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 COMMISSIONER 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' COMBINED REPLY
IN SUPPORT OF MYLAN'S MOTION FOR A PRELIMINARY INJUNCTION

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INTRODUCTION

Mylan's position on the merits of its motion for preliminary injunctive relief rests on a logical foundation consisting of three premises:

1. At the "magic moment of midnight" on March 25, 2007 when the '303 patent expired, Apotex's ANDA either was converted to a paragraph II certification under the FDA's rules and long-standing practice, or it remained a paragraph IV certification.

2. If Apotex's application was converted to a paragraph II certification, then it is barred by pediatric exclusivity.

3. If, on the other hand, Apotex was permitted to maintain its paragraph IV certification, then it is barred by Mylan's 180-day exclusivity.

The FDA in its opposition makes clear that Apotex's ANDA did indeed convert to a paragraph II certification "when the '303 patent expired on March 25, 2007[.]" FDA Opp.[1] at 32. Because the FDA leaves no doubt that Apotex, like the other applicants, *was* converted to a paragraph II applicant when the patent expired, the FDA is correct that any further debate about whether the FDA was *required* to convert Apotex's ANDA to a paragraph II has been "render[ed] irrelevant." *Id*. at 33.[2]

Likewise irrelevant, or at least premature, are the FDA and Apotex's[3] arguments that Mylan's 180-day generic exclusivity terminated at patent expiration. *See id.* at 40-45; Apotex Opp. at 8-12. The April 18 FDA decision held that "for all intents and purposes, Mylan's 180-

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[1] *Government Defendants' Combined Memorandum in Opposition to Motions for Injunctive Relief Filed by Teva, Apotex, and Mylan* [Dkt. No. 52] (hereinafter "FDA Opp.").

[2] For the same reason, Apotex's arguments concerning the "rebuttable presumption" of paragraph II conversion (Part I.B.) and "necessary and sufficient conditions" for paragraph II conversion (Part I.C.) need not be addressed. *Apotex's Opposition to Mylan's Motion for a Preliminary Injunction* [Dkt. No. 55] (hereinafter "Apotex Opp.").

[3] Teva did not file an opposition to Mylan's motion for a preliminary injunction.

day exclusivity will terminate with the expiration of the patent[.]" Ltr.[4] at 13, *see generally id.*, Part 4 at 10-13. Mylan did not challenge that aspect of the decision in its preliminary injunction motion because the FDA's 180-day ruling does not threaten Mylan with immediate harm, the *sine qua non* for preliminary injunctive relief.

The propriety of the FDA's Part 4 ruling on 180-day exclusivity will not become ripe unless and until pediatric exclusivity is terminated. Mylan intends to amend its complaint to challenge the FDA's April 18 Part 4 ruling that Mylan's 180-day marketing exclusivity terminated when the patent expired, and to brief the issue on the summary judgment schedule issued at last week's telephonic status conference. It is neither necessary nor desirable for the Court to rule on 180-day exclusivity now.[5]

On the merits, the FDA's defense of its newly-created "Apotex exception" is exceptionally weak. First, the FDA points out that the facts of this case present "a new situation not previously presented to FDA . . . ." FDA Opp. at 33. That may be so, and is presumably why the FDA delayed the ruling to receive public comment, but mere novelty does not insulate an agency's decisions from proper APA review. Beyond that, the FDA can point only to its desire to effectuate a perceived "'clear Congressional intent that pediatric exclusivity not block the approval of an ANDA where the ANDA applicant has prevailed . . . .'" FDA Opp. at 32-33

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

[5] It may be that the seeds of confusion were sown by a vagary of the ECF filing system, which on April 23, 2007, the same day that Mylan filed its preliminary injunction papers that are at issue here, electronically distributed *Mylan's Supplemental Memorandum and Points and Authorities* [Dkt. No. 51], filed on April 16 in support of Mylan's amended motion for preliminary injunction. The supplemental memorandum does address 180-day exclusivity; however, that preliminary injunction was rendered moot by the FDA's April 18 decision. Mylan's current motion for a preliminary injunction does not depend on the Court's finding that it is entitled to 180-day exclusivity.

(quoting Ltr. at 9). Why the FDA believes this Congressional intent is so "clear," or how that intent can trump the plain language of the *Best Pharmaceuticals for Children Act*, Pub. L. No. 107-109, 115 Stat. 1408 (2002) ("the BPCA"), the FDA does not say.

Apotex's argument fares no better because, like the FDA's, it is directed to the wrong subsection of the BPCA's exclusivity provisions. Apotex's chart breaking down the elements of § 355a(c)(2)**(B)** is rendered irrelevant by the FDA's conversion of its paragraph IV certification to a paragraph II certification. The application of pediatric exclusivity to paragraph II ANDAs is governed by § 355a(c)(2)**(A)**, which plainly provides that "the period during which [a paragraph II] application may not be approved . . . shall be extended by a period of six months after the date the patent expires . . ." without regard to any court determination. Because the statutory language bars approval of paragraph II filers irrespective of the status of any paragraph IV litigation, the FDA's attempt to create an exception for successful paragraph IV litigants cannot survive step one *Chevron* scrutiny.

ARGUMENT

I. THE FDA HAS NO LEGAL BASIS TO REWARD APOTEX FOR "PREVAILING" IN ITS PARAGRAPH IV LITIGATION BY EXEMPTING IT FROM PARAGRAPH II PEDIATRIC EXCLUSIVITY

The following sentence, which appears at page 33 of the FDA Opposition, may be the most significant line in all the varied briefing submitted by the parties:

> The reasoning for [the Apotex] exception *renders irrelevant* Mylan's argument that Apotex should automatically be converted to a paragraph II because of past FDA policy and the rulings in *Ranbaxy* and *Mylan (fentanyl)*.

FDA Opp. at 33 (emphasis added). The FDA's April 18 decision did not precisely address *how* the Apotex exception would be effectuated in conformity with the statutory scheme. In particular, it was unclear (1) whether the FDA converted Apotex's ANDA to a paragraph II, as it did with the other paragraph IV filers (like Teva), and then created an "exception" to

§ 355a(c)(2)**(A)**, which governs paragraph II applications, or (2) whether the FDA had allowed Apotex to maintain its paragraph IV certification after patent expiration and had derived the exception from § 355a(c)(2)**(B)**, which governs paragraph IV applications.

In its opening brief, Mylan argued that the FDA was required to treat Apotex's ANDA as having converted to a paragraph II certification when the patent expired because of past FDA policy and the *Ranbaxy* and *Mylan (fentanyl)* rulings. *See Memorandum of Points and Authorities in Support of Plaintiffs' Application for a Preliminary Injunction* [Dkt. No. 44-2], at 7-8. The FDA asserts in its opposition that Mylan's argument is "irrelevant," which can *only mean* that the FDA is conceding that it *did* convert Apotex's ANDA to a paragraph II, thus obviating the need for argument about whether it was *required* to do so. FDA Opp. at 33.

Section 355a(c)(2)(A) of the BPCA, which governs paragraph II applications, provides that "if the drug is the subject of a listed patent for which certification has been submitted under [paragraph II] . . . and for which pediatric studies were submitted prior to the expiration of the patent . . . the period during which [a paragraph II] application may not be approved . . . *shall be* extended by a period of six months . . . ." 21 U.S.C. § 355a(c)(2)(A) (emphasis added). When the '303 patent expired, all of "the unapproved ANDAs," including Apotex's, "were required to change (or were deemed to have changed) to paragraph II certifications and became subject to Pfizer's pediatric exclusivity at that time." FDA Opp. at 32. Because "one or more remaining claims" of the '303 patent at least potentially cover the listed drug, the '303 patent "should remain in the Orange Book and the remaining unapproved ANDAs are potentially subject to Pfizer's pediatric exclusivity." *Id*. at 34. All "unapproved ANDAs," that is, except Apotex's.

The FDA bases its decision to exempt Apotex from pediatric exclusivity on what it terms "'clear Congressional intent that pediatric exclusivity not block the approval of an ANDA where

the ANDA applicant has prevailed.'" FDA Opp. at 32-33 (quoting Ltr. at 9). That rationale is the only one offered by the FDA, and it is the only one that matters. Apotex's speculation, such as its suggestion that the FDA wished to "recogni[ze]" its "actual victory before the '303 patent expired" by exempting Apotex from pediatric exclusivity, is not only implausible, it is entitled to no legal force. Apotex Opp. at 5; *see Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1067 (D.C. Cir. 1998) ("[I]t is on an agency's own justifications that the validity of its regulations must stand or fall.")(citing *SEC v. Chenery Corp.*, 318 U.S. 80, 87 (1943)).

The FDA's Congressional intent rationale cannot survive even the most deferential scrutiny because it turns on the FDA's reading of § 355a(c)(2)**(B)** when, as we have shown, the applicable subsection is § 355a(c)(2)**(A)**. *See* FDA Opp. at 32-33 ("[T]he language of subsection 355a(c)(2)**(B)** 'manifests a clear Congressional intent . . . .'" (emphasis added) (internal citation omitted)). Section 355a(c)(2)**(A)** flatly provides that pediatric exclusivity bars the approval of a paragraph II application "for a period of six months after the patent expires," *without reference to any court determination.*

Where a statute is clear on its face, the inquiry into its meaning ends because Congress's intent is unmistakable. "When a court reviews an agency's construction of the statute which it administers, it is confronted with two questions. First, always, is the question whether Congress has directly spoken to the precise question at issue. If the intent of Congress is clear, that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress." *Chevron, U.S.A., Inc. v. NRDC, Inc.*, 467 U.S. 837, 842-43 (1984). And "when the statute's language is plain, the sole function of the courts—at least where the disposition required by the text is not absurd—is to enforce it according to its terms." *Lamie v. United States Trustee*, 540 U.S. 526, 534 (2004) (quotations and citations omitted); *see also*

Ratzlaf v. United States, 510 U.S. 135, 147-48 (1994) ("[W]e do not resort to legislative history to cloud a statutory text that is clear.")

Here, § 355a(c)(2)(A) makes clear that no paragraph II ANDA may be approved for six months after patent expiration. Apotex has a paragraph II ANDA. The FDA thus may not approve Apotex's ANDA for six months. *Q.E.D.*

II. ALL OF THE EQUITABLE FACTORS FAVOR MYLAN

A. MYLAN FACES IRREPARABLE HARM

Both the FDA and Apotex fail to address the harm that, in this case, is unique to Mylan and heavily militates in favor of a preliminary injunction here. The FDA acts as though Mylan, Teva and Apotex are all large and similarly situated companies and that the economic impact of any mistaken FDA policy decisions are not material for purposes of analyzing irreparable harm. *See* FDA Opp. at 47. Apotex, on the other hand, argues that imposition of a preliminary injunction – even for a short period of time – would result in harm to it that is equivalent or greater than those Mylan would suffer in the absence of such an injunction. *See* Apotex Opp. at 16. Both are mistaken.

The preliminary injunctive relief sought by Mylan is appropriate in light of the real danger that the Federal Circuit's mandate will issue and Apotex's ANDA will be approved before this Court can consider the merits of Mylan's objections. Under this scenario, the Court would be presented with a *fait accompli* and Mylan would be denied the opportunity to be heard before the *status quo* is altered – a result that would cause Mylan irreparable harm and render the FDA's action effectively unreviewable. Preliminary injunctive relief is proper to protect a movant from imminent harm when another party threatens to suddenly alter the *status quo* in a manner that would deprive the movant of its rights. *See Barrow v. Graham*, 124 F. Supp. 2d

714, 716 (D.D.C. 2000) ("In the absence of facts that would enable a court fully to assess the merits of the parties' respective positions, a TRO may issue to preserve the *status quo* and to prevent imminent harm until a hearing on the request for a preliminary injunction may be held."); *Jackson v. District of Columbia*, 254 F.3d 262, 268 (D.C. Cir. 2001) ("[F]ederal courts possess a 'traditional power to issue injunctions to preserve the *status quo* while administrative proceedings are in progress and prevent impairment of the effective exercise of appellate jurisdiction.'") (internal citations omitted)).

The FDA's proposed actions would deprive Mylan of its 180-day exclusivity rights – a deprivation of legal rights that many courts, including this one, have held to constitute irreparable harm. *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"); *Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 29 (D.D.C. 1997) (granting preliminary injunction and acknowledging that "there is a significant economic advantage to receiving first approval and being the first company to enter the market, *an advantage that can never be fully recouped through money damages or by 'playing catch-up'*") (emphasis added)). Unless the Court takes steps to preserve the *status quo* – even if only for a short period of time – Mylan will be deprived of these important rights.

Finally, the FDA's summary deprivation of Mylan's right to be the only ANDA with final, effective approval leaves Mylan with no other opportunity for legal redress. The FDA's decision is contrary to its past policies and the plain language of the Hatch-Waxman Act, and it deprives Mylan of its exclusivity rights granted by Congress – before having any opportunity to be heard. Mylan would lose all of the benefits that it has worked for more than five years to obtain, causing it to suffer millions of dollars in lost sales per day, impaired access to customers,

and long-term losses in market share. *See Declaration of Brian S. Roman in Support of Mylan's Emergency Application for a Temporary Restraining Order* [Dkt. No. 44-5], at ¶ 6; *see also, TorPharm Inc. v. Shalala*, No. 97-1925, 1997 U.S. Dist. LEXIS 21983, at *13-14 (Sept. 15, 1997) ("early market entry is critical … because competitors will vie for a small number of long-term contracts"). The D.C. Circuit has recognized that economic deprivations can constitute irreparable harm where – as here – the injured party would be left with no legal recourse. *See Hoffman-Larouche, Inc. v. Califano*, 453 F. Supp. 900, 903 (D.D.C. 1978) (noting that where a party "will suffer loss of sales and good will for which it would have *no right of recourse*, … its injury will be irreparable" (emphasis added)); *Express One Int'l, Inc. v. United States Postal Serv.*, 814 F. Supp. 87, 91 (D.D.C. 1992) (finding irreparable harm in light of "non-recoverable monetary losses"). When the FDA unlawfully deprives Mylan of its rights without any notice, Mylan will be left without legal remedies. *See Komongnan v. United States Marshals Serv.*, 471 F. Supp. 2d 1, 4 (D.D.C. 2006) ("In the absence of an express waiver, sovereign immunity precludes suits against the United States and its agencies.").

B. THE BALANCE OF THE RELATIVE HARMS FAVORS ENTRY OF THE INJUNCTION

The injunctive relief that Mylan requests is limited in nature. Mylan is asking only that it be granted the right to be heard *before* the FDA effectuates any approval of Apotex's ANDA. Such limited injunctive relief would harm no other interested party in this case. In fact, such injunctive relief would provide broad-based benefits to all of the parties – all of whom will benefit from both the opportunity to be heard and resolution of these issues *before* any change to the *status quo* is effectuated. This is particularly true in light of the high likelihood that this Court would find any intervening FDA approval of Apotex's ANDA to have been unlawful, thereby necessitating the *post-hoc* rescission of that approval. No party's interests would be served by the uncertainty and confusion that would result from such an *ultra*

vires FDA action. Apotex, 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 AN INJUNCTION

By enabling the Court to forestall the FDA's unlawful action, the injunction will promote the well-recognized public interest in ensuring that federal agencies faithfully comply with their statutory mandates as prescribed by Congress. *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 injunction likewise will enable this Court to avoid the wasted resources and the potential for public confusion that would result from a mistaken FDA decision that would be subject to subsequent reversal.

III. IF THE COURT DECIDES TO ORDER THE FDA TO APPROVE ADDITIONAL ANDAS AT ONCE, IT SHOULD BRIEFLY DELAY THE EFFECTIVE DATE OF THE ORDER TO PERMIT MYLAN TO SEEK A STAY

In the unlikely event that the Court decides to enter a preliminary injunction requiring the FDA to approve other ANDAs for amlodipine without delay,[6] Mylan respectfully asks that the Court briefly delay the effective date of the order to permit Mylan to seek a stay in this Court and, if necessary, in the D.C. Circuit. *See* Fed. R. Civ. P. 62, Fed. R. App. P. 8. Courts routinely delay the effective date of preliminary injunctions, particularly of the mandatory variety, to preserve the *status quo*. *See e.g.*, *Mylan Pharms., Inc. v. Shalala*, 81 F. Supp. 2d 30, 48 (D.D.C. 2000) (denying mandatory injunction that would disrupt the *status quo*). Delaying the effective date would be particularly justified in this case because once the FDA issues approval and the

[6] Such an injunction would require the Court to uphold Apotex and Teva's challenges to the FDA's April 18 decision while rejecting Mylan's.

other generics enter the market, there is no turning back the clock. Mylan would have lost its hard-won market leadership position and would never be able to get it back, even if the Court of Appeals were to later rule that the additional approvals were not warranted.

CONCLUSION

For these reasons and those discussed in plaintiffs' opening brief, the Court should enjoin the FDA from approving Apotex's ANDA following issuance of the *Pfizer v. Apotex* mandate until further proceedings by this Court.

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Respectfully submitted,

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