IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

TEVA PHARMACEUTICALS USA, INC., Plaintiff, v. KATHLEEN SEBELIUS, et al., Defendants.	Case No. 1:09-cv-01111 (RMC)

OPPOSITION OF INTERVENOR-DEFENDANT APOTEX, INC.
TO PLAINTIFF TEVA PHARMACEUTICALS USA, INC.'S
MOTION FOR PRELIMINARY INJUNCTIVE RELIEF

Apotex, Inc. ("Apotex") hereby opposes Teva Pharmaceuticals USA, Inc.'s ("Teva") motion for a preliminary injunction. In the underlying action, Teva seeks a declaration that it has not forfeited its right to exclusivity for certain generic losartan products. It also seeks to compel the Food and Drug Administration ("FDA") to act in a manner not inconsistent with such a declaratory ruling. What this means is that Teva seeks to enjoin FDA from approving any Abbreviated New Drug Application ("ANDA") for generic losartan, other than Teva's, for 180 days after Teva begins to commercially market its losartan drug products. Although the earliest date at which Teva could obtain approval to market its generic losartan products is April 2010, Teva also filed a motion for preliminary injunctive relief, seeking a declaration that Teva has not forfeited its claim to 180-day exclusivity for its losartan drug products.

Teva is not entitled to preliminary injunctive relief because it cannot show that it is likely to succeed on the merits; it will not be irreparably harmed if preliminary relief is not granted; the issuance of relief will harm Apotex, other generic competitors, patients, the government and

third party payers; and because the public interest does not favor the issuance of preliminary relief.

Teva brings this motion even though FDA has not yet issued a decision as to whether Teva has forfeited any right to 180-day exclusivity. In some situations, FDA has opened administrative dockets, called for comments and issued decisions in advance of the dates on which it issues a final approval of generic products; in other situations FDA has refused to do so. Apotex believes it would be appropriate for FDA to consider Teva's arguments now. Until FDA does so, however, there is no agency decision to review. The lack of an agency decision by itself makes it unlikely that Teva can succeed on the merits.

Teva anticipates that FDA will decide that Teva has forfeited any claim to exclusivity based on U.S. Patent No. 5,608,075 ("the '075 patent") for losartan products. Teva Pharm. USA, Inc.'s Mem. Pts. & Auth. in Supp. of Mot. for Prelim. Inj. ("Teva Mem.") at 6. Teva's apprehension is well-based. The clear language of the governing statute results in Teva's forfeiture of 180-day exclusivity. FDA has consistently applied the clear language to all previous similar situations. As a result, even apart from the lack of an agency decision, Teva cannot show a likelihood of success on the merits. Consumers are entitled to benefit from full generic competition once the relevant patent and associated pediatric exclusivity for brand name losartan products expire in April 2010 and all otherwise eligible applicants, including Apotex, are entitled to receive final approval.

BACKGROUND

Statutory and Regulatory Framework

This case arises under the Hatch Waxman provisions of the Food, Drug, and Cosmetic Act ("FDCA") as amended by the Medicare Modernization Act of 2003 ("MMA"), Pub. L. No. 108-173, § 1102, 117 Stat. 2066, 2457-2460 (2003).

Under the FDCA, pharmaceutical companies seeking to market an innovator drug (the first drug of its kind) must first obtain approval from FDA by filing a New Drug Application ("NDA") containing data demonstrating the safety and effectiveness of the drug. 21 U.S.C. §§ 355(a), (b). An NDA applicant must also submit information on any patent that claims the drug or a method of using the drug and for which a claim of patent infringement could reasonably be asserted for an unauthorized use. 21 U.S.C. §§ 355(b)(1), (c)(2). Once the application is approved, FDA publishes or "lists" the patent information in "Approved Drug Products With Therapeutic Equivalence Evaluations," a publication known as the Orange Book. Id.; see also 21 C.F.R. § 314.53(e).

Companies seeking approval of generic versions of approved drug products must submit an ANDA, supported by data showing, among other things, that the proposed product is bioequivalent to the innovator drug referenced in the application. 21 U.S.C. § 355(j). The ANDA also must contain one of four specified certifications for each patent that "claims the listed drug." 21 U.S.C. § 355(j)(2)(A)(vii); 21 C.F.R. § 314.3(b). The patent certification must state one of the following:

> (I) that the required patent information relating to such patent has not been filed;
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> (II) that such patent has expired;
>
> (III) that the patent will expire on a particular date; or

(IV) that such patent is invalid or will not be infringed by the drug for which approval is being sought.

See 21 U.S.C. § 355(j)(2)(A)(vii).

A certification under paragraph III indicates that the ANDA applicant does not intend to market the drug until after the applicable patent expires, and approval of the ANDA may be made effective on the expiration date. 21 U.S.C. § 355(j)(5)(B)(ii). A paragraph IV certification indicates that the ANDA applicant wishes to challenge the validity of the patent, or to claim that the patent would not be infringed by the product proposed in the ANDA. The ANDA applicant submitting a paragraph IV certification must also provide a notice to the NDA holder and the patent owner stating that an application containing a paragraph IV certification has been submitted and explaining the factual and legal basis for the applicant's opinion that the patent is invalid or not infringed. 21 U.S.C. § 355(j)(2)(B).

The filing of a paragraph IV certification "for a drug claimed in a patent or the use of which is claimed in a patent" is an act of infringement, 35 U.S.C. § 271(e)(2)(A), thus enabling the NDA holder and patent holder to sue the ANDA applicant. If the NDA or patent holder sues the ANDA applicant within 45 days of the date it receives notice of the paragraph IV certification, FDA will stay approval of the ANDA for 30 months from the date that the patent holder and NDA holder received notice, unless a final court decision issues earlier in the patent case or the patent court otherwise orders a longer or shorter period. 21 U.S.C. § 355(j)(5)(B)(iii). If no action is brought within 45 days, FDA may approve an ANDA with a paragraph IV certification, and the approval may become effective immediately despite the unexpired patent, provided that other conditions for approval have been met. Id.; 21 C.F.R. § 314.107(f)(2).

Under certain circumstances, the statute makes the first applicant that submits an ANDA containing a paragraph IV certification eligible for a 180-day period of marketing exclusivity.

Other ANDA applicants cannot obtain FDA approval during this period and may not market their products. 21 U.S.C. § 355(j)(5)(B)(iv); 21 C.F.R. § 314.107(c). The MMA added new provisions to the FDCA specifying that an ANDA applicant that is initially eligible for 180-day exclusivity will forfeit exclusivity if it fails to meet any one of several specified conditions. One of these is the failure to market the drug within certain specific time periods. See 21 U.S.C. § 355(j)(5)(D).

The statute provides that 180-day exclusivity "shall be forfeited by a first applicant if a forfeiture event occurs with respect to that first applicant." 21 U.S.C. § 355(j)(5)(D)(ii). In relevant part, a forfeiture event is defined to include a failure to market by the later of:

> (aa) the earlier of the date that is –
>
> > (AA) 75 days after the date on which the approval of the application of the first applicant is made effective under subparagraph (B)(iii); or
> >
> > (BB) 30 months after the date of submission of the application of the first applicant, or
>
> (bb) . . . the date that is 75 days after the date as of which . . .
>
> > (CC) The patent information submitted under subsection (b) or (c). . . is withdrawn by the holder of the application approved under subsection (b) of this section.

21 U.S.C. § 355(j)(5)(D)(i)(I). This forfeiture provision was added by Congress as part of a 2003 restructuring of Hatch Waxman, in which Congress sought to preserve the incentives for applicants to challenge as many patents as possible, but also ensure that a first applicant's eligibility for 180-day exclusivity will not unreasonably delay the approval of subsequent ANDAs. See 149 Cong. Rec. S15746 (daily ed. Nov. 24, 2003) (statement of Sen. Schumer).

FDA has not issued new regulations interpreting the forfeiture provisions of the MMA; it has, however, otherwise addressed and applied certain aspects of the forfeiture provisions in

public letter decisions, after providing notice and an opportunity for comment. See, e.g., Letter from Gary Buehler, Director, Office of Generic Drugs, to William A. Rakoczy ("Acarbose Decision") at 4-5 (May 7, 2008), FDA Docket No. 2007-N-0445 (Complaint at Exh. 5); Letter from Gary Buehler, Director, Office of Generic Drugs, to ANDA Applicant ("COSOPT Decision") (Oct. 28, 2008), FDA Docket No. 2008-N-0483 (Complaint at Exh. 9). In a matter involving an ANDA for acarbose, FDA applied the subsection (aa)(BB) deadline, which requires marketing within "30 months after the date of submission of the application of the first applicant," as running from the date on which FDA receives a substantially complete application. Acarbose Decision at 6, 9 n.15. FDA also applied the subsection (bb)(CC) deadline, which requires marketing within 75 days from when the patent information "is withdrawn by the holder of the application," as running from the date on which FDA receives the patent holder's request to remove the patent from the Orange Book. Id. at 7-9. Similarly, in a matter involving generic COSOPT®, FDA determined that an applicant that had failed to market by the later of 30 months after the date of submission of the ANDA or 75 days after the patent information is withdrawn, forfeits 180-day exclusivity. COSOPT Decision at 2.

Factual Background

Merck currently holds approved NDA No. 20-386 for losartan potassium ("losartan") tablets and NDA No. 20-0387 for losartan potassium/hydrochlorothiazide ("losartan HCTZ") tablets, which are sold under the brand-names Cozaar® and Hyzaar® for the treatment of hypertension. Merck originally provided patent information on three patents to FDA for listing in the Orange Book as patents that claim these drugs: U.S. Patent No. 5,138,069 ("the '069 patent"), U.S. Patent No. 5,153,197 ("the '197 patent") and U.S. Patent No. 5,608,075 ("the '075

patent"). The '069 patent and its associated pediatric exclusivity expire on February 11, 2010.[1] The '197 patent and its associated pediatric exclusivity expire on April 6, 2010. The '075 patent expires in March 2014 and its pediatric exclusivity expires in September 2014. Merck also claims that U.S. Patent No. 5,210,079, which is a method of use patent, claims the approved use of Cozaar. This patent is not relevant to this litigation because Teva does not seek approval for this method of use. Teva Mem. at 21 n.2.

Teva claims to be the first applicant to have certified to each of the '069, '197 and '075 patents. According to Teva, it submitted its ANDA for losartan on December 18, 2003, and FDA acknowledged it received the ANDA on February 11, 2004. Id. at 21-22. Teva also claims that it subsequently submitted an ANDA for losartan HCTZ on May 24, 2004, and FDA acknowledged it received the ANDA on July 15, 2004. Id. at 22-23. Teva sent a notice of its paragraph IV patent certification to Merck. Id. at 23. Merck did not sue Teva for patent infringement within 45 days. Id.

Apotex is a pharmaceutical company that develops and manufactures generic drugs for sale in the United States and throughout the world. Declaration of Ellen Gettenberg ("Gettenberg Dec.") ¶ 1. Apotex also submitted ANDAs seeking approval to market generic versions of Cozaar and Hyazaar, also containing paragraph IV certifications to the '075 patent. Id. ¶ 10. Apotex intends to launch its products immediately upon receiving final approval from FDA, which, like Teva, it anticipates receiving in April 2010. Id. If Teva receives the 180-day exclusivity to which it claims it is entitled, Apotex's ANDAs will not be approved until October 2010, 180 days after Teva's approvals.

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1. Pediatric exclusivity adds to a patent an additional six months of exclusivity when the innovator has fulfilled certain requirements relating to testing the drugs in children. 21 U.S.C. § 355a(b).

ARGUMENT

I. The Standard for Issuance of a Preliminary Injunction

Teva's motion for a preliminary injunction must be denied because Teva fails to meet the stringent standards for injunctive relief. A preliminary injunction is an "extraordinary remedy that should be granted only when the party seeking the relief, by a clear showing, carries the burden of persuasion." Cobell v. Norton, 391 F.3d 251, 258 (D.C. Cir. 2004) (citing Mazurek v. Armstrong, 520 U.S. 968, 972 (1997)). In order to prevail on a motion seeking this extraordinary relief, Teva bears the burden of showing: (1) that it is likely to succeed on the ultimate merits of the claim; (2) that it will be irreparably harmed if the preliminary relief is denied; (3) that the issuance of relief will not significantly harm other interested parties; and (4) that the public interest favors the issuance of a preliminary injunction. Serono Labs., Inc. v. Shalala, 158 F.3d 1313, 1317 (D.C. Cir. 1998); Mova. Pharm. Corp. v. Shalala, 140 F.3d 1060, 1066 (D.C. Cir. 1998). Teva cannot meet any of these standards.

II. Teva Has Not Shown a Likelihood of Success on the Merits

The burden is on Teva to demonstrate "by a clear showing a probability of success on the merits," Pharm. Research & Mfrs. of Am. v. Walsh, 538 U.S. 644, 662 (2003); see also Mylan Labs, Inc. v. Leavitt, 484 F. Supp. 2d 109, 117 (D.D.C. 2007), quoting Am. Bankers Ass'n v. Nat'l Credit Union Admin., 38 F. Supp. 2d 114, 140 (D.D.C. 1999) ("[A]bsent a 'substantial indication' of likely success on the merits, 'there would be no justification for the court's intrusion into the ordinary process of administration and judicial review.'"). "[E]ven where denial of a preliminary injunction will harm the plaintiff, the injunction should not be issued where it would work a great and potentially irreparable harm to the party enjoined, unless an overwhelming case in the plaintiff's favor is present on the merits and equities of the controversy." Dofrmann v. Boozer, 414 F.2d 1168, 1173 (D.C. Cir. 1969) (citation omitted); see

also Taylor v. Resolution Trust Corp., 56 F.3d 1497, 1507 (D.C. Cir. 1995). Teva cannot satisfy its burden because it is not likely to succeed on the merits.

The lack of any administrative decision leaves Teva's request for injunctive relief tenuously perched. See Hi-Tech Pharmacal Co., Inc. v. FDA, 587 F. Supp. 2d 1, 10 (D.D.C. 2008). See also Collagenex Pharm., Inc. v. Thompson, No. 03-1405, 2003 U.S. Dist. LEXIS 12523, at *9 (D.D.C. July 22, 2003). Even in the absence of an agency decision or an administrative record, however, it is clear that Congress intended, as evidenced by the clear language of the statute, that the failure of an applicant to market within the statutory deadlines opens the door to full generic competition.

A. Teva's Reliance on the Ranbaxy Case is Misplaced

Teva's argument in this case rests heavily on its assertion that Ranbaxy Labs. Ltd. v. Leavitt, 469 F.3d 120 (D.C. Cir. 2006), should govern the outcome here. Teva is incorrect for two key reasons. First, the Court is not interpreting the same statute that it was in Ranbaxy. Second, the Ranbaxy case fundamentally concerned whether FDA could award or decline to award 180-day exclusivity based on whether there had been litigation over the patents.

The governing statute in this case is not only different from the governing statute in Ranbaxy, but is different in ways that are central to this case. There was no provision for forfeiture of 180-day exclusivity in the statute construed in Ranbaxy. There is a statutory provision governing forfeiture of 180-day exclusivity in this case.[2] In this case, the court is

2. The statute was amended to include forfeiture provisions in the MMA. Although the MMA preceded the Ranbaxy case, the Ranbaxy decision is based on the pre-MMA version of the statute because the MMA provided that the pre-MMA version would continue to apply where an ANDA had already been submitted at the time the MMA was enacted, which was the situation in Ranbaxy. The Ranbaxy case noted that the decisions rendered by the FDA and the district court had been made pursuant to the FDCA "as it stood before the MMA and, because the MMA was not made retroactive. . . this decision is also geared to the Act pre-MMA." Ranbaxy, 469 F. 3d at 122.

being asked to construe the forfeiture provision that did not apply in Ranbaxy. Consequently, Ranbaxy cannot possibly govern the outcome of this case.

In Ranbaxy, FDA had determined that an ANDA applicant's eligibility for 180-day exclusivity would be extinguished if the NDA holder both delisted the patent on which the ANDA applicant's exclusivity was based and did not sue the ANDA applicant for patent infringement. The agency had also determined that an ANDA applicant's eligibility for 180-day exclusivity would be preserved in the same circumstances if the NDA holder did sue the ANDA applicant. Ranbaxy and Teva sued FDA, arguing that FDA could not make 180-day exclusivity decisions based on the presence or absence of a lawsuit. Both this Court and the Court of Appeals agreed. The Court of Appeals held that "FDA's requirement that a generic manufacturer's patent challenge give rise to litigation as a condition of retaining exclusivity when a patent is delisted is inconsistent with the [FDCA], which provides that the first generic manufacturer to file an approved application is entitled to exclusivity when it either begins commercially to market its generic drug or is successful in patent litigation." Id. at 121. In this case, FDA has not made a litigation distinction.

In addition, the logic of Ranbaxy is no longer applicable. Teva makes much of the Ranbaxy language to the effect that patent delistings should not be permitted to affect an ANDA applicant's entitlement to 180-day exclusivity. This is not precisely what the Ranbaxy case said, but, even if it were, it would not be applicable here because the current version of the statute contains a provision expressly permitting patent withdrawals to affect an ANDA applicant's eligibility for 180-day exclusivity. The statute no longer provides that the "first generic manufacturer to file an approved application is entitled to exclusivity," id.; it now provides that the first generic manufacturer is entitled to exclusivity if it has not forfeited its exclusivity.

B. The Governing Statute Should Resolve This Case

The appropriate point of reference for resolving this case is not the Ranbaxy case, but rather the provisions of the statute that govern this case. "The preeminent canon of statutory interpretation requires [a court] to 'presume that [the] legislature says in a statute what it means and means in a statute what it says there.' Thus, [a court's] inquiry begins with the statutory text, and ends there as well if the text is unambiguous." BedRoc Ltd., LLC v. U.S., 541 U.S. 176, 183 (2004), citing Connecticut Nat. Bank v. Germain, 503 U.S. 249, 253-54 (1992) and Lamie v. U.S. Trustee, 540 U.S. 526, 533-34 (2004). The language of the relevant forfeiture provision of the FDCA is clear and unambiguous, and the Court need look no further to decide this case.

The current version of the statute still provides that an ANDA applicant may obtain 180-day exclusivity if it is the first applicant to file a paragraph IV certification for the drug. Congress added provisions governing forfeiture of eligibility for 180-day exclusivity. There are six different forfeiture provisions in the current version of the statute. The one at issue in this case is the so-called "failure to market" forfeiture provision. It provides that an ANDA applicant forfeits eligibility for 180-day exclusivity if it fails to market its product within prescribed time periods. These are defined as follows:

(I) Failure to Market. The first applicant fails to market the drug by the later of –

(aa) the earlier of the date that is –

(AA) 75 days after the date on which the approval of the application of the first applicant is made effective under subparagraph (B)(iii); or

(BB) 30 months after the date of submission of the application of the first applicant; or

(bb) with respect to the first applicant or any other applicant (which other applicant has received tentative approval), the date that is 75 days after the date as of which, as to each of the patents with respect to which the first applicant submitted and

> lawfully maintained a certification qualifying the first applicant for the 180-day exclusivity period under subparagraph (B)(iv), at least 1 of the following has occurred:
>
> (AA) In an infringement action brought against that applicant with respect to the patent or in a declaratory judgment action brought by that applicant with respect to the patent, 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.
>
> (BB) In an infringement action or a declaratory judgment action described in subitem (AA), a court signs a settlement order or consent decree that enters a final judgment that includes a finding that the patent is invalid or not infringed.
>
> (CC) The patent information submitted under subsection (b) or (c) is withdrawn by the holder of the application approved under subsection (b).

21 U.S.C. § 355(j)(5)(D)(i)(I)(bb). The statute directs that a forfeiture event occurs when an ANDA applicant eligible for 180-day exclusivity fails to market its drug by the later of two dates. One of these is calculated under subsection (aa) by determining the earlier of the date that is 75 days after the eligible applicant's approval or 30 months after the submission date of the eligible applicant's ANDA. The second date is calculated under subsection (bb) by determining the date that is 75 days after the date that one of the three enumerated events occurs.

In this case, the dates specified in subsection (aa) are known. Teva's ANDA applications have not yet been approved. Therefore, part (AA) has not occurred. The part (BB) date – the date that is thirty months after Teva's Cozaar ANDA submission – is June 19, 2006, thirty months from December 18, 2003, the date on which Teva submitted its ANDA. Teva Mem. at 21. The relevant part (BB) date for Teva's Hyzaar ANDA submission is November 25, 2006, thirty months from May 24, 2004, the date on which Teva submitted its ANDA. The earlier of the two dates is the date that is 30 months from submission of Teva's ANDAs. Thus, the

forfeiture date under subsection (aa) for Cozaar is June 18, 2006 and for Hyzaar November 24, 2006.

As to subsection (bb), the first two events, both of which involve litigation, have not occurred. Merck did not sue Teva over the '075 patent. The third event, which is described in part (CC) of subsection (bb), has occurred. Part (CC) of subsection (bb) describes the situation in which the NDA holder withdraws patent information on which an ANDA applicant's eligibility for exclusivity is based. The undisputed facts here show that Merck, the NDA holder, withdrew the patent information on the '075 patent with respect to which Teva was eligible for exclusivity. Merck withdrew the patent information by January 1, 2009, a date that is far longer than 75 days ago. Id.

Because both the (aa) and (bb) dates have long since passed, Teva has forfeited its eligibility for exclusivity.

As Judge Robertson once observed in construing a different portion of the 180-day exclusivity provision, "[t]he language of the statute may be complex, and even cumbersome, but it is plain and unambiguous." Mova Pharm. Corp. v. Shalala, 955 F. Supp. 128 (D.D.C. 1997), aff'd, 140 F.3d 1060 (D.C. Cir. 1998). That is true of this statutory language as well. Nevertheless, its complexity should not be allowed to obscure its plain meaning.

C. FDA's Previous Reading of the Relevant Statutory Provision is Correct

In the past, FDA has had no difficulty in determining the correct reading of the statute. As described above in the statutory and regulatory background section of this memorandum and in Teva's memorandum, Teva Mem. at 18-20, FDA has been called upon to construe the statutory language regarding the effect on forfeiture of 180-day exclusivity when an NDA holder withdraws information on a patent at least twice before. In both the Acarbose Decision and the COSOPT Decision, FDA construed the language using the analysis above. As FDA explained in

its COSOPT Decision, "on its face, 21 U.S.C. 355(j)(5)(D)(i)(I)(bb)(CC) applies when '[t]he patent information....is withdrawn by the holder of the [NDA].' FDA reads the plain language of 21 U.S.C. § 355 (j)(5)(D)(i)(I)(bb)(CC) to apply wherever a patent is withdrawn (or requested to be 'delisted') by the NDA holder." COSOPT Decision at 14, n.15.[3] To our knowledge, FDA has never taken a contrary or inconsistent position.[4]

D. Teva's Arguments That the Statute Does Not Mean What It Says Have No Merit

Teva does acknowledge that the current version of the statute provides for forfeiture, stating that "[t]o be sure, FDA is right that the delisting trigger makes clear that it now is possible in certain circumstances for a patent to be delisted despite a first applicant's exclusivity-qualifying certification to that patent." Teva Mem. at 31.

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3. Teva attempts to bolster its argument by pointing out that the language in 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb) provides that the action creating forfeiture must be "with respect to" a generic applicant, and argues that the action can only be "with respect to" a generic applicant if it results from litigation. Teva Mem. at 33. The words "with respect to" mean "insofar as concerns" or "with reference to." Webster's Third New Int'l Dictionary (2002). Merck's withdrawal of the information on the '075 patent is with respect to Teva because it affects Teva's 180-day exclusivity. It is not more or less "with respect to" Teva if a court orders that the patent information be withdrawn or if Merck withdraws the information on its own initiative.

4. Teva terms the result of FDA's decision the "Delisting Rule." Apotex declines to use this incorrect terminology. There is no "rule" involved. The Administrative Procedure Act defines a rule, in relevant part as "any rule for which the agency publishes a general notice of proposed rulemaking pursuant to section 553(b) of this title... or any other law... for which the agency provides an opportunity for notice and public comment." 5 U.S.C. § 601(2). In short, the term "rule" is usually used synonymously with the term "regulation." There is no regulation here. The relevant provisions are provisions of the governing statute, and FDA's decisions are administrative interpretations of the statute. Further, the statutory provision does not speak of "delisting." The statute refers to an NDA holder's decision to withdraw patent information from its NDA application. "Delisting" is a term commonly used to refer to FDA's action to remove the patent from the Orange Book after it has received such a request from the NDA holder. A correct understanding of the statutory provisions is central to this case and Teva should not be permitted to use incorrect terminology to further confuse an already complex issue. Finally, FDA does not "delist" these patents from the Orange Book. It notes in the Orange Book that the NDA holder has requested that that patent information on the patent be withdrawn.

Teva, however, rejects the plain meaning of the statute, offering a variety of arguments to persuade this Court that the statute should not be interpreted to mean what it says. None of Teva's arguments comes close to offering a valid, or even sensible interpretation of the Hatch Waxman statutory provisions.

The Effect of Patent Delisting Versus the Permissibility of Patent Delisting: Teva first argues that the current version of the statute governs only the effect when a patent is delisted, but does not address the circumstances in which a patent may be delisted. Teva Mem. at 4. The statute, of course, does not speak of delistings at all. It provides for forfeiture when an NDA holder withdraws from its NDA application information on a patent. The statute creates no limitation on the NDA holder withdrawal of patent information. The forfeiture provision itself recognizes an NDA holder's right to withdraw patent information. Further, the statute establishes that an NDA holder must submit information on patents that claim the drug and, by necessary implication, must not maintain patent information in its application on patents that do not claim the drug. 21 U.S.C. § 355(b). FDA has always interpreted the statute to permit NDA holders to submit and withdraw patent information in accordance with their best understanding of their statutory obligations, and the courts have upheld FDA's practice in this regard. Teva Pharms., USA, Inc. v. Leavitt, 548 F.3d 103, 106 (D.C. Cir. 2008) ("When it comes to the veracity of patent information supplied by NDA holders, FDA operates in a purely ministerial role, relying on the NDA holders to provide the Agency with accurate patent information."); Apotex, Inc. v. Thompson, 347 F.3d 1335, 1348-49 (Fed. Cir. 2003). Had the Congress intended to establish limits on an NDA holder's ability to withdraw patent information to preserve an ANDA applicant's eligibility for 180-day exclusivity, it would certainly have said so, as this would establish an entirely new burden on NDA holders.

Further, the NDA holder could not know whether it could withdraw a patent at any given time. An NDA holder does not know which ANDA applicant is first to file or whether an ANDA applicant has forfeited in some other way when the NDA holder chooses to withdraw information on a patent. An entirely new administrative mechanism would have to be created to provide the NDA holder sufficient information to know whether it was precluded from withdrawing its patent information.[5]

Lastly, if Teva's objection is to Merck's action in withdrawing the information on the '075 patent, it is suing the wrong party. It should be looking to Merck, not FDA.[6]

The Counterclaim Provision of the FDCA: Teva next argues that the withdrawal of patent information is only relevant to forfeiture when a court has ordered the NDA holder to withdraw information on a patent. Teva Mem. at 31-33. Teva is correct that the current version of the statute includes a provision that would allow ANDA applicants sued for patent infringement to counterclaim to force innovators to withdraw patent information. 21 U.S.C. § 355(j)(5)(C)(ii). It is not correct, however, that this provision is linked to the forfeiture provision of 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(CC). There is certainly no language in the statute to support Teva's argument. The counterclaim provision does not refer to forfeiture. The forfeiture provision makes no mention of a court, counterclaim or patent litigation. The provision refers only to patent information withdrawn by the NDA holder, and is not limited to patent

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5. This raises another important difference from the Ranbaxy case. The issue there was not whether an NDA applicant could withdraw patent information from its NDA, but rather whether FDA could give effect to such a request by delisting the patent from the Orange Book.

6. Teva's use of the term "delisting" makes it difficult to discern whether Teva is arguing that the NDA holder cannot withdraw the patent information or that FDA cannot publish in the Orange Book the NDA holder's request to withdraw the patent information. Given the statutory language referring to an NDA holder's withdrawal of the patent information, Apotex assumes the former and addresses that argument in this section of its memorandum. If Teva is arguing the latter, its argument is truly specious. By the terms of the statute, forfeiture does not depend on what FDA does, but rather on the NDA holder's action in withdrawing the patent information.

information withdrawn by the NDA holder as a result of litigation. A patent may be withdrawn for any number of reasons. An NDA holder could realize it made a mistake in submitting the patent, or decided to disclaim a patent or otherwise withdraw a patent for any number of valid reasons. Once withdrawn, the patent no longer serves as a barrier to generic entry. Congress certainly could rationally conclude that a withdrawn patent should not delay generic entry and require prompt marketing upon penalty of forfeiture. There is no reason to link forfeiture to litigation and Congress did not do so.[7]

Further, the two provisions appear to have different purposes. The counterclaim provision remedies a situation in which an innovator has submitted information on a patent that does not claim the drug and then sues the ANDA application for patent infringement in order to block ANDA approval for 30 months. The forfeiture provision remedies a situation in which an ANDA application delays marketing its drug, thereby delaying generic competition. The two are not related.

FDA has already considered and rejected this argument in both the Acarbose and COSOPT decisions. Acarbose Decision at pp. 8, 9; COSOPT Decision at 14, n.15. FDA's decision rested on the plain language of the statute:

> We agree that, if a patent were withdrawn by the NDA holder as a result of a counterclaim by an ANDA applicant, a first applicant's continued eligibility for 180-day exclusivity would be governed by section 505(j)(5)(D)(i)(I) [21 U.S.C. § 355(j)(5)(D)(i)(I)]; however, the scope of the patent delisting forfeiture provision is much broader. Section 505(j)(5)(D)(i)(I)(bb)(CC) [21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(CC)] applies to more than just those patents withdrawn as a result of a counterclaim; on its face, it applies when

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7. It is more than a little ironic that Teva, which argued so forcefully in the Ranbaxy case that FDA could not create a distinction based on litigation when the statute makes no such distinction, now argues that FDA must create a distinction based on litigation when the statute still makes no such distinction.

> "[t]he patent information. . .is withdrawn by the holder of the [NDA]."

COSOPT Decision at 14, n.15.

The Commercial Marketing Trigger: Teva next argues that NDA holders should not be allowed to effectuate a forfeiture by withdrawing patent information when a different patent precludes the ANDA applicant from marketing its product.[8] This, argues Teva, effectively writes the commercial marketing trigger out of the statute, in contravention of the decision in the Ranbaxy case. Teva Mem. at 26. In fact, permitting the withdrawal of patent information and subsequent forfeiture does not write the commercial marketing trigger out of the statute. Teva's argument mixes two separate concepts. The forfeiture provision addresses whether an ANDA applicant is entitled to 180-day exclusivity. The commercial marketing trigger fixes the point at which an ANDA applicant's 180-day exclusivity begins to run. It is true that an ANDA applicant that has forfeited its exclusivity can never trigger exclusivity by commercial marketing. It is not true, however, that this circumstance reads the commercial marketing trigger out of the statute. Any ANDA applicant that does not forfeit its exclusivity will still trigger its exclusivity by commercial marketing.

Brand Manufacturer Manipulation: Teva's next point is that effecting a forfeiture through withdrawal of patent information allows NDA holders to "unilaterally and strategically"

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8. Whether Merck solely responsible for effectuating a forfeiture in this case in highly debatable. Had Teva challenged all three of the patents covering losartan, Merck's withdrawal of the patent information on the '075 patent would not have affected Teva's exclusivity. Instead, Teva chose to challenge only the patent that it could easily claim it was not infringing. Teva itself made a significant contribution to its failure to obtain 180-day exclusivity. In any event, FDA has rejected the argument that exclusivity should not be forfeited when the ANDA applicant's approval is blocked by a different patent or exclusivity "because the 180-day exclusivity provisions contain language demonstrating that Congress knew how to address [these] circumstances....and did not do so in the failure-to-market forfeiture provision." COSOPT Decision at 9.

divest first applicants of 180-day exclusivity. Teva Mem. at 25. Teva's memorandum presumes a grand conspiracy by Merck to deprive Teva of its exclusivity. Teva advances no facts to support this assertion. There are any number of reasons why Merck might have chosen to withdraw information on the '075 patent. For example, the patent may have been erroneously listed, Merck's interest in it may have lapsed, or Merck may have been responding to a change in FDA's regulations.[9] Further, Teva's argument assumes that Merck is free to submit or withdraw patent information at its option. This is not the case. An NDA holder has a statutory obligation to submit information if a patent claims the drug that is the subject of its application for approval. 21 U.S.C. § 355(b). Teva's assertion that Merck would ignore that statutory obligation purely for the purpose of disadvantaging Teva is unwarranted.

Evisceration of Exclusivity: Teva argues that allowing NDA holders to withdraw patent information so as to cause a forfeiture "eviscerates the exclusivity reward" by eliminating the incentive for ANDA applicants to challenge patents. Teva Mem. at 27. This argument is remarkably overstated. The new version of the statute may change the incentives; in fact, the whole idea of forfeiture changes the incentives by reducing an ANDA applicant's level of certainty that it will ever achieve 180-day exclusivity even if it is the first ANDA applicant to file a paragraph IV certification. Congress plainly wanted to change the incentives; otherwise it would not have created forfeiture provisions. But Congress was careful not to eviscerate the 180-day exclusivity provisions. It maintained 180-day exclusivity with some limitations. As

9. In 2003, FDA issued a regulation providing new guidance on circumstances in which a patent can be said to claim a drug. 21 C.F.R. § 314.53(b). The regulation established new requirements regarding polymorph patents. The '075 patent at issue is a polymorph patent. Teva Mem. at 27. It may be that Merck's decision to withdraw information in the '075 patent was a response to the regulation.

this case illustrates, ANDA applicants continue to pursue exclusivity under the new statute, just as they did under the old statute.

Teva's Entitlement to 180-Day Exclusivity: Teva argues that it has earned 180-day exclusivity by challenging Merck's patent, and should be rewarded for its effort. Teva Mem. at 27-29. Teva did challenge the validity of Merck's patent. So did other ANDA applicants. There is no basis for assuming a causal connection between Teva's or any other applicant's paragraph IV certification and Merck's withdrawal. Even assuming it was Teva's certification that succeeded in convincing Merck to withdraw the patent as an obstacle to approval, this is not all that the current version of the statute requires. The statute requires not only that an ANDA applicant earn exclusivity, but also that it not forfeit its exclusivity. Teva's quarrel is not with FDA, but rather with Congress, which adopted the forfeiture provisions.

III. The Balance of Harms Favors Apotex

Teva's plea for preliminary injunctive relief is fundamentally flawed because Teva does not seek to preserve the status quo; it seeks to change it. Gold ex rel NLRB v. State Plaza, Inc., 435 F. Supp. 2d 110, 118 (D.D.C. 2006) (quoting Univ. of Texas v. Camenisch, 451 U.S. 390, 395 (1981)) (stating that "[t]he purpose of a preliminary injunction is merely to preserve the relative positions of the parties until a trial on the merits can be held."); EMILY's List v. FEC, 362 F. Supp. 2d 43, 52 (D.D.C. 2005) (same).

The language of the forfeiture provisions is clear, as is FDA's interpretation and application of the statute. As Teva itself recognizes, it has already forfeited any exclusivity for its generic losartan products. See Teva Mem. at 6 ("Teva already has been stripped of its right to 180-day exclusivity for generic losartan potassium products…"). "Teva's investors know that. Teva's suppliers know that. Teva's customers know that." Id. Teva is correct. Apotex's

customers currently can confidently expect that Apotex will be able to supply them with generic losartan come April 2010. A preliminary injunction would not preserve Apotex's position any more than it would preserve Teva's position.

A preliminary injunction would improve Teva's position – making it appear more likely that Teva will be the only supplier of generic losartan in April 2010 and for the following six months. By the same token, Apotex's customers may fear that it is now less likely that Apotex will be able to supply generic losartan during the six month period following April 6, 2010. Teva will benefit from a preliminary injunction but Apotex will suffer. Moreover, this is an advantage Teva can leverage onto other products. Gettenberg Dec. ¶¶ 13, 15. Teva is a subsidiary of Teva Pharmaceutical Industries Ltd., which, by its own account, is among the top 20 pharmaceutical companies in the world and the leader in generic pharmaceuticals. Teva Pharmaceutical Industries Ltd., Fact Sheet: First Quarter 2009 (May 5, 2009), available at http://www.tevapharm.com/pdf/Q109FSheet.pdf (last accessed July 1, 2009).

While Teva would benefit from a preliminary injunction, preliminary relief brings it no closer to its avowed goal: a decision on the merits of the forfeiture provision that allows it to decide how much losartan to manufacture. Apotex, like Teva, has to make decisions as to what resources to commit to meet anticipated demand. A preliminary injunction will increase uncertainty and interfere with the existing calculus. See Gettenberg Dec. ¶¶ 12, 13.

Teva alleges that it will be irreparably harmed if a preliminary injunction is not granted essentially because "is virtually impossible for a first applicant to obtain effective judicial relief after FDA approves competing generic products for commercial marketing." Teva Mem. at 35. It then bootstraps its injury argument by pointing to the harm of losing 180-day exclusivity. Id. at 35-37.

Of course, it is not impossible to obtain judicial review even if FDA defers its decision until the day of approval. In the Hi-Tech case, Judge Bates dealt with FDA's refusal to consider the exclusivity issues in advance of approval by requiring FDA to give advance notice of when it would issue its decision and requiring the parties to be present in Court on the day when FDA's decision would be issued. Hi-Tech, 587 F. Supp. 2d at 13. On that day, the Court issued a short stay of all approvals to allow Hi-Tech to move for an injunction. Hi-Tech had the opportunity to seek an injunction then, but choose not to do so. Hi-Tech Pharmacal Co. v. FDA, 587 F. Supp. 2d 13, 17 (D.D.C. 2008). Certainly the procedure devised by Judge Bates, though unnecessarily cumbersome due to FDA's refusal to issue its decision prior to approval, provided Hi-Tech a meaningful opportunity for judicial review.

To be sure, there are unique benefits to exclusivity, but in this case, Teva seeks a preliminary injunction only, which cannot, in fact, result in a final determination of exclusivity. Even if an award of exclusivity were at stake at the preliminary injunctive stage, Teva will still achieve a significant profit even if it must compete with Apotex and others, just not as much as it wants. Any gains to Teva from exclusivity are offset by losses to competitors, and to consumers.

As this Court has noted, the irreparable injury requirement erects a very high bar for a movant. Apotex, Inc. v. FDA, No. 06-0627, 2006 U.S. Dist. LEXIS 20894, at *53 (D.D.C. 2006), aff'd, 449 F.3d 1249 (D.C. Cir. 2006), citing Varicon Int'l v. OPM, 934 F. Supp. 440, 447 (D.D.C. 1996). The harm alleged must be certain, great, actual, and imminent. Id., citing Wisconsin Gas v. FERC, 758 F.2d 669, 674 (D.C. Cir. 1985).

Teva cannot make the requisite showing because the harm it faces is that it will have to compete with Apotex and others come April 2010. "The mere existence of competition is not

irreparable harm, in the absence of substantiation of severe economic impact." Washington Metropolitan Area Transit Com. v. Holiday Tours, Inc., 559 F.2d 841, 843 n.3 (D.C. Cir. 1977).

If the injunction is not granted, Teva will still be able to compete for sales with Apotex. But an order effectively giving Teva exclusivity would mean that Apotex will lose entirely the opportunity to compete in the market for its share of sales. "The D.C. Circuit has recognized that generic drug makers 'face continued harm [when they are] denied access to the market . . .'" Mylan Pharms., Inc. v. Shalala, 81 F. Supp. 2d 30, 43 (D.D.C. 2000) (quoting Teva Pharms., USA, Inc. v. FDA, 182 F.3d 1003, 1011 n.8 (D.C. Cir. 1999) (citing Byrd v. EPA, 174 F.3d 239, 244 (D.C. Cir. 1999))).

In conservative terms, Apotex estimates that it would attain a 15-20% share of the market if it were allowed to compete, achieving $24.7 million in sales during the first 12 months. Gettenberg Dec. ¶ 16. If, however, Teva is awarded exclusivity, Apotex will be lucky to achieve a 5-10% share of the market, with annual sales of $4.1 million. Id.

The harm to Apotex will be greater even than the considerable loss in sales during the initial six months. If Teva is the only generic with the opportunity to market during the six months beginning April 6, 2010, it will have the opportunity to enter into contracts with and cement relationships with its customers, making it more difficult for Apotex to compete after the period of exclusivity expires. Id. ¶¶ 14, 15. Moreover, the effects can spread across product lines. Id. Wholesalers and pharmacies prefer to order from a manufacturer that is able to supply a full line of products. When a supplier cannot meet the demand for a full line, a wholesaler may well shift to a competitor who can do so, rather than juggle multiple orders from multiple suppliers. Customers who shift for this reason may never return.

The kind of injury that Apotex would suffer – the loss of the opportunity to compete, the erosion of its client base and loss of potential new customers in the market – cannot be compensated financially. Because Apotex will suffer substantial loss from relief conferring exclusivity on Teva, the balance of harm weighs against Teva.

IV. The Public Interest Favors Denial of Preliminary Relief

There is a strong public interest, evidenced by the enactment of Hatch Waxman, in encouraging competition in the prescription drug market and making more low cost generics available. See H.R. Rep. No. 98-857, at 18-19 (1984), reprinted in 1984 U.S.C.C.A.N. at 2651-2652. By purchasing generic equivalents of brand name drugs consumers save billions of dollars every year. See Comment of the Staff of the Bureau of Competition and Policy Planning of the FTC, In re: 180-Day Exclusivity for Abbreviated New Drug Applications ("FTC Comment"), FDA Docket No. 85N-0214, at 2 (Nov. 4, 1999).

Patients will achieve substantial savings if there is true generic competition. FDA, "Savings from Generic Drugs Purchased at Retail Pharmacies" (2009), available at http://www.fda.gov/Drugs/EmergencyPreparedness/BioterrorismandDrugPreparedness/ucm134205.htm (last accessed July 1, 2009). Prices will be lower if FDA can approve all otherwise eligible ANDAs than if Teva is awarded exclusivity because the average price of a drug declines even more when the number of manufacturers and distributors of that drug increases. See Prepared Statement of the Federal Trade Commission Before the Committee on Energy and Commerce ("FTC Statement") at 12 (Oct. 9, 2002) ("Studies indicate that the first generic typically enters the market at 70 to 80 percent of the price of the corresponding brand and rapidly secures as much as a two-thirds market share. The second generic typically enters at an even lower price. . . ."); FTC Statement at 4 ("Three or more companies offering a generic version of a

listed drug can lower the price by at least fifty percent, if not substantially more, from the branded price.").[10] Consumers will benefit if Apotex and others can compete with Teva. Gettenberg Dec. ¶¶ 19-22. The public interest lies in a regulatory framework that increases competition.

Finally, the public interest always strongly favors the faithful application of the FDCA. Mova Pharm. Corp. v. Shalala, 955 F. Supp. 128, 131 (D.D.C. 1997), aff'd, 140 F.3d 1060 (D.C. Cir. 1998); Bracco Diagnostics v. Shalala, 963 F. Supp. 20, 30 (D.D.C. 1997) ("Requiring [FDA] to act lawfully is also very much in the public interest."); Whitaker v. Thompson, 248 F. Supp. 2d 1, 16 (D.D.C. 2002) ("[I]t is clearly in the public interest to ensure that governmental agencies, such as the FDA, fully comply with the law. . ."). The public interest therefore favors the denial of a preliminary injunction in this case.

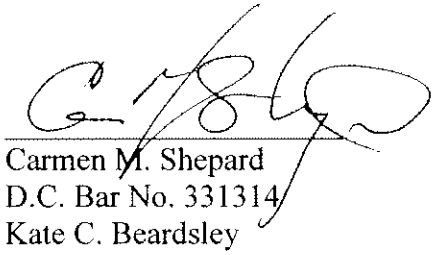
10. As the Congressional Budget Office has recognized in a study of generic drugs, when all other aspects of a drug product are the same, as they are in a generic version of a brand name product, "price competition can be intense." Congressional Budget Office, How Increased Competition from Generic Drugs has Affected Prices and the Returns in the Pharmaceutical Industry, at 18 (July 1998).

CONCLUSION

For the reasons stated above, Apotex respectfully requests that the Court deny Teva's Motion for Preliminary Injunctive Relief.

Dated: July 1, 2009

Respectfully submitted,



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