IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

MYLAN LABORATORIES INC. and MYLAN PHARMACEUTICALS INC., Plaintiffs, and MUTUAL PHARMACEUTICAL CO., INC., Intervenor-Plaintiff, v. MICHAEL O. LEAVITT, in his official capacity as SECRETARY OF HEALTH AND HUMAN SERVICES, ANDREW C. VON ESCHENBACH, M.D., in his official capacity as COMMISSION OF FOOD AND DRUGS, and UNITED STATES FOOD AND DRUG ADMINISTRATION, Defendants, and TEVA PHARMACEUTICALS USA, INC., and APOTEX INC., Intervenor-Defendants.	Civil Action No. 07-CV-579 (RMU)

PLAINTIFFS' OPPOSITION TO TEVA'S APPLICATION
FOR DECLARATORY AND INJUNCTIVE RELIEF

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INTRODUCTION

Teva filed its paragraph IV certification on March 23, 2007, a scant two days before Pfizer's last Orange Book patent expired, and now complains that the FDA's April 18 decision "penalize[s] paragraph IV applicants" like itself, particularly "where the brand manufacturer does not initiate litigation against a patent-challenging generic applicant at all." Mem.[1] at 5, 18. According to Teva, the FDA denied its short-lived paragraph IV application because the FDA decided that "each generic applicant" must prevail in "its own [Hatch-Waxman] litigation" with the brand manufacturer, which Teva sees as an attempt by the FDA to "revive its discredited 'successful defense requirement[.]'" Mem. at 5. As we show in Part I, however, Teva's argument is a straw man – the FDA did not block Teva's ANDA because it failed to prevail in "its own litigation," but rather because the pediatric exclusivity provisions of the Best Pharmaceuticals for Children Act ("BPCA")[2], as interpreted by the FDA, prevent the FDA from approving any unapproved ANDAs, including Teva's.

Teva also argues that the "plain text" of the BPCA is "unambiguous" and requires the FDA to immediately treat the *Pfizer v. Apotex* panel decision[3] as a "court determin[ation]" rather than awaiting the mandate from the Federal Circuit. Mem. at 22. As we show in Part II, Teva finds plain meaning where there is none. Section 355a(c)(2)(B) does not tell the FDA when to terminate pediatric exclusivity in the event a "court determin[ation] that the patent is valid and would be infringed" is overturned on appeal. That is why, in this case, the FDA had to resort to

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[1] *Brief of Teva Pharmaceuticals USA, Inc. in Support of Its Cross-Claim and Application for Declaratory and Injunctive Relief* [Dkt. No. 48-2] (hereinafter "Mem.").

[2] Pub. L. No. 107-109, 115 Stat. 1408 (2002).

[3] *Pfizer Inc. v. Apotex, Inc.*, No. 2006-1261, 2007 U.S. App. LEXIS 6623 (Fed. Cir. March 22, 2007)

a call for comments to aid its construction of the relevant statutory language. The FDA's decision to require a mandate before terminating pediatric exclusivity was reasonable and based on substantial legal and policy considerations, and this Court must afford that decision full *Chevron* deference. Likewise, in Part III we show that Teva has provided no reason the Court should not afford full *Chevron* deference to the other basis for the FDA's refusal to approve Teva's ANDA – the fact that "the *Apotex* decision addressed only claims 1-3 of an 11 claim patent" and that unless it is shown that "the remaining claims do not . . . claim the approved drug substance . . .," the '303 patent "remains validly listed." Ltr.[4] at 9.

Finally, as we show in Part IV, any harm to Teva from being denied entry into a multi-generic market until September is slight indeed. Moreover, any comparison of the balance of harms must favor Mylan, and the public interest will be served by maintaining the *status quo*.

For all of these reasons, Teva's application for declaratory and injunctive relief should be denied in its entirety.

ARGUMENT

I. THE FDA DID NOT DECIDE "THAT GENERIC APPLICANTS MUST PREVAIL IN THEIR OWN LITIGATION WITH THE BRAND MANUFACTURER."

Teva devotes the first section of its brief to a battery of arguments against the FDA's supposed decision "that generic applicants must prevail in *their own litigation* with the brand manufacturer." Mem. at 15 (emphasis added); *see also id.* at 16 (". . . FDA's Letter Decision reads the statute to provide that each generic applicant must secure *its own* 'court determination that the patent is invalid or would not be infringed' in order to defeat the brand manufacturer's

[4] Letter from Gary Buehler to ANDA Applicant/Holder for Amlodipine Besylate Tablets, dated April 18, 2007 [Dkt. No. 40-2].

pediatric exclusivity — even where the brand manufacturer does not initiate litigation against a patent-challenging generic applicant at all") (emphasis added); *id.* at 20 ("[I]t makes no sense to have a rule requiring the generic applicant to await the onset of that litigation"). This decision to require each paragraph IV filer to prevail in "its own litigation," Teva argues, prejudices a "patent-challenging generic applicant" like itself, who having amended to a paragraph IV two days prior to patent expiration, not unexpectedly, was not sued by the patent-holder. *Id*. at 16.

But Teva has constructed a straw man. Despite Teva's creative use of snippets from the April 18 decision, the FDA did *not* decline to approve Teva's application because Teva had not prevailed in "its own" paragraph IV litigation, but because (1) at least until the *Pfizer v. Apotex* mandate issues, the only final "court determin[ation]" in effect is the final judgment of the district court for the Northern District of Illinois finding the '303 valid and infringed; and (2) the Federal Circuit panel decision only invalidated three claims of the '303 patent, leaving the remaining eight claims presumptively valid, and the '303 patent "validly listed" in the Orange Book. Ltr. at 10.

II. THE FDA DID NOT ERR BY CONSTRUING THE BPCA TO REQUIRE AN APPELLATE MANDATE BEFORE A PATENT HOLDER WHO PREVAILS IN THE DISTRICT COURT IS DEPRIVED OF PEDIATRIC EXCLUSIVITY

The BPCA provides that pediatric exclusivity applies to a paragraph IV filer if "in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed. . . ." 21 U.S.C. § 355a(c)(2)(B).[5] The statute is silent with

[5] The six-month period of pediatric exclusivity does not apply to Mylan's ANDA because it received final approval in October of 2005, and "therefore, under the literal terms of the statute, [Mylan's] ANDA cannot be delayed." Ltr. at 5 n.4.

regard to what happens when, as in this case, that "court determin[ation]" is overturned on appeal.

The FDA decided, based on a number of substantial legal and policy considerations, that in these circumstances, it will not terminate pediatric exclusivity until a court of appeals decision is final, as evidenced by the issuance of a mandate. As we show in our opposition to Apotex's motion for a preliminary injunction, which raises the same APA objections as Teva, the FDA's reading is, at the very least, a reasonable interpretation of the statutory text.[6] That is all that is required; the question is not whether the agency's interpretation is the best one, but rather whether it is a permissible one. *See Chevron U.S.A., Inc. v. Natural Resources Defense Council*, 467 U.S. 837, 842-43 (1984). Therefore, until a mandate issues overruling the district court's determination, the '303 patent is valid and infringed and, according to the plain language of the statute, Pfizer's pediatric exclusivity continues.

III. TEVA VIRTUALLY IGNORES THE SECOND BASIS FOR THE FDA'S DECISION NOT TO APPROVE ITS ANDA — THE REMAINING VALID CLAIMS OF THE '303 PATENT.

In Part III of the April 18 decision, the FDA ruled that, even if the *Pfizer v. Apotex* mandate issues before the expiration of pediatric exclusivity next September 25, "ANDAs other than Apotex [such as Teva] may not be eligible for immediate approval." Ltr. at 9. The FDA noted "that the Apotex decision addressed only claims 1-3 of an 11 claim patent." *Id*. Unless it can be shown that "one or more of the remaining claims" do not "claim the approval drug substance, drug product or an approved method of use," the "FDA will assume the '303 patent remains validly listed." *Id.* at 9-10.

[6] *See Plaintiffs' Opposition to Apotex's Motion for Preliminary Injunction* (Apr. 26, 2007) at 8-9.

In its preliminary injunction brief, Teva buries its two-paragraph argument against this aspect of the FDA's decision in the section otherwise devoted to arguing that the FDA has wrongly decided that "each generic applicant" must prevail in "its own litigation." *See* Mem. at 16, 20-21. In the first of those paragraphs, Teva dismisses Part III of the FDA's April 18 decision as a "red herring." It is unclear from Teva's argument why this is so. Part III sets out a separate and additional reason why pediatric exclusivity blocks Teva's ANDA, regardless of the correctness of the mandate ruling in Part I. In Part III, the FDA explains that a patent may remain in the Orange Book if "one or more of the remaining claims claims the approved drug substance, approved drug product, or approved method of use, . . . the patent should remain in the Orange Book. . . ." Ltr. at 9. The responsibility for determining whether particular claims cover a listed drug or method of use is with the parties; the FDA "has neither the expertise nor the resources to resolve patent issues," therefore, in the absence of a court decision invalidating all potentially assertable claims, the "FDA will assume the patent remains validly listed." *Id.* at 10. The FDA's Part III ruling is based on clearly articulated legal and policy considerations, and, just like the Part I mandate ruling, is entitled to full *Chevron* deference.

In the second paragraph of its argument, Teva, without even acknowledging the *Chevron* deference due to the FDA's Part III ruling, weakly argues that the FDA's approach "subjects the entire process to manipulation by the brand manufacturer" by permitting the brand manufacturer to "selectively assert patent claims in paragraph IV litigation." Mem. at 20. But, at most, the ruling requires a generic applicant to challenge all claims that might cover the listed drug. To the extent all of those claims are not asserted by the patent holder, it is an easy matter for the generic applicant to bring a declaratory judgment counterclaim to ensure that all claims are covered. *See, e.g., Teva Pharms. USA, Inc. v. Novartis Pharms. Corp.*, No. 06-1181, 2007 U.S. App.

LEXIS 7383 * 24 (Fed. Cir. March 30, 2007) ("The [ANDA] declaratory judgment provisions . . . simply levels the playing field by making it clear that the generic applicant can also seek a prompt resolution of these patent issues by bringing a declaratory judgment action[.]"). And in any event, Teva's policy argument does nothing more than contend that one interpretation of the statute is better than another. That is not the issue; *Chevron* requires only that the agency's interpretation be a permissible one, not the only one or the best one. *Chevron*, 467 U.S. at 843 and n.11.

IV. ALL EQUITABLE FACTORS WEIGH IN MYLAN'S FAVOR.

Because Teva has shown no likelihood of success on the merits, it must make a "very strong" showing of irreparable harm to obtain a temporary restraining order. *Sandoz, Inc. v. Food & Drug Admin.*, 439 F. Supp. 2d 26, 32 (D.D.C. 2006), *aff'd*, No. 06-5204, 2006 U.S. App. LEXIS 22343 (D.C. Cir. Aug 30, 2006) (quoting *Apotex, Inc. v. FDA*, No. 06-627, 2006 U.S. Dist. LEXIS 20894, at *16 (D.D.C. April 19, 2006)). With allegations of economic losses that are speculative and remote at best, Teva has simply failed to make out a showing of irreparable injury sufficient to sustain that burden.

A. TEVA IS NOT HARMED AT ALL BY FDA'S DECISION.

Teva argues that, but for the FDA's decision letter denying generic ANDA approvals until the end of the pediatric exclusivity period, it "reasonably could have expected to make [tens of millions of dollars] from selling generic amlodipine drug products." Mem. at 30. But Teva has no right to market access. It is blocked by both the six-month period of pediatric exclusivity *and* by Mylan's 180-day exclusivity. Teva cannot overcome the legal barriers that prevent it from receiving final FDA approval for its ANDA under any scenario. Teva has no prospect of

receiving final approval and no prospect of participating in the amlodipine besylate market until the end of September 2007, at the earliest. It is damaged not at all by the FDA's decision.

Because Teva lacks any reasonable legal expectation of FDA approval, its asserted harms – including its professed ability to secure amlodipine besylate sales in the "tens of millions of dollars" – are completely speculative. Teva acknowledges that, even if it were legally permitted to enter the amlodipine besylate market in the near future, it would likely follow Pfizer, Mylan and Apotex into that market. As the fourth market entrant, it is highly unlikely that Teva would occupy more than a marginal position in the market – especially since the earlier entrants are likely to have secured many of the valuable long-term contracts by then. Indeed, Teva's assumption that it would be one of four players in the market is also flawed. If the FDA were forced to approve Teva in spite of Teva's precarious legal posture, the FDA would also presumably approve all of Teva's other competitors that are similarly situated, leading to a glut of generic manufacturers in the amlodipine besylate market. Such a development would undermine any expectation that Teva might have of enjoying a preeminent market position. Correspondingly, Teva can cite only to speculative and theoretical harms, which are insufficient to constitute irreparable harm. *See Power Mobility Coalition v. Leavitt*, 404 F. Supp. 2d 190, 205 (D.D.C. 2005) (finding no irreparable injury where harm is speculative); *Wisconsin Gas Co. v. Federal Energy Regulatory Com.*, 758 F.2d 669, 674 (D.C. Cir. 1985) (In order to qualify as irreparable injury, "injury must be both certain and great; it must be actual and not theoretical.").

More fundamentally, Teva's asserted harms are purely economic in nature, and – as the D.C. Circuit has held repeatedly held – such harms do not give rise to claims of irreparable harm – especially where the plaintiff has other legal recourse. *See Wisconsin Gas*, 758 F.2d at 674

(per curiam) ("It is also well settled that economic loss does not, in and of itself, constitute irreparable harm").

B. THE HARM TO MYLAN OUTWEIGHS ANY HARM TO TEVA.

In contrast to Teva's speculative harms, if the Court granted Teva's request for a mandatory injunction resulting in final approval of its ANDA, Mylan would face harm that is imminent and certain. Mylan's harms – unlike Teva's – are not merely economic in nature; at their core they are legal harms.

If Teva's demand for immediate final approval is granted, Mylan would lose its 180-day exclusivity rights. Courts have repeatedly recognized that a generic drug manufacturer is irreparably harmed when it is wrongfully deprived of its 180-day period of marketing exclusivity *vis-à-vis* other generic manufacturers. *See Mova Pharm. Corp. v. Shalala,* 955 F. Supp. 128, 131 (D.D.C. 1997) (finding irreparable harm where the FDA deprived a party of its "180-day statutory grant of exclusivity"); *aff'd,* 140 F.3d at 1067, n. 6 (1998) (confirming that Mova's loss of its "'officially sanctioned head start' … suffices to show a severe economic impact to Mova," for purposes of satisfying the irreparable harm standard).

Denial of the relief requested by Teva would – ultimately – benefit all parties. Issuance of a mandatory injunction requiring the FDA to approve Teva's ANDA immediately would be disruptive – and should such mandatory injunction ultimately be reversed upon appeal – it would necessitate the *post-hoc* rescission of any such forced approval. No party's interests would be served by the uncertainty and confusion that would result from such reversals in policy. Teva, the FDA, and Mylan all share an interest in preserving the *status quo* pending judicial consideration of the issues raised by this motion.

C. THE PUBLIC INTEREST WILL BENEFIT FROM A DENIAL OF THE MANDATORY INJUNCTION REQUESTED BY TEVA.

Teva misrepresents the public interest as elevating the importance of open market access for generic drugs over all other considerations – including statutory and regulatory requirements, patent-holder pediatric exclusivity periods, and first-to-file generic company's 180-day exclusivity – to name a few of the interests that Teva would sacrifice. Teva's analysis – and its characterization of the FDA as "simply a government agency with no particular stake in this dispute" – is deeply flawed. Mem. at 32.

The public interest depends upon the faithful compliance of federal agencies with their statutory mandates. *See, e.g.*, *Mylan Pharms. Inc. v. Shalala*, 81 F. Supp. 2d 30, 45 (D.D.C. 2000) ("It is in the public interest for courts to carry out the will of Congress and for an agency to implement properly the statute it administers."). The importance of abiding by statutory requirements and the will of Congress cannot be understated. The FDA – which bears responsibility for the administration of the Hatch-Waxman Act and the BPCA – must ensure that it complies with, and administers, the laws in a manner that heeds the broader implications of the underlying incentive structure of the Hatch-Waxman Act. If the Court were to accept Teva's invitation not to recognize either pediatric exclusivity or Mylan's 180-day exclusivity, it would be undermining the policies underlying these statutory frameworks, and it would also be forcing the FDA to violate express its statutory obligations relating to pediatric and 180-day exclusivity. Such an outcome would not serve the public interest.

The public interest will be best served by a denial of Teva's request for a mandatory injunction. Such a denial would avoid the wasted resources and the potential for public confusion that would result if the court required the FDA to approve Teva's ANDA, only to

rescind its approval (and force Teva to pull its products off the shelves) thereafter if the appellate court chose to reverse the mandatory injunction.

CONCLUSION

For all of these reasons, Teva's application for declaratory and injunctive relief should be denied in its entirety.

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Respectfully submitted,

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