silent and ambiguous statute in this complex arena, and has chosen a method that it believes strikes the delicate balance between the competing legislative policies of incentivizing new pharmaceutical developments and encouraging lower-cost generic competition. Hence, the deference to which the agency is entitled is at its apex. See Mead, 533 U.S. at 226-27. Under such circumstances, the Court cannot say that the FDA has acted irrationally or outside the scope of its authority. See Cal. Indep. Sys. Operators Corp., 372 F.3d at 399-400 (citing Chevron, 467 U.S. at 843-44; Motion Picture Ass'n of Am., Inc. v. FCC, 309 F.3d 796, 801 (D.C. Cir. 2002)). Operating, as it must, within the constraints of these principles, the Court concludes that the FDA's interpretation must be deemed reasonable.

III. Was the FDA's Decision to Grant Exclusivity to Andrx, Rather than to Apply Shared Exclusivity, Arbitrary and Capricious?

Apotex also contends that, even if the FDA's patent-based approach is permissible under Chevron, FDA's action in this case was nonetheless arbitrary and capricious. Specifically, Apotex submits that the FDA's November 2001 exclusivity determination was incorrect -- instead of awarding exclusivity to Andrx based upon the originally-listed patents, the FDA should have awarded exclusivity for those patents to DRL. See Pl.'s Mem. Supp. Mot. Summ. J. at 7; Pl.'s Reply at 22; Pl.'s Surreply at 1-4. According to Apotex, Andrx failed to follow the FDA's "notice-plus-amendment" rule, under which an amendment to an already-submitted ANDA does not become effective until the later of the date on which the amendment is submitted or the date on which satisfactory notice of the amendment is provided to the NDA-holder. See Pl.'s Reply at 23-24. Andrx amended its ANDA to include the 40 mg strength of omeprazole on September 28, 1998, but it did not provide sufficient notice (in Apotex's view) to AstraZeneca until June 2, 1999. Between those dates, in February 1999, DRL submitted its ANDA for the 40 mg strength of omeprazole. Because DRL submitted its ANDA before Andrx's amendment became effective, Apotex argues that DRL, not Andrx, was entitled to exclusivity based on the originally-listed patents. Apotex concedes that Andrx was the first to certify to the later-listed patents in connection with the 40 mg strength of omeprazole. The result, according to Apotex, is that the FDA should have applied its shared exclusivity rule to Andrx and DRL. If the FDA had done so, then all exclusivity associated with the 40 mg strength of omeprazole would have expired 180 days following the October 2002 court decision on the '499 patent (because, under shared exclusivity, the triggering of one exclusivity period triggers all other exclusivity

periods), and Apotex would now be entitled to final approval for its ANDA.

The FDA responds that Andrx satisfied the notice-plus-amendment rule constructively, when it provided the relevant ANDA to AstraZeneca in a litigation production before the date on which DRL filed its ANDA. Apotex counters that the statute -- and FDA's rules -- clearly establish a framework that requires formal, not constructive, notice. But the FDA contends that, even if that were true, the notice-plus-amendment rule does not apply to Andrx here because the rule was not formulated until January 2003. See Def.'s Mem. Supp. Cross-Mot. Summ. J. at 38. Although the FDA admits to having applied the rule retroactively, it claims never to have done so regarding a "settled exclusivity determination." Def.'s Reply at 20-21 n.12, 24 n.16. The Court understands this to mean that although the FDA has applied the rule retroactively to situations arising before January 2003, it has only done so in cases in which the FDA had not yet determined which ANDA applicant was entitled to exclusivity based upon the patents at issue.

Moreover, the FDA claims that shared exclusivity would still not apply because any true blocking situation was eradicated by the October 2002 court decision. The FDA describes shared exclusivity as a narrow exception to the patent-based approach that is only applied if an ANDA applicant is unable to market its generic product solely because of an exclusivity entitlement held by another ANDA applicant. So long as there is some other event or object preventing an ANDA applicant from legally going to market, then, the FDA does not apply the shared exclusivity rule. See Admin. Rec. Exh. 75; Def.'s Reply at Exh. C.

The Court concludes that the FDA's challenged actions were not arbitrary and capricious. The FDA's justification for not retroactively applying the notice-plus-amendment rule is rational: retroactive application to situations in which the FDA has already determined which applicant is

entitled to exclusivity would disturb settled agency decisions and increase administrative burdens. See Landgraf v. USI Film Prods., 511 U.S. 244, 265 (1994). It is arguably for this reason that retroactive applications of the law are not favored in the administrative law context. See Bowen v. Georgetown Univ. Hosp., 488 U.S. 204, 208 (1988); Marrie v. SEC, 374 F.3d 1196, 1206 (D.C. Cir. 2004). Although Apotex has identified cases in which the FDA has applied the notice-plus-amendment rule to ANDA amendments that precede the January 2003 formulation of the rule, it does not argue that the FDA has ever re-opened a previous exclusivity determination solely to apply retroactively the subsequently-formulated notice-plus-amendment rule. Nor does Apotex appear to argue that the notice-plus-amendment rule pre-dates Andrx's ANDA amendment in this case. Even if circumstances were otherwise, Apotex would at most be able to show evidence of administrative error. But administrative error alone does not make agency action arbitrary and capricious. The hallmark of the APA's highly deferential standard of judicial review is that agencies are not required to make decisions that are correct; they are merely foreclosed from making decisions that are irrational. See Volpe, 401 U.S. at 416.

In any event, whether the notice-plus-amendment rule should have been applied to the facts of this case is ultimately insignificant, because there would still be no basis for applying the shared exclusivity rule. At least as far back as March 28, 2002, the FDA refused to apply the shared exclusivity rule in the absence of a true blocking situation. See Admin. Rec. Exh. 75 at 4, 5. Indeed, the FDA refused DRL's request that the shared exclusivity rule be applied based upon DRL's certification to the '431 patent, because the FDA determined that the expiration of that patent -- not the exclusivity entitlement of another ANDA applicant -- is what actually blocked DRL from marketing its product. See id. Similarly, it is the October 2002 court decision here,

rather than any blocking exclusivity period, that prevents Andrx and DRL from marketing their generic products until October 2007. See Def.'s Reply at Exh. C. Accordingly, the FDA's justifications for its actions appear to be consistent with its patent-based approach and cannot be deemed arbitrary or capricious.[7]

CONCLUSION

For the foregoing reasons, the Court concludes that the FDA's patent-based interpretation of § 355(j)(5)(B)(iv) is permissible under Chevron and the FDA's actions in this case were not "arbitrary and capricious, an abuse of discretion, or otherwise contrary to law" under the APA. Accordingly, Apotex's motion for summary judgment will be denied and the FDA's motion for summary judgment will be granted. A separate order has been issued on this date.

/s/ John D. Bates
JOHN D. BATES
United States District Judge

Dated: February 13, 2006

[7]Apotex has described the FDA's "supplement" to the Administrative Record in this case as a "litigation-driven tactic[]" that, under Bowen, 488 U.S. at 213, and Mead, 533 U.S. at 228-31, should not be accepted by the Court. The Court is not convinced, however, that "the FDA's interpretations constitute a post-hoc rationale made only to defend its decisions from . . . challenge or that the decisions fail to reflect the agency's fair and considered judgment." Dr. Reddy's Labs., 302 F. Supp. 2d at 348-49. The reasoning supplied by the FDA here has been consistent throughout this case, as evidenced by the March 28, 2002 letter in response to DRL's inquiry regarding shared exclusivity based upon the '431 patent. See id.; see also Admin. Rec. Exh. 75. "Though [Apotex] contends that the FDA's positions in this action appear for the first time in the briefs, that is true because [Apotex] itself [admittedly] presented new arguments through its briefs, before the FDA had the opportunity to consider them [at the administrative level]." See Dr. Reddy's Labs., 302 F. Supp. 2d at 348-49; see also Def.'s Reply at 20 (recognizing that Apotex had not previously presented its shared-exclusivity argument at the administrative level).

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