UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

APOTEX INC., Plaintiff,	)	
v.	)	Civil Action No. 07-1194 (RMU)
FOOD AND DRUG ADMINISTRATION, *et al.*, Defendants.	)	

FEDERAL DEFENDANTS' MEMORANDUM IN OPPOSITION TO PLAINTIFF'S MOTION FOR TEMPORARY RESTRAINING ORDER AND/OR PRELIMINARY INJUNCTION

Plaintiff Apotex Inc. ("Apotex") seeks an order from this Court compelling the Food and Drug Administration ("FDA") to disregard the order of a sister federal court in the Southern District of New York – an order that effectively requires Apotex to stop marketing a drug product that has been held to infringe the patents of proposed intervenor-defendant AstraZeneca ("Astra"). Upon holding that Apotex had infringed Astra's patents covering omeprazole capsules (brand name Prilosec), a drug used in the treatment of gastroesophageal reflux disease, the New York court ordered that the approval date of Apotex's abbreviated new drug application ("ANDA") for generic omeprazole be reset to no earlier than October 20, 2007. FDA thereafter took administrative action to comply with the court's order, converting Apotex's previously approved ANDA to a "tentatively" approved ANDA for which "final" approval cannot be granted until October 20, 2007.

As a result of the New York court's order, and FDA's implementation thereof, Apotex will be unable to lawfully market its omeprazole product for approximately four months. Although Apotex has appealed the New York court's decision to the United States Court of

Appeals for the Federal Circuit (where it has unsuccessfully sought a stay of the New York court's order), it now comes to this Court claiming that the New York court lacked authority to award such relief and faulting FDA for complying with the New York court's order. Apotex's attempt to collaterally attack the New York order in this forum is utterly meritless. FDA's action in giving effect to the New York court's order in this matter can in no way be characterized as "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law," nor has Apotex shown that it will suffer irreparable harm in the absence of the preliminary injunctive relief it seeks. Accordingly, Apotex's motion for a temporary restraining order and/or preliminary injunction enjoining FDA to reinstate final approval of its ANDA should be denied.

BACKGROUND

Astra manufactures omeprazole under the brand name Prilosec. Brand drugs like Prilosec are also known as "pioneer," or "innovator" drugs (in contrast to "generic" drugs), and are generally protected by various patents that cover their chemical composition or formulation. Apotex, along with several other generic applicants, including Impax Laboratories, Inc. ("Impax"), filed ANDAs with FDA, seeking approval to market generic versions of omeprazole. As part of its ANDA, Apotex challenged two patents that are relevant to this action: U.S. Patent Nos. 4,786,505 ("the '505 patent") and 4,853,230 ("the '230 patent"). Astra sued Apotex (and other generic manufacturers) for infringement of those two patents in the United States District Court for the Southern District of New York ("New York court"). After the 30-month stay of approval under 21 U.S.C. § 355(j)(5)(B)(iii) expired, FDA granted final approval to Apotex's application for the 10 and 20 mg products on October 6, 2003.

After receiving final approval, Apotex made the calculated risk to market its generic omeprazole products, despite the possibility that the New York court would later determine that

Apotex's products infringed one or more of Astra's patents. After the patents expired on April 20, 2007, Impax moved to dismiss Astra's infringement claims case for lack of jurisdiction, arguing that pediatric exclusivity no longer applied after the patents had expired, and that there was nothing left for the court to adjudicate. AR Tab 2, Order of May 25, 2007, at 8.[1] The New York court denied that motion by order dated May 25, 2007, determining that it retained the power to delay the effective date of the ANDAs (if they were found to infringe) under both 35 U.S.C. § 271(e)(4)(A) and its inherent equitable powers. *Id.* at 26.[2]

Subsequently, on June 14, 2007, the New York court held that Apotex's and Impax's products infringed the '505 and '230 patents. AR Tab 1 (attaching court's order). As relief for that infringement, the New York court ordered: "Pursuant to 35 U.S.C. § 271(e)(4)(A), the effective date of approval for the aforementioned products and related ANDAs shall be not earlier than October 20, 2007, the date on which the six-month period of pediatric exclusivity under 21 U.S.C. § 355a(b)(2)(B) expires." *Id.* Apotex unsuccessfully sought a stay of the court's order in both the district court and in the Federal Circuit. AR Tab 2, pp. 30-32 (denying Apotex's request for reconsideration and a stay in the district court); AR Tab 5 (Federal Circuit's denial of a stay). Apotex's motion for reconsideration of the Federal Circuit's denial of its request for a stay remains pending.

Shortly after entry of the New York court's order, Astra requested that FDA change the approval status of Apotex's and Impax's ANDAs from final to tentative. AR Tabs 1, 2. On June

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[1] "AR" denotes the Administrative Record in this case, which federal defendants filed on July 5, 2007.

[2] Apotex apparently made a similar challenge to the court's jurisdiction, albeit belatedly, after the court had found infringement. AR Tab 2 at 2. The court also rejected Apotex's challenge. *Id.*

21, 2007, Apotex and Impax submitted a joint letter to the agency setting forth their view that, because the patents had expired before the New York court ruled as to their infringement, no six-month period of pediatric exclusivity should apply. AR Tab 3. Astra responded on June 25, 2007, observing that Apotex and Impax were essentially asking FDA to join them in disputing the New York court's decision. AR Tab 4.

Nothing in the submission from Apotex and Impax persuaded the agency that it could defy a court order regarding the approval status of the ANDAs. Accordingly, on June 28, 2007, FDA gave effect to the district court's decision by changing the approval status of the applications from final to tentative. AR Tabs 6,7. Apotex sued FDA in this Court on July 2, 2007, seeking a temporary restraining order and/or preliminary injunction to require FDA to reinstate Apotex's final approval.

STATUTORY AND REGULATORY FRAMEWORK

A. New Drug Applications ("NDAs")

FDA approves applications to market drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 355. Pursuant to this provision, pharmaceutical companies seeking to market "pioneer" or "innovator" drugs must first obtain FDA approval by filing an NDA containing extensive scientific 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 against an unauthorized party. 21 U.S.C. § 355(b)(1), (c)(2). FDA publishes the patent information it receives in "Approved Drug Products With Therapeutic Equivalence Evaluations" (the "Orange Book"). *Id.*; *see also* 21 U.S.C. § 355(j)(7); 21 C.F.R. § 314.53(e).

B. Abbreviated New Drug Applications ("ANDAs")

The Drug Price Competition and Patent Term Restoration Act of 1984 (known as the "Hatch-Waxman Amendments"), codified at 21 U.S.C. §§ 355, 360cc, and 35 U.S.C. §§ 156, 271, 282, permits the submission of ANDAs for approval of generic versions of approved drug products. 21 U.S.C. § 355(j). The ANDA process shortens the time and effort needed for approval by, among other things, allowing the applicant to demonstrate its product's bioequivalence[3] to a drug already approved under an NDA (the "listed" drug) rather than having to reproduce the safety and effectiveness data for that drug. *Eli Lilly and Co. v. Medtronic, Inc.*, 496 U.S. 661, 676 (1990). If an ANDA applicant establishes that its proposed drug product has the same active ingredient, strength, dosage form, route of administration, labeling, and conditions of use as a listed drug, and that it is bioequivalent to that drug, the applicant can rely on FDA's previous finding that the listed drug is safe and effective. *See id.* The FDCA sets forth in detail additional information that an ANDA must contain, and lists the numerous deficiencies that may prevent or delay approval of an ANDA. *See* 21 U.S.C. §§ 355(j)(2), 355(j)(4).

1. Patent Certifications

The timing of approval of ANDAs depends in part on patent protections for the pioneer drug. An ANDA must contain one of four specified certifications for each patent that "claims the listed drug" or "a use for such listed drug for which the applicant is seeking approval." 21 U.S.C. § 355(j)(2)(A)(vii). The 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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[3] Two drugs are considered bioequivalent if, in general, the rate and extent of absorption of the proposed drug is not significantly different from the rate and extent of absorption of the listed drug. 21 U.S.C. § 355(j)(8)(B).

(II) that such patent has expired;

(III) that such 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 id. If a certification is made under paragraph I or II indicating that patent information pertaining to the drug or its use has not been filed with FDA or the patent has expired, then the patent, by itself, will not delay approval of the ANDA. 21 U.S.C. § 355(j)(5)(B)(I). A certification under paragraph III indicates that the ANDA applicant does not intend to market the drug until after the applicable patent has expired, and FDA will not approve the ANDA until after the patent has expired. 21 U.S.C. § 355(j)(5)(B)(ii).

If an applicant wishes to challenge a patent's validity, or to claim that the patent would not be infringed by the product proposed in the ANDA, the applicant must submit a paragraph IV certification to FDA. The applicant must also provide notice of the paragraph IV certification to the NDA holder and the patent owner and describe 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). This enables the NDA holder and patent owner to sue the ANDA applicant.

If the patent owner or NDA holder brings a patent infringement suit against the ANDA applicant within 45 days after receiving notice of the paragraph IV certification, the suit triggers an automatic stay of FDA approval for 30 months from the date the patent owner or NDA holder received notice of the certification ("30-month stay"). 21 U.S.C. § 355(j)(5)(B)(iii). The 30-month stay can be modified or lifted if the patent court reaches a decision before 30 months

expires or otherwise orders a longer or shorter stay period. *Id.* At the end of 30 months (or such shorter or longer period as the court orders), FDA will approve the ANDA in spite of the patent and ongoing litigation if the ANDA is otherwise ready for approval.

2. Tentative and Final ANDA Approval

FDA's approval of an ANDA becomes effective on the date the agency issues a letter approving the drug, "unless the approval letter provides for a delayed effective date." 21 C.F.R. § 314.105(d). If there is a delayed effective date, the approval is "tentative and does not become final until the effective date." *Id*. For example, when FDA reviews an ANDA and concludes that the drug described in the ANDA is safe and effective for the uses recommended in the labeling, but patent protections or other exclusivities prevent the approval from becoming immediately effective, FDA will issue a "tentative approval." *See* 21 C.F.R. § 314.105(d). A tentative approval indicates that the technical and scientific requirements for approval have been met as of a particular date but that approval cannot be made effective (and marketing is not permitted) until after some future event (such as expiration of a 30-month stay, a patent, or a period of marketing exclusivity). *See id.*; *see generally Barr Labs. v. Thompson*, 238 F. Supp. 2d 236, 245-50 (D.D.C. 2002).

A tentative approval "does not constitute 'approval' of an application and cannot, absent a final approval letter from the agency, result in an effective approval . . . ." 21 C.F.R. § 314.107(b)(3)(v). The products covered by an ANDA that has received tentative approval "may not be introduced or delivered for introduction into interstate commerce until approval of the [ANDA] is effective." 21 C.F.R. § 314.105(d). Moreover, a tentative approval cannot become effective without a final approval letter from the agency resulting in a final effective approval. 21 C.F.R. 314.107(b)(3)(v); *see also* 59 Fed. Reg. 50338, 50352 (October 3, 1994) (a

tentative approval becomes "final and, therefore, effective only when the agency sends an approval letter to the applicant").

3. Patent Litigation Stays of Approval

In addition to amending the FDCA, the Hatch-Waxman Amendments amended the patent code to specify the consequences that follow when an NDA holder or patent owner sues the ANDA applicant and wins – that is, the court hearing the patent infringement litigation finds the patent valid and infringed. In these circumstances, the patent code provides that "the court shall order the effective date of any approval of the drug . . . involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed." 35 U.S.C. § 271(e)(4)(A). In other words, as part of the relief to be entered in the event of a finding of patent infringement, approval of the ANDA that was the subject of the suit must be delayed – or delayed from taking effect – until "not earlier than" the date the patent has expired. The statute does not differentiate between unapproved ANDAs that are pending with FDA and ANDAs that have already received FDA approval.[4]

Accordingly, when patent litigation between an ANDA applicant and NDA holder or patent owner results in a court order under 35 U.S.C. § 271(e)(4)(A) stating that the effective date of ANDA approval shall be no earlier than the date the patent expires, FDA may not issue a

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[4] As the legislative history makes clear, Congress explicitly recognized that this requirement would affect previously approved as well as unapproved applications:

> If the infringing party has not begun commercial marketing of the drug, injunctive relief may be granted to prevent any commercial activity with the drug and the FDA would be mandated to make the effective date of any approved ANDA not earlier than the expiration date of the infringed patent . . . *In the case where an ANDA had been approved, the order would mandate a change in effective date.*

H.R. Rep. No. 98-857, pt. 1, at 46 (1984) (emphasis added).

final effective approval until after the date in the order has passed. When an ANDA has already been approved by FDA, but a court, having found the patent at issue valid and infringed, issues an order under 35 U.S.C. § 271(e)(4)(A) stating that the approval of the ANDA may not be made effective until after the date the patent expires, the ANDA loses it full effective approval status, becoming instead an approval with a delayed effective date, that is, a tentative approval. *See Mylan Laboratories, Inc. v. Thompson*, 389 F.3d 1272, 1281-82 (D.C. Cir. 2004) ("*Mylan (duragesic)*") (upholding FDA's conversion of an approved ANDA from final to tentative approval following a finding of patent infringement).

4. Pediatric Exclusivity

Congress amended the FDCA in 1997 to provide an economic incentive for drug manufacturers to invest the resources necessary to conduct and submit studies of the effects of drugs in the pediatric population. The pediatric exclusivity statute, 21 U.S.C. § 355a, provides an additional six months of marketing exclusivity beyond the term of applicable patents and other marketing exclusivities to drug manufacturers that conduct such pediatric studies at FDA's request. S. Rep. No. 105-43, at 52. In general terms, if an ANDA applicant has submitted a paragraph II (the patent has expired) or paragraph III (the patent will expire on a specified date) certification, and pediatric studies have been submitted prior to the expiration of the patent, pediatric exclusivity will delay approval of the ANDA for six months after the date the patent expires. 21 U.S.C. § 355a(c)(2)(A). If the ANDA applicant submitted a paragraph IV certification (patent is invalid or will not be infringed), and the patent court determines that the patent is valid and infringed, "the period during which an [ANDA] may not be approved under . . . [21 U.S.C. §] 355(j)(5)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions)." 21 U.S.C. § 355a(c)(2)(B). FDA has

determined that Astra successfully completed pediatric studies for Prilosec and is therefore eligible for pediatric exclusivity for that drug.[5] Depending on the type of patent certification filed by an ANDA applicant and the outcome of any related patent litigation, Astra's pediatric exclusivity may delay for six months the approval of ANDAs referencing Prilosec.

ARGUMENT

To obtain either a TRO or a preliminary injunction, a party must demonstrate that: (1) it has a substantial likelihood of success on the merits; (2) it will suffer irreparable injury in the absence of preliminary relief; (3) other interested parties will not be substantially injured if the requested relief is granted; and (4) granting such relief would serve the public interest.[6] *See Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1066 (D.C. Cir. 1998); *Mylan Laboratories, Inc. v. Leavitt*, 484 F. Supp. 2d 109, 117 (D.D.C. 2007) ("*Mylan (amlodipine)*"); *Boehringer Ingelheim Corp. v. Shalala,* 993 F. Supp. 1, 1 (D.D.C. 1997). Although the four factors are to be balanced on a sliding scale, "[i]t is particularly important for the movant to demonstrate a substantial likelihood of success on the merits." *Mylan (amlodipine)*, 484 F. Supp. 2d at 117.

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[5] *See* Electronic Orange Book, *available at* http://www.accessdata.fda.gov/scripts/cder/ob/docs/patexclnew.cfm?Appl_No=019810&Product_No=001&table1=OB_Rx (showing pediatric exclusivity for the '505 and '230 patents).

[6] Because the facts necessary for a resolution of this case are not disputed, summary judgment may be appropriate. A party is entitled to summary judgment when "the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any material fact and that the moving party is entitled to a judgment as a matter of law." Fed. R. Civ. P. 56(c). The federal defendants have filed an administrative record in this case, and there is no known dispute about the contents of that record. Courts have held that it is appropriate to provide judgment for the non-moving party in such cases if the court's determination of the legal issues establishes that the defendant is entitled to such a judgment. *See Celotex Corp. v. Catrett*, 477 U.S. 317, 326 (1986) (noting that courts may grant summary judgment *sua sponte*).

Moreover, "if a party makes no showing of irreparable injury, the court may deny the motion for injunctive relief without considering the other factors." *Id.*

The interim injunctive relief Apotex seeks is "an extraordinary form of judicial relief" that is not to be entered lightly; such motions are thus granted sparingly. *Id.*; *Bristol-Myers Squibb Co. v. Shalala*, 923 F. Supp. 212, 215 (D.D.C. 1996). Moreover, Apotex's request that this Court order FDA to reinstate final approval of Apotex's ANDA is a "mandatory injunction" that must be reviewed "with even greater circumspection." *Mylan Pharm., Inc. v. Shalala*, 81 F. Supp. 2d 30, 36 (D.D.C. 2000); *see also Mylan v. Thompson*, 139 F. Supp. 2d 1, 18 (D.D.C.), *rev'd other grounds*, 268 F.3d 1323 (Fed. Cir. 2001).

I. Apotex Is Not Likely to Succeed on the Merits

A. FDA Properly Gave Effect to the New York Court Order

Apotex's challenge rests on the premise that the district court's order only "purports to reset the effective date of Apotex's approval to the expiration of Astra's supposed 'pediatric exclusivity' on October 20, 2007," and that FDA was not obligated to follow that order. Br. 2. Apotex could not be more wrong. As an administrative agency, it is not FDA's role to second-guess a district court's order granting relief in a patent infringement suit between two private parties. Nor is FDA free to simply ignore the order of the New York court. This is particularly true here, where the district court issued its order pursuant to its "general equitable powers" (AR Tab 2, at 26), and 35 U.S.C. § 271(e)(4)(A), which is not part of the FDCA and which FDA is not charged with administering. *See Mylan (duragesic)*, 389 F.3d at 1279 n.5.

Once the New York court determined that Apotex's ANDA should have a delayed effective date until October 20, 2007, FDA gave effect to that order, in recognition of the New York court's judicial power to grant relief. Although FDA was not a party to that case, FDA

properly determined in *Mylan (duragesic)* and here that it would respect the authority of a district court to issue orders that collaterally require the agency to take action. *See Mylan (duragesic)*, 389 F.3d at 1282. Indeed, the district court's authority to issue orders awarding relief under 35 U.S.C. § 271(e)(4)(A) inherently depends upon FDA's compliance with those orders, even when, as here, FDA is not a party to a private patent infringement litigation.

1. The District Court's Decision, Not FDA's Decision in the Amlodipine Case, Controls in this Case

Apotex argues that previous agency precedent must compel the conclusion that pediatric exclusivity does not apply in this case, citing an unrelated decision that FDA recently issued regarding pediatric exclusivity for another drug, amlodipine besylate. Br. 13-14. Apotex, however, omits a key fact in its discussion of the amlodipine matter that readily distinguishes that matter. There, FDA approved Mylan's ANDA; Mylan's product was later found to infringe a patent. AR Tab 3, Ex. 4, at 4. The district court enjoined the approval of Mylan's ANDA until the patent expired, ***but Mylan successfully sought a stay of that decision in the Federal Circuit***. *Id.* FDA therefore determined that it would not apply any pediatric exclusivity against Mylan because Mylan's ANDA was already approved, and, "[a]fter that stay, FDA had no basis to convert the approval status of Mylan's ANDA from approved to tentatively approved." *Id.* at 5-6, n.4; *see also Mylan (amlodipine)*, 484 F. Supp. 2d at 116 ("The Federal Circuit's stay meant that Mylan had FDA approval for its generic version of amlodipine besylate.").

Here, however, FDA does have a reason to convert the approval status of Apotex's ANDA from final to tentative: the district court's order pursuant to 35 U.S.C. § 271(e)(4)(A) (and the court's general equitable powers) still stands, following two failed attempts by Apotex to obtain a stay of that order. Indeed, the district court's order leaves no room for FDA to

exercise its discretion regarding whether the agency believes application of pediatric exclusivity would be appropriate for Apotex's ANDA in the absence of the court's order. Thus, FDA has not impermissibly "depart[ed] from the amlodipine precedent in this case," or otherwise afforded Apotex inconsistent treatment, as Apotex alleges. Br. 14-15. FDA simply implemented the New York court's order by changing the approval status of Apotex's ANDA from final to tentative.

2. The District Court's Decision Controls, Notwithstanding Apotex's Preferred Interpretation of the Pediatric Exclusivity Statute

Apotex additionally argues that FDA's decision to change the status of its ANDA to tentative approval contravenes the pediatric exclusivity statute, 21 U.S.C. § 355a. Br. 16. As Apotex's brief makes clear, however, Apotex primarily takes issue with the district court's determination that pediatric exclusivity applies in this case, not with FDA's administrative implementation of that decision. Br. at 12 ("Here, FDA has revoked or converted Apotex's final approval solely on the basis of a court order that purports to reset the effective date of approval of Apotex's ANDA . . . ."). Apotex is collaterally estopped from challenging that order in this Court. Under the doctrine of collateral estoppel, "'once a court has decided an issue of fact or law necessary to its judgment, that decision may preclude relitigation of the issue in a suit on a different cause of action involving a party to the first case.'" *McLaughlin v. Bradlee*, 803 F.2d 1197, 1201 (D.C. Cir. 1986) (quoting *Allen v. McCurry*, 449 U.S. 90, 94, 101 S. Ct. 411, 66 L. Ed. 2d 308 (1980)).

Here, the New York court concluded that it had jurisdiction pursuant to 35 U.S.C. § 271(e)(4)(A) and its inherent equitable powers to order that the approval of Apotex's ANDA be delayed until the pediatric exclusivity period expired, even when the patents had expired before the court found infringement. AR Tab 2 (attaching May 25, 2007, Order, at 26); AR Tab 1

(attaching June 14, 2007, judgment against Apotex, at ¶ 3). Although Apotex is free to challenge that ruling on appeal to the Federal Circuit, it may not do so here. The relief that Apotex seeks from this Court (an order requiring FDA to immediately reinstate Apotex's final approval) would directly conflict with that judgment (an order directing that the effective date of approval be reset to October 20, 2007). Having failed to persuade the New York court to construe the patent statute and pediatric exclusivity provision in the manner it would prefer, Apotex's avenue of review lies with the appellate court, not with FDA (which is bound by the New York court's order) or this Court (which should not revisit the ruling of its sister court). While Apotex may hope to find a more receptive audience for its statutory construction arguments in these venues, consideration of such issues by this Court would amount to an unwarranted collateral attack upon the New York court's judgment and is not permissible under the law.

Apotex also incorrectly argues that FDA cannot revoke ANDAs that have already been approved under 35 U.S.C. § 271(e)(4)(A). Apotex's argument misses the point: that statute speaks to the authority of the district court, not FDA, following a determination of patent infringement. Nor did FDA "revoke" Apotex's ANDA. It merely changed its status from "final" approval to "tentative" approval pursuant to a district court's order finding infringement and resetting the effective date of approval under 35 U.S.C. § 271(e)(4)(A) – an administrative action the D.C. Circuit squarely upheld in *Mylan (duragesic)*, 389 F.3d at 1281-82.[7]

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[7] FDA's June 28, 2007, letter states that the agency is "convert[ing]" the final approval to a tentative approval, an action that is statutorily and administratively distinct from revoking or withdrawing approval of an ANDA. *See* 21 U.S.C. § 355(e); *Mylan (duragesic)*, 389 F.3d at 1282 n.8 (Mylan's ANDA approval was never "withdrawn" or "revoked" but "merely underwent a change of status or classification from final to tentative after the Vermont district court delayed its effective date). Apotex's repeated characterization of FDA's action as a "revocation" of approval (*e.g.,* Br. 1, 10, 12, 13) is thus erroneous.

B. FDA Was Bound to Comply with the New York Court's Order

Apotex contends that FDA's conversion of its ANDA from final approval to tentative approval was arbitrary and capricious because the agency was "not even remotely bound by the New York court's order . . . ." Br. 19. Unsurprisingly, Apotex offers no support for the remarkable proposition that a federal agency is free to disregard an order of a federal court. Contrary to Apotex's claim, the New York court hearing the patent action did not enter an order that merely "purports" to reset the effective date of Apotex's ANDA to on or after October 20, 2007. Br. 2, 12. The court explicitly "ordered, adjudged and decreed" that "the effective date of approval for the aforementioned products and related ANDAs shall be not earlier than October 20, 2007 . . . ." AR Tab 1 (Judgment) at ¶ 3. Thus, the New York court did not "purport" to reset the effective date of Apotex's ANDA, it *did* reset the effective date of Apotex's ANDA – thereby necessitating that FDA formally change the status of Apotex's ANDA from "final" approval to "tentative" approval in order to reflect the changed effective date entered by the court.

Whatever the legal merit of the New York court's action (which Apotex has challenged on appeal to the Federal Circuit – the only proper forum for the consideration of such issues), FDA was not free to ignore the court's order and the changed circumstances that resulted therefrom. Rather, as the D.C. Circuit has recognized, FDA was bound to take the administrative steps necessary to comply with the court's order by converting Apotex's ANDA to "tentatively approved." *See Mylan (duragesic)*, 389 F.3d at 1281-82. The New York court did not consult FDA prior to entering the order or seek its views on the underlying legal issue, nor did the court ask FDA to fashion a remedy for Apotex's infringement of Astra's patents. Rather, the court determined, based upon its own reading of the relevant statutes, its authority thereunder, and its

inherent equitable power, that the appropriate remedy for infringement would be to reset the effective date of an infringing ANDA to no earlier than October 20, 2007, the date that Astra's pediatric exclusivity period would expire, thereby returning the parties, in the court's view, to the *status quo* before infringement – *i.e.*, the position they would have been in had an infringing ANDA not been submitted. *See* AR Tab 2 (May 25, 2007, Order), at 14.[8]

Whether the New York court's patent ruling and the remedy it fashioned are sustainable under 35 U.S.C. § 271(e)(4) – or the district court's inherent equitable powers – is for the Federal Circuit to decide, not FDA or this Court. Once the Federal Circuit declined to stay the New York court's order, FDA's role was limited simply to administratively implementing the binding order by converting Apotex's ANDA from final approval to tentative approval – just as it did in *Mylan (duragesic)*, a case that, in all meaningful respects, is identical to the case at bar. In *Mylan (duragesic)*, as in this case, the district court found that Mylan infringed certain patents covering the brand name product and ordered that the effective date of Mylan's already-approved ANDA be reset to a date no earlier than the expiration of the patent. As the D.C. Circuit explained, the patent court's action meant that FDA – although not itself a party to the patent

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[8] As the court explained (with respect to Impax's similarly situated ANDA):

> [S]uch an order would have the effect of returning the parties to the status quo before infringement – that is before Impax filed its ANDA with a Paragraph IV certification. . . . This remedy would put the parties in the position they would have been in had the act of infringement never occurred: It would subject Impax to Astra's six-month period of pediatric exclusivity, as it would have had it filed an ANDA with a Paragraph II or Paragraph III certification. Moreover, such an order would give effect to, and is in accordance with the goal of the statutory scheme enacted by Congress when it authorized the grant of market exclusivity to patent holders who conduct pediatric studies.

AR Tab 2 (May 25, 2007 Order), p. 14-15.

litigation – was duty bound to convert the status of Mylan's approved ANDA from "final" approval to "tentative" approval in order to administratively implement the court's remedy:

> First, the FDA concluded that, as a consequence of the Vermont district court's determination under 35 U.S.C. § 271(e)(4)(A) that "the effective date of any approval of Mylan's ANDA product shall be no earlier than the date of expiration of the '580 patent family," the FDA's approval of Mylan's ANDA was no longer "immediately effective" – its effective date had changed, as the Congress had contemplated it would under such circumstances when it enacted 35 U.S.C. § 271 . . . . The FDA next determined, logically enough, that the effective date was then "delayed" and therefore "tentative," rather than "immediate" and "final," under the FDA's own regulation which provides that "[a]n approval with a delayed effective date is tentative and does not become final until the effective date." 21 C.F.R. 314.105(a).

Mylan (duragesic), 389 F.3d at 1281 (citations omitted).

Under these circumstances, the court concluded, FDA was required to respond administratively to the Vermont district court's order by converting Mylan's previously approved ANDA to tentative approval status, just as it did in this case in response to the New York court's order resetting the effective date of Apotex's ANDA:

> [T]he patent remedy statute directs that upon a finding of infringement the district court establish a new effective date for approval which is "not earlier than the date of the expiration of the patent which has been infringed," 35 U.S.C. § 271(e)(4)(A), and the ***FDA was bound under the district court's order to treat the status of Mylan's ANDA under the FDCA "the same as that of other ANDAs blocked from final approval by patent or exclusivity rights***."

Id. at 1282 (emphasis added). Thus, as the *Mylan (duragesic)* decision makes clear, FDA did exactly what it was supposed to do in this case – indeed what it was *bound* to do – when it converted Apotex's ANDA to tentative approval status.

In claiming that FDA was not "bound" by the New York court's order, Apotex confuses the concept of binding *precedent* with a binding court *order*. Regardless of whether the New York court's decision would be binding on FDA as a matter of precedential authority, there is no

question that FDA, like any federal agency, must comply with an order of a federal court. Thus, it matters not for purposes of this case whether, in a subsequent administrative proceeding, FDA would be free to construe the pediatric exclusivity provision as it sees fit, and perhaps reach a different outcome than the New York court did here. The only question in this case is whether FDA was obliged to carry out the New York court's order resetting the effective date of Apotex's ANDA approval by changing the approval status from final to tentative. The answer to that question is most assuredly "yes." *See Mylan (duragesic)*, 389 F.3d at 1282.

As such, Apotex's reliance on *Nat'l Cable & Telecomms. Ass'n v. Brand X Internet Servs.*, 545 U.S. 967 (2005), and *Teva Pharms. USA, Inc. v. FDA*, 441 F.3d 1 (D.C. Cir. 2006), is unavailing. Br. 21-24. Whatever those cases have to say about an agency's prerogative to construe its own statute under *Chevron* and its progeny, nothing in those decisions authorizes an agency to disregard a controlling court order. Apotex is likely correct that FDA would not be bound, in a subsequent case, by the New York court's construction of the pediatric exclusivity provision as a matter of judicial precedent, but there is no gainsaying the fact that FDA was bound to comply with the court's *order* resetting the effective date of Apotex's ANDA – whether it agrees with the court's underlying reasoning or not.

C. FDA Was Not Required to Issue a Formal Administrative Decision in Response to Apotex's Submission

Apotex fares no better with its request that FDA's decision be vacated "pending the Agency's preparation of a complete response to the issues raised by Apotex in its June 21, 2007 submission to the Agency." Br. 24. FDA's June 28, 2007, letter to Apotex clearly explains what action the agency is taking and the basis for that action. The letter references the New York court's June 14, 2007, decision in the omeprazole patent litigation in New York, which ordered

that the effective date of approval of Apotex's ANDA "shall be not earlier than October 20, 2007 . . . ." AR Tab 6 at 1. The letter advises Apotex that "in light of this court order, the Agency hereby converts the final approval of ANDA 76-048 issued on October 6, 2003, to a tentative approval. Therefore your ANDA is now **tentatively approved**. Final approval cannot be granted earlier than October 20, 2007." *Id.* (emphasis in original).

Apotex complains that FDA did not address the issues raised in its submission to the agency, and contrasts its action with the process that the agency recently underwent with respect to amlodipine. Br. 25. Unlike the amlodipine matter, however, there were no novel issues of statutory construction or administrative practice for the agency to resolve in this case. Here, in contrast to amlodipine, the relevant issues had already been ruled upon by a federal court which had then issued an order that obligated FDA to take a specific administrative action. Once the court issued its order resetting the effective date of Apotex's ANDA, the only role left for FDA was to acknowledge the administrative consequence of the new effective date – namely, the changed status of Apotex's ANDA from "final" approval to "tentative" approval.

Whatever process FDA engaged in with respect to amlodipine, the circumstances here did not call for FDA to weigh competing views, exercise its discretion, or make any sort of independent administrative determination; indeed, there was nothing for the agency to determine. The circumstances called not for administrative decisionmaking, but for administrative action. FDA's letter, which is neither "slipshod" nor "conclusory," as Apotex alleges (Br. 25), reflects the action that the agency took and the basis of that action. Nothing further was required.

II. Apotex Will Not Suffer Irreparable Harm Absent Preliminary Injunctive Relief

Not only has Apotex failed to make the requisite showing of likely success on the merits, it has also failed to demonstrate that it will suffer irreparable harm absent injunctive relief or that

the balance of hardships tips in its favor. Courts insist that only *irreparable* harm justifies the issuance of a preliminary injunction. Indeed, "[t]he *sine qua non* of granting any preliminary injunctive relief is a clear and convincing showing of irreparable injury to the plaintiff." *Experience Works, Inc. v. Chao*, 267 F. Supp. 2d 93, 96 (D.D.C. 2003). Because Apotex's likelihood of success on the merits is exceedingly slim, Apotex "would have to make a very substantial showing of severe irreparable injury" to prevail on its motion. *Nat'l Pharm. Alliance v. Henney,* 47 F. Supp. 2d 37, 41 (D.D.C. 1999).

Irreparable injury is a "very high standard." *See Varicon Int'l v. OPM*, 934 F. Supp. 440, 447 (D.D.C. 1996); *Bristol-Myers,* 923 F. Supp at 220. The injury alleged must be certain, great, actual, and imminent, and economic harm alone is not enough. *Wisconsin Gas Co. v. FERC*, 758 F.2d 669, 674 (D.C. Cir. 1985); *Apotex, Inc. v. FDA*, No. 06-0627, 2006 WL 1030151 (D.D.C. April 19, 2006) at *16 ("*Apotex (pravastatin)*") ("In this jurisdiction, harm that is "merely economic" in character is not sufficiently grave under this standard.""); *Boivin v. US Airways, Inc*., 297 F. Supp. 2d 110, 118 (D.D.C. 2003); *Bristol-Myers*, 923 F. Supp. at 220. As this Court recently explained:

> To satisfy the standard of irreparable injury to justify a preliminary injunction, the movants' loss must be "more than simply irretrievable." *Mylan Labs., Inc. v. Thompson*, 139 F. Supp. 2d 1, 27 (D.D.C. 2001); *see also Wisc. Gas Co. v. FERC*, 758 F.2d 669, 674 (D.C. Cir. 1985). Instead, the injury must be such that it "cause[s] extreme hardship to the business, or even threaten[s] destruction of the business." *Gulf Oil Corp. v. Dep't of Energy*, 514 F. Supp. 1019, 1025 (D.D.C. 1981); *see also, Sandoz, Inc. v. FDA*, 439 F. Supp. 2d 26 (D.D.C. 2006) (noting that "[t]o successfully shoehorn potential economic loss into the irreparable harm requirement, a plaintiff must establish that the economic harm is so severe as to 'cause extreme hardship to the business' or threaten its very existence.").

Mylan (amlodipine), 484 F. Supp. 2d at 123; *see also Experience Works*, 267 F. Supp. 2d at 96 ($21.1 million reduction in funding is serious financial blow, but one frequently faced by other

similar entities, and not an economic loss that threatens survival of the business); *Sociedad Anonima Vina Santa Rita v. Dep't of Treasury*, 193 F. Supp. 2d 6, 14 (D.D.C. 2001) ("financial harm alone cannot constitute irreparable injury unless it threatens the very existence of the movant's business").

In the present case, Apotex does not come close to establishing that it would suffer irreparable injury in the absence of the preliminary injunctive relief it seeks. Indeed, Apotex's ANDA will again be eligible for final approval on or about October 20, 2007 – less than four months from now. Although Apotex claims that omeprazole sales are a "major component" of its overall sales, accounting for some 20 percent of total U.S. sales during the fiscal year ending March 2007 (McIntire Dec. ¶ 12), nowhere does Apotex allege that a four-month moratorium on omeprazole sales would cause serious financial hardship to the company, let alone threaten its destruction. As this Court observed in *Mylan (amlodipine)*: "Monetary figures are relative, and depend for their ultimate quantum on a comparison with the overall financial wherewithal of the corporation involved." 484 F. Supp.2d at 123. Thus, when, as here, a company seeking preliminary injunctive relief does not argue that its alleged losses "would threaten the continued existence of [its] business," it "fail[s] to demonstrate irreparable injury." *Id.*

Apotex's assertion that it will suffer "unquantifiable, intangible losses," such as "loss of good will and damage to . . . customer relations," is equally unavailing. Br. 26. Apotex's claims are speculative and unsupported, and are merely forms of economic loss that do not meet the high standards set forth above. Moreover, Apotex well knew, when it began marketing its generic omeprazole product while patent litigation was still ongoing, that it ran the risk of an adverse outcome in the patent case that could result in an award of damages and the removal of its product from the market. In these circumstances, Apotex's claim of reputational harm and

loss of good will ring particularly hollow. Apotex has to stop distributing its omeprazole product because it was found to infringe Astra's patent; its asserted fear that customers might believe there is something wrong with the product is purely speculative and, in any event, was part of the risk Apotex knowingly undertook when it decided to "launch at risk" while patent litigation was ongoing.

III. The Balance of Harms Weighs Against Apotex's Request for Relief

Apotex has also failed to show that any harm it would suffer in the absence of injunctive relief outweighs the potential harm to others, or that the entry of such relief would further the public interest. Although FDA has no commercial stake in the outcome of this litigation, FDA is the government agency charged with implementing the statutory scheme governing the approval of generic drugs. As such, FDA's interest coincides with the public interest. *Apotex (pravastatin),* 2006 WL 1030151 at *18 (FDA interest "is deemed to be aligned with that of the public" when administering a statute placed within its charge); *Serono Laboratories, Inc. v. Shalala*, 158 F.3d 1313, 1326 (D.C. Cir. 1998) (determining that the public interest is "inextricably linked" to Congress' purpose in passing the Hatch-Waxman Amendments); *Mylan (amlodipine)*, 484 F. Supp. 2d at 123-24 ("With regard to FDA, the risk of harm, as an agency tasked with carrying out its duties to the public, is in equipoise with that of Hatch-Waxman itself.").

FDA agrees that the public benefits from lower-cost generic competitors in the pharmaceutical marketplace, but it is also important to ensure that the rewards and incentives contained in the statute are properly allocated in the manner Congress intended – including the incentive for brand name companies to research and develop new drug treatments, and to test those products in pediatric populations. *See Mylan (amlodipine)*, 484 F. Supp. 2d at 124. Here,

the New York patent court – exercising the authority granted to it by the Hatch-Waxman Amendments, as well as its own inherent equitable power – entered a remedy that sought to ensure that Astra obtained the full statutory benefit it would have received but for Apotex's infringement of its patents. Although its judgment is subject to review by the Federal Circuit, granting the relief Apotex seeks in this Court would improperly short-circuit the appellate review process and disregard the role Congress assigned to the patent court within the Hatch-Waxman scheme.

In any event, Apotex cannot claim that generic competition will be significantly weakened in the absence of preliminary injunctive relief. There are currently no less than three other approved versions of generic omeprazole that have not been found to infringe Astra's patents and that are currently being marketed in competition with brand-name Prilosec. Thus, the public will not be substantially harmed by the four-month absence of Apotex's version of the drug from the market.

Moreover, any financial harm Apotex would suffer in the absence of injunctive relief would be at least equaled by the harm that both Astra and Apotex's generic competitors would suffer should the requested relief be granted. In such event, Astra would lose the full benefit of the pediatric exclusivity it earned by conducting pediatric studies of its product (and which the New York court determined it should enjoy), while those generic manufacturers on the market who have not been found to infringe Astra's patents (and who are not subject to the pediatric exclusivity period) would be subject to additional competition from Apotex prior to the expiration of the period on October 20, 2007. Thus, the balance of the harms does not support Apotex's motion for relief. *See Serono*, 158 F.3d at 1326 ("[Serono's] injury must be weighed against the next factor – the extent to which an injunction will substantially injury the other party.

. . . [a]nd that balance of harms results roughly in a draw.").

Accordingly, Apotex has failed to demonstrate that the balance of harms and the public interest support its request for temporary and/or preliminary injunctive relief.

CONCLUSION

For the foregoing reasons, Apotex's Motion for Temporary Restraining Order and/or Preliminary Injunction should be denied.

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that I caused a copy of the foregoing Memorandum in Opposition to Plaintiff's Motion for Temporary Restraining Order and/or Preliminary Injunction to be served via the District Court's electronic filing (ECF) system upon:

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