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, UNITED STATES FOOD AND DRUG ADMINISTRATION, Defendants, and TEVA PHARMACEUTICALS USA, INC., and APOTEX INC., Intervenor-Defendants.	)	Civil Action No. 07-cv-579 (RMU)

MEMORANDUM IN SUPPORT OF PLAINTIFFS' EMERGENCY APPLICATION TO TEMPORARILY RESTRAIN THE FDA FROM APPROVING ANY ADDITIONAL AMLODIPINE ANDAS IN DEROGATION OF MYLAN'S RIGHT TO 180-DAY MARKET EXCLUSIVITY

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Federal Cases

Federal Statutes

Other Authorities

INTRODUCTION

In April, this Court denied Mylan's motion for a preliminary injunction seeking to enjoin the FDA from approving Apotex's amlodipine ANDA when the Federal Circuit mandate issued in *Pfizer v. Apotex*. In that motion, Mylan argued that Apotex's application was barred both by pediatric exclusivity and 180-day generic exclusivity.[1] Subsequently, although Mylan appealed the Court's denial, the mandate issued, and Apotex was approved and entered the market. The FDA refused to approve any other amlodipine ANDAs, however, because it had determined that Pfizer's pediatric exclusivity applied to all other pending ANDAs. As things stood until last Friday, Mylan and Apotex were the only two ANDA filers marketing amlodipine.

On Friday, June 22, without notice to Mylan or anyone else, the FDA, at Pfizer's request, "delisted" the '303 patent on the hypertension drug Norvasc, that is, the FDA removed the '303 patent from the Orange Book.[2] As a result, according to the FDA notice letter announcing the delisting, "there is no pediatric exclusivity barrier to approval of ANDAs for amlodipine." Bloodworth Decl.,[3] Exh. A at 2. Moreover the FDA stated in its letter that the D.C. Circuit's recent decision[4] holding that the FDA "must leave a patent listed in the Orange Book, notwithstanding an NDA holder's request to delist, if an ANDA applicant is eligible for 180-day exclusivity" does not apply "where the patent has expired." Bloodworth Decl., Exh. A at 2, n.2.

---

[1] *Memorandum of Points and Authorities in Support of Plaintiffs' Application for a Preliminary Injunction* [Dkt. No. 44-2].

[2] *Approved Drug Products with Therapeutic Equivalence Evaluations* (hereinafter the "Orange Book").

[3] *Declaration of Shannon M. Bloodworth in Support of Plaintiffs' Emergency Application to Temporarily Restrain the FDA from Approving Any Additional Amlodipine ANDAs in Derogation of Mylan's Right to 180-Day Market Exclusivity*.

[4] *Ranbaxy Labs. Ltd. v. Leavitt*, 469 F.3d 120 (D.C. Cir. 2006).

Absent maintaining the *status quo* until Mylan's right to 180-day exclusivity is finally determined, at least eight other generic competitors who filed ANDAs on amlodipine will enter the market, much to Mylan's detriment.

Now that the FDA has delisted the Pfizer patent, Mylan's claim to 180-day exclusivity has moved to the forefront. One of the issues in the pending appeal to the D.C. Circuit from the Court's denial of a preliminary injunction in this case is whether the FDA's position that Mylan's 180-day exclusivity did not survive the expiration of the '303 patent is in conflict with the governing provisions of the Hatch-Waxman Act. Mylan is well aware that the Court in its Memorandum Opinion summarily addressed Mylan's contention that 180-day exclusivity, once triggered, does not terminate upon patent expiration. With respect, however, the Court did not have the benefit of full briefing on this complex issue, and, as a result, got it wrong. Mylan is likely to prevail on its claim to 180-day exclusivity in the Court of Appeals, but its victory will be hollow unless the Court maintains the status quo until the appeal has been decided. Mylan therefore asks this Court for a temporary restraining order to enjoin the FDA from approving any additional ANDAs on amlodipine in derogation of Mylan's right to 180-day exclusivity until the issue is finally decided on appeal.

FACTUAL BACKGROUND

For 15 years, beginning in 1992, Pfizer enjoyed a patent monopoly on a best-selling hypertension drug called Norvasc® (amlodipine besylate). Pfizer's patent went unchallenged until May 22, 2002, when Mylan filed an ANDA that included a paragraph IV certification asserting that Pfizer's patents on Norvasc were invalid. Pfizer sued Mylan in the Western District of Pennsylvania for patent infringement, although it did not file within the 45 days required to invoke the "automatic stay" provisions of the Hatch-Waxman Act (the "*Mylan*

action"). *Pfizer, Inc. v. Mylan Laboratories Inc., et al.*, No. 2:06-3462 (W.D. Pa.). When Mylan filed its paragraph IV certification, the expiration of Pfizer's last patent was almost five years away—March 25, 2007. Not until a year after Mylan filed its paragraph IV certification challenging Pfizer's patent did another generic company follow Mylan's lead. That company was Apotex, which Pfizer proceeded to sue in the Northern District of Illinois (the "*Apotex* action").

On October 3, 2005, while both the *Mylan* and *Apotex* actions were pending, the FDA granted final approval of Mylan's ANDA. Bloodworth Decl., Exh. B. In the approval letter, the FDA confirmed that because Mylan had been the first applicant to file an ANDA with a paragraph IV certification, "Mylan is eligible for 180-days of market exclusivity." *Id.* at 2. The letter went on to state, consistent with the plain language of the Hatch-Waxman Act, that Mylan's 180-day generic marketing exclusivity "will begin to run from the earlier of the commercial marketing or court decision dates identified in [21 U.S.C.] section 505(j)(5)(B)(iv)." *Id.* The FDA approved Mylan's amlodipine ANDA even though the FDA had previously granted Pfizer a six-month period of pediatric exclusivity. *See* Bloodworth Decl., Exh. C ("FDA Ltr.") at 4.

Although Mylan beat Apotex to the punch by a year, the *Apotex* action was the first to proceed to judgment. On January 29, 2006, the district court for the Northern District of Illinois entered judgment against Apotex, declaring that Pfizer's patent was valid, enforceable, and infringed by Apotex's amlodipine tablets. The district court ordered that the effective date of Apotex's ANDA be reset to September 25, 2007 (reflecting the patent term plus six months of pediatric exclusivity). Bloodworth Decl., Exh. D. Apotex appealed the district court judgment to the Federal Circuit. Bloodworth Decl., Exh. E.

Just over a year later, on February 27, 2007, while the *Apotex* action was pending on appeal, the district court for the Western District of Pennsylvania in the *Mylan* action reached the same conclusion as the district court in the *Apotex* action. The Pennsylvania district court ordered that the approval of Mylan's ANDA would not be made effective until after Pfizer's patent expired a month later, on March 25, 2007, and enjoined Mylan from going to market with its generic version of the drug until then. Bloodworth Decl., Exh. F.

On March 22, 2007, just days before Pfizer's patent expired, the Federal Circuit issued its decision in the *Apotex* case, holding Pfizer's patent invalid as obvious. *Pfizer Inc. v. Apotex, Inc.*, No. 2006-1261, 2007 U.S. App. LEXIS 6623 (Mar. 22, 2007). The following day, the Federal Circuit stayed the district court's order in the *Mylan* action. *See* Bloodworth Decl., Exh. G. Mylan began commercial marketing of its generic amlodipine besylate tablets that same day. *See id.* at Exh. H.

On April 18, 2007, the FDA issued a formal letter decision ruling *inter alia* that Mylan's marketing exclusivity rights did not survive the expiration of the Pfizer patent because at patent expiration all unapproved applications, including those with paragraph IV certifications, are deemed to have been converted to paragraph II certifications, which may be approved without regard to generic exclusivity. Bloodworth Decl., Exh. C. In its preliminary injunction ruling, this Court held Mylan's 180-day generic exclusivity under § 355(j)(5)(B)(iv) did not survive patent expiration. This Court found that the plain language of the 180-day generic exclusivity provision only blocks paragraph IV ANDAs and, since all unapproved paragraph IV ANDAs, such as Apotex's, were deemed to contain paragraph II certifications upon the patent's expiration, the plain language of § 355(j)(B)(iv) did not apply to Apotex. Mem. Op. at 18-19 ("[Section 355(j)(5)(B)(iv)] by its terms, applies only to paragraph IV certification, which cease

to exist upon patent expiration."). Mylan filed a motion for reconsideration of the district court's April 30 decision, which was denied without opinion on May 14, 2007.

On May 21, 2007, the Court of Appeals for the Federal Circuit denied Pfizer's Petition for Rehearing and Rehearing *En Banc* and issued an immediate mandate. Bloodworth Decl., Exh. I. On May 23, 2007, the FDA granted final approval of Apotex's amlodipine ANDA and Apotex has entered the market.

In addition to Mylan and Apotex, there are at least eight other generic manufacturers that are awaiting final FDA approval for their amlodipine ANDAs. *See* Bloodworth Decl., Exh. J. The FDA's decision to delist the '303 patent from the Orange Book clears the way for these applicants to also receive final FDA approval.

LEGAL BACKGROUND - The Hatch-Waxman Act

The purpose of the Hatch-Waxman Act[5], formally known as the Drug Price Competition and Patent Term Restoration Act of 1984, was to "make available more low cost generic drugs by establishing a generic drug approval procedure." H.R. Rep. No. 98-857 (Part I), at 14-15 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647. In the Hatch-Waxman Act, Congress struck an intricate balance among multiple competing interests. On the one hand, Congress wished to promote the interest in "quickly getting lower-cost generic drugs to market." *Teva Pharms. Indus. Ltd. v. Crawford*, 410 F.3d 51, 54 (D.C. Cir. 2005). On the other hand, Congress "also wanted to protect the patent rights of the pioneer applicants," thereby fostering innovation.

[5] Certain Hatch-Waxman provisions have been superseded by the *Medicare Prescription Drug, Improvement and Modernization Act of 2003* ("MMA"), Pub. L. 108-173, 117 Stat. 2066 (Dec. 8, 2003). But the 1984 version of the Hatch-Waxman Act applies to the provisions at issue here because the MMA provisions control only those ANDAs filed after December 3, 2003. *See* FDA Ltr. at 1 n.1; MMA, at § 1102(b)(1). Unless indicated otherwise, all references herein will be to 21 U.S.C. § 355, *et seq.* (2002).

Andrx Pharms., Inc. v. Biovail Corp. Int'l, 256 F.3d 799, 802 (D.C. Cir. 2001); *see Bristol-Myers Squibb Co. v. Royce Labs. Inc.*, 69 F.3d 1130, 1133-34 (Fed. Cir. 1995) ("Congress's objective . . . was to strike a 'careful balance between the policies of fostering the availability of generic drugs and of providing sufficient incentives for research on breakthrough drugs.'") (citations omitted). Congress adopted an incentive structure that awarded certain generic drug companies preferential treatment, and accorded certain brand name drug makers additional benefits, depending upon whether they took steps that Congress wished to reward.

To expedite the approval process for generic drugs, the Hatch-Waxman Act permits a generic drug company to submit an Abbreviated New Drug Application, or ANDA, to the FDA. The ANDA must include studies showing that the generic product is "bioequivalent" to the name brand drug that has already been approved. *See Dr. Reddy's Labs., Inc. v. Thompson*, 302 F. Supp. 2d 340, 343 (D.N.J. 2003) ("*DRL*") (citing 21 U.S.C. § 355(j)(2)(A)(iv)). The ANDA must also contain a certification that relates to the patent rights of the branded drug manufacturer that are listed in the Orange Book. The generic drug company must file one of four possible certifications to each patent listed in the Orange Book. The four certifications are labeled according to the paragraph number in the statute that describes them—paragraphs I through IV.

The first three certifications pose no threat to the brand name drug maker's patent rights. A "paragraph I" certification informs the FDA that there are no patents listed in the Orange Book for the drug in question. 21 U.S.C. § 355(j)(2)(A)(vii)(I). A "paragraph II certification" informs the FDA that there is a patent listed in the Orange Book, but that the patent has expired. *Id.* at § 355(j)(2)(A)(vii)(II). A "paragraph III" certification informs the FDA that the Orange Book lists unexpired patents on the drug in question and certifies that the applicant does not intend to enter the market until those patents have expired. *Id*. at § 355(j)(2)(A)(vii)(III). A paragraph I,

II or III certification means that the brand name manufacturer's patents, if any, will not be at stake by the filing of the ANDA.

A paragraph IV certification, in contrast, is a declaration of war—the filer asserts that the brand name drug has no valid patent protection. 21 U.S.C § 355(j)(2)(A)(vii)(IV). A paragraph IV certification often triggers a lawsuit by the brand name drug maker asserting its patent rights. *See* 21 U.S.C. § 355(j)(5)(B)(iii); 35 U.S.C. § 271(e)(2) (2006).

But litigating a patent challenge against a pharmaceutical giant is a time consuming and expensive proposition, so Congress decided to provide generic drug companies with an incentive to file such challenges. The reward is the right of the first paragraph IV filer to enter the market for 180-days free from competition from other generics. Mechanically, Congress accomplished this end by directing the FDA to delay approval of later paragraph IV ANDAs. The relevant provision directs that "[i]f the [ANDA of a competing generic company] contains a [paragraph IV certification] and is for a drug [with an ANDA already containing] such a certification, the application shall be made effective not earlier than one hundred eighty days after . . . the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application . . . ." 21 U.S.C. § 355(j)(5)(B)(iv). As this Court has emphasized, the meaning of the "literal language" of this provision is clear: "Section 355(j)(5)(B)(iv) says that, if an applicant has already filed a paragraph IV ANDA, later applications shall be approved 'not earlier than one hundred and eighty days after' the commercial-marketing trigger or the court-decision trigger is satisfied." *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1069 (D.C. Cir. 1998) (quoting 21 U.S.C. § 355(j)(5)(B)(iv) (2002)).

ARGUMENT

Mylan is entitled to a temporary restraining order because it can show "1) a substantial likelihood of success on the merits, 2) that [plaintiff] would suffer irreparable injury if the injunction is not granted, 3) that any injunction would not substantially injure other interested parties, and 4) that the public interest would be served by the injunction." *Canales v. Paulson*, No. 06-1330, 2006 U.S. Dist. LEXIS 61915, at *8 (D.D.C. Aug. 30, 2006) (quoting *Katz v. Georgetown Univ.*, 246 F.3d 685, 687-88 (D.C. Cir. 2001)). These factors "interrelate on a sliding scale and must be balanced against each other." *Id*. (quoting *Sereno Lab. v. Shalala*, 158 F.3d 1313, 1318 (D.C. Cir. 1998). Furthermore, "'[i]f the arguments for one factor are particularly strong, an injunction may issue even if the arguments in the other areas are rather weak.'" *Id*. (quoting *CityFed Financial Corp. v. Office of Thrift Supervision*, 58 F.3d 738, 746 (D.C. Cir. 1995)).

I. MYLAN IS LIKELY TO SUCCEED ON APPEAL BECAUSE ITS 180-DAY EXCLUSIVITY HAD VESTED BEFORE PATENT EXPIRATION AND THE FDA'S REGULATIONS AND PRECEDENT CLEARLY REQUIRE A PATENT TO REMAIN LISTED IN THE ORANGE BOOK UNTIL THE 180-DAY EXCLUSIVITY OF THE FIRST-TO-FILE COMPANY HAS EXPIRED

The portion of the FDA's regulations relied upon in the FDA's April 18, 2007 letter decision to find that Mylan's eligibility for 180-day generic exclusivity does not extend beyond the '303 patent's expiration is arbitrary, capricious, and contrary to law because Mylan's right to the 180-day generic exclusivity reward vested *prior to* the patent's expiration and under the plain language of 21 U.S.C. § 355(j)(5)(B)(iv), the FDA does not have authority to cut short Mylan's generic exclusivity period. Mylan is likely to succeed on the merits because the FDA's own regulations prohibit it from delisting patents held invalid based on a paragraph IV challenge, such as the '303 patent, during that challengers entitled reward of 180-day generic exclusivity.

A. ONCE MYLAN'S 180-DAY GENERIC EXCLUSIVITY RIGHT VESTED, IT COULD NOT BE DIVESTED BY THE '303 PATENT'S EXPIRATION

1. The Statute's Plain Language Requires That Vested 180-Day Generic Exclusivity Extends Beyond Patent Expiration

Throughout the years, the FDA has repeatedly attempted to narrow the scope of the application of the exclusivity. The Courts have likewise repeatedly thwarted those attempts and overturned the FDA's 180-day determinations. *See, e.g.*, *Mova*, 140 F.3d at 1069 (rejecting FDA's "successful defense" prerequisite to 180 day exclusivity); *Granutec, Inc. v. Shalala*, Nos. 97-1873, 97-1874, 1998 U.S. App. LEXIS 6685, at *20-21 (4th Cir. Apr. 3, 1998) (same); *Inwood Labs., Inc. v. Young*, 723 F. Supp. 1523, 1526 (D.D.C. 1989) (same); *Teva Pharms. USA, Inc. v. FDA*, 182 F.3d 1003, 1010-1011 (D.C. Cir. 1999) *on remand*, 1999 U.S. Dist. LEXIS 14575 (D.D.C. Aug. 18, 1999), *aff'd*, 2000 U.S. App. LEXIS 38667 (D.C. Cir. Nov. 15, 2000) (rejecting FDA's interpretation of a "decision of court"); *Mylan Pharms. Inc. v. Henney*, 94 F. Supp. 2d 36, 52-54 (D.D.C. 2000) (same); *TorPharm Inc. v. Shalala*, No. 97-1925, 1997 U.S. Dist. LEXIS 21983, *11-12 (D.D.C. Sept. 15, 1997) (same). The regulations at issue here are these same regulations that have been piecemeal rejected by the Courts.

"[T]he courts are the final authorities on issues of statutory construction," and "must reject administrative constructions . . . that are inconsistent with the statutory mandate or that frustrate the policy that Congress sought to implement." *FEC v. Democratic Senatorial Campaign Comm.*, 454 U.S. 27, 32 (1981). In its April 18 decision, the FDA stated its "longstanding position that 180-day exclusivity expires with the patent." FDA Ltr. at 10. But this conclusion is precluded by the plain language of the 180-day generic exclusivity provision of the Hatch-Waxman Act, which reads:

> If the application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) [*i.e.*, a paragraph IV certification] and is for a drug for which a previous application has been submitted under this subsection continuing [sic]

> such a certification, the application shall be made effective not earlier than one hundred and eighty days after—
>
> > (I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or
> >
> > (II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed,
>
> whichever is earlier.

21 U.S.C. § 355(j)(5)(B)(iv) (2002). Mylan was the first to file a paragraph IV certification and its 180-day generic exclusivity began on March 23, 2007, when it notified the FDA that it had begun commercial marketing. *See Mylan*, 94 F. Supp. 2d at 40 ("By its terms, the [180-day generic exclusivity statute] affords the first filer protection from competition from subsequent generic makers for 180 days beginning from the earlier of a commercial marketing or court decision.").

The plain language of § 355(j)(5)(B)(iv) is not limited to patent terms. As the D.C. Circuit has emphasized, the meaning of the "literal language" of this provision is clear: "Section 355(j)(5)(B)(iv) says that, if an applicant has already filed a paragraph IV ANDA, later applications shall be approved 'not earlier than one hundred and eighty days after' the commercial-marketing trigger or the court-decision trigger is satisfied." *Mova*, 140 F.3d at 1069 (quoting 21 U.S.C. § 355(j)(5)(B)(iv)); *see also Lamie v. United States Trustee*, 540 U.S. 526, 534 (2004) ("[W]hen 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.") (quotations and citations omitted). Since 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). Accordingly, Mylan's 180-day generic exclusivity bars the FDA from approving any other

ANDAs with paragraph IV certifications, even though the '303 patent has expired.

2. The Statute's Legislative History and Purpose Require that Vested 180-Day Generic Exclusivity Extends Beyond Patent Expiration

Nothing in the text or legislative history of the 180-day generic exclusivity statute indicates that the right created thereby is cut short upon patent expiration. In fact, Congress adopted the 180-day generic exclusivity statute, *inter alia*, to encourage generics to file paragraph IV challenges to the validity of pharmaceutical patents and to reward such challengers for their risk and expense.[6] According to a 2002 Federal Trade Commission report, the 180-day generic exclusivity statute has worked, encouraging challenges to patents and resulting in 73% of those challenges succeeding in removing the barriers created by an invalid patent. *See* Federal Trade Commission, "Generic Drug Entry Prior to Patent Expiration," July 2002, at 16, available

[6] *See, e.g.*, 152 Cong. Rec. S7922, at S7928 (daily ed. July 19, 2006) (statement of Sen. Leahy) ("[T]he original intent of the Hatch-Waxman law . . . was to provide incentives for generic companies to challenge the validity of patents on medicines and provide incentives for generic companies to manufacture low-cost medicines" and "that [a] generic company would have the exclusive right for 180 days to make the generic version of the patented medicine); 149 Cong. Rec. S15670-03, at S15746 (daily ed. Nov. 24, 2003) (statement of Sen. Schumer) ("Fourth, the generic provisions revamp the 180-day exclusivity incentive provided in the Hatch-Waxman Act. Under the act, the first generic drug company to challenge a patent on a brand drug has the exclusive right to market its drug for 6 months before any other generic can compete. This feature encourages generic applicants to challenge weak patents and brings consumers much quicker access to affordable generic drugs."); 149 Cong. Rec. S8686-03, at S8691 (daily ed. June 26, 2003) (statement by Sen. Hatch) ("The Waxman-Hatch law provides an incentive for generic firms to challenge patents. To encourage generic competitors to pursue patent challenges in a vigorous fashion, the 1984 law provided 180 days of marketing exclusivity in situations where a generic drug firm could show the pioneer's patents were invalidated or not infringed."); Proposed Rule, 180-Day Generic Drug Exclusivity for Abbreviated New Drug Applications, 64 Fed. Reg. 42873, 42874 (Aug. 6, 1999), *withdrawn on other grounds by* 67 Fed. Reg. 212, 66593 (Nov. 1, 2002) ("Given this risk of patent infringement litigation, section 505(j)(5)(B)(iv) of the act provides an incentive for generic drug applicants to file paragraph IV certifications challenging patents that may be invalid, unenforceable, or not infringed by the product that is the subject of the ANDA."); 54 Fed. Reg. 28872, 28895 (July 10, 1989) ("The purpose of [the 180-day exclusivity provision] of the act is to reward the first applicant to test the scope or validity of a patent. . . .").

at http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf.

But Congress's purpose can only be accomplished if the first filer challenging the invalid patent is assured of 180-day generic exclusivity, regardless of how long the litigation takes. If potential challengers must consider factors such as the speed of various courts' dockets, the possibility that various presiding judges may retire, and other uncontrollable events in deciding whether to challenge invalid patents, this inevitably will deter the challenges that Congress intended to encourage, particularly as the end of the patent term draws closer. The D.C. Circuit has rejected previous attempts to reduce the period of 180-day generic exclusivity, there in the related context of delisting, because it would be contrary to the intent of Congress:

> By thus reducing the certainty of receiving a period of marketing exclusivity, the FDA's delisting policy diminishes the incentive for a manufacturer of generic drugs to challenge a patent listed in the Orange Book in the hope of bringing to market a generic competitor for an approved drug without waiting for the patent to expire. The FDA may not, however, change the incentive structure adopted by the Congress, for the agency is bound "not only by the ultimate purposes Congress has selected, but by the means it has deemed appropriate, and prescribed, for the pursuit of those purposes."

Ranbaxy, 469 F.3d at 126 (quoting *MCI Telecomms. Corp. v. AT&T Co.*, 512 U.S. 218, 231 n.4 (1994)). The FDA's decision that vested 180-day generic exclusivity does not survive patent expiration "change[s] the incentive structure adopted by the Congress" in the same manner the D.C. Circuit has rejected.

Mylan was the first to file under paragraph IV and the first to be sued by Pfizer for patent infringement. Mylan's patent infringement case, the Pennsylvania action, was delayed due to circumstances outside of its control, including a lengthy delay caused by a change of trial judges. That resulted in the unique situation in which Apotex, which Pfizer sued later, was able to use Mylan's arguments and expert reports in the Pfizer-Apotex litigation. Mylan took the risk that was recognized by Congress as critical, and Mylan is entitled to the reward of 180-day generic

exclusivity regardless of how long its case took to resolve. The FDA's ruling that Mylan's 180-day generic exclusivity does not survive patent expiration cannot justify a "departure from the plain meaning of statutory language," and its reliance on vague notions of Congressional intent cannot satisfy this "considerable burden." *Mylan*, 94 F. Supp. 2d at 55; *id.* at 56 (noting that, to depart from the plain language of a statute, there must be a "clear indication of congressional intent at odds with the text of the statute").

The FDA agrees that Congress created the 180-day generic exclusivity statute for these purposes. But it argues that, "[o]nce a listed patent expires and is no longer a barrier to ANDA approval, there is no longer a need to provide an incentive to challenge it in court." FDA Ltr. at 11. The FDA's analysis is focused on today, which is the wrong time; of course there need be no incentive to challenge a patent once it expires. The critical time period is 2002, when Mylan filed its ANDA with a paragraph IV certification. Mylan's filing came nearly five years before the '303 patent was to expire and brought the '303 patent's validity before the courts. Thus, Congress's intent in creating incentives to the challenge of pharmaceutical patents was fulfilled. Had Mylan known in 2002 that a combination of events out of its control would deprive it of that 180-day generic exclusivity, Mylan would not have filed a paragraph IV certification. It would have filed with a paragraph III certification (thus insulating itself from the burden of patent infringement litigation) and it would have waited until the '303 patent expired. That series of events would have been directly contrary to Congress's purpose in adopting the 180-day generic exclusivity statute.

3. This Is A Case of First Impression: The FDA Has Never Before Cut Short A First Filer's 180-Day Exclusivity Period Once It Has Vested

The two cases that the FDA relies upon are inapposite. Neither *Ranbaxy Labs. Ltd. v. Leavitt*, 469 F.3d 120, 126 (D.C. Cir. 2006) nor *Dr. Reddy's Labs., Inc. v. Thompson*, 302 F.

Supp. 2d 340, 354-55 (D.N.J. 2003) ("*DRL*") addressed vested exclusivity rights. In *Ranbaxy*, the Court of Appeals recognized that the issue of whether 180-day generic exclusivity survived the patent's expiration was not before it. *See Ranbaxy*, 469 F.3d at 126 ("We need not address the question of patent expiration in this case."). The FDA often points out that the *Ranbaxy* opinion goes on to note in *dicta* "that the text and structure of the statute suggest a distinction between expiration and delisting such that the first generic applicant may no longer retain exclusivity when the patent has expired." *Id.* But importantly, in neither *Ranbaxy* nor *DRL* had the first filer triggered its period of 180-day exclusivity – as Mylan did here – when the FDA cut short that exclusivity.

In *DRL*, the court upheld the FDA's decision that DRL's tentatively approved ANDA was no longer *eligible* for exclusivity because once the underlying patent expires, its ANDA was deemed to convert from a paragraph IV certification to a paragraph II certification. 302 F. Supp. 2d at 351 (noting FDA's explanation that "a paragraph IV certification on a patent loses its eligibility for exclusivity based upon that patent when the patent expires *before either of the triggering events occurs*) (emphasis added). Without a paragraph IV certification, DRL was not eligible for exclusivity under the plain language of the generic exclusivity provision. *Id.* at 351 ("[T]he FDA will not grant exclusivity based upon a paragraph IV certification on a patent that has expired at the time the exclusivity decision is made."). That reasoning does not apply here because, prior to the '303 patent's expiration, the FDA had approved Mylan's ANDA with a paragraph IV certification, the 180-day exclusivity period had begun, and Mylan's 180-day generic exclusivity had vested. The FDA has conceded as much. *See* FDA Ltr. at 13.

The FDA's principal argument is based on the statute's explicit focus on ANDAs with paragraph IV certifications. Although Congress certainly was concerned about subsequent

paragraph IV filers, that concern was not to the exclusion of all other filers. Moreover, Congress certainly did not know when it enacted the statute in 1984 that, ten years later, the FDA would deem all paragraph IV certifications to be paragraph II certifications after the relevant patent had expired.[7] The FDA therefore is incorrect when it argues that, after the patent expires, subsequent filers avoid 180-day generic exclusivity because their paragraph IV certifications are required "[b]y the terms of the statute" to change to certifications under paragraph II. FDA Ltr. at 10. The FDA itself has argued just the opposite in the Apotex proceedings, where it has continued to treat Apotex's certification as a paragraph IV, even after the '303 patent had expired, so that Apotex can avoid Pfizer's pediatric exclusivity. *Id*. at 8-9. Under the construction adopted by the FDA in the pediatric exclusivity context, Apotex's ANDA still contains a paragraph IV certification and, by the express terms of the statute, cannot be approved during Mylan's 180-day generic exclusivity. *Id.*; *see also Apotex's Opposition to Mylan's Motion for a Preliminary Injunction* [Dkt. No. 55] ("Apotex Br.") at 5 (agreeing with the FDA's "decision to not automatically convert Apotex's paragraph IV certification to a paragraph II certification").

The rest of the ANDAs are subject to Mylan's 180-day generic exclusivity as well, even if they contain or are changed to paragraph II certifications. "*Exclusivity*" was the term that Congress itself chose to describe the right it was bestowing on the first to challenge patents (*i.e.*, the title of the statutory paragraph is "180-day exclusivity period"). The term "exclusivity" demonstrates an intent to make the first-filer's right to sell exclusive of other generics, regardless of the paragraph under which they certified. On the other hand, the FDA's interpretation would lead to the absurd result that filers that certified under paragraph IV, and thus took on the risk of

[7] A paragraph II certification states that that the relevant patent "has expired." 21 U.S.C. § 355(j)(2)(A)(vii)(II). An ANDA filer will not be sued for patent infringement when it certifies under paragraph I (certifying the relevant patent has not been filed), paragraph II, or paragraph III (certifying the date on which the relevant patent will expire).

litigation (such as Apotex), were blocked by Mylan's 180-day generic exclusivity, while the FDA would be free to approve those who merely certified under paragraphs II and III and took no risk at all.

Such a result would fly in the face of Congress's intent in adopting the 180-day generic exclusivity statute and its expectations regarding how the FDA would treat the various certifications *vis-à-vis* each other. For example, Congress has expressed its intent that ANDAs with paragraph IV certifications must be treated better than those with certifications under paragraphs II and III by providing that the former "shall" be approved after the 180-day generic exclusivity period ends, but the latter only "may" be approved. *Compare* 21 U.S.C. § 355(j)(5)(B)(iii) ("If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval *shall* be made effective immediately. . . .") *with* 21 U.S.C. § 355(j)(5)(B)(i) ("If the applicant only made a certification described in subclause (I) or (II) of paragraph (2)(A)(vii) . . . the approval *may* be made effective immediately") *and* 21 U.S.C.§ 355(j)(5)(B)(ii) ("If the applicant made a certification described in subclause (III) of paragraph (2)(A)(vii), the approval *may* be made effective on the date certified. . . .") (emphases added).

Thus, the FDA's interpretation of the statute produces absurd results, which "are to be avoided if alternative interpretations consistent with the legislative purpose are available." *Griffin v. Oceanic Contractors, Inc.*, 458 U.S. 564, 575 (1982); *see also Clinton v. New York*, 524 U.S. 417, 429 (1998) (rejecting interpretation of statute that "would produce an absurd . . . result which Congress could not have intended" (quotations omitted)); *Fleischmann Constr. Co. v. United States ex rel. Forsberg*, 270 U.S. 349, 360-62 (1926) (interpreting a statutory term "'within one year from the completion of the work' to mean 'within one year after

the performance and final settlement of the contract'" to avoid "unjust or absurd consequences"); *Quinn v. Butz*, 510 F.2d 743, 753 (D.C. Cir. 1975) ("[A] construction of a statute leading to unjust or absurd consequences should be avoided.").

Both the D.C. Circuit and the FDA applied this principle in recognizing that a certification that a patent is "unenforceable" suffices for purposes of the Paragraph IV certification, even though the statute only mentions patents that are "invalid" or "will not be infringed." *See Teva Pharms.*, 182 F.3d at 1009; 59 Fed. Reg. 50,338, 50,339 (Oct. 3, 1994) (explaining that the FDA included "unenforceability" because "the alternative interpretation . . . would be contrary to Congress' obvious intent in allowing patent challenges under [the Hatch-Waxman Act] and would lead to absurd results."). Even if the result of the FDA's interpretation did not rise to the level of absurdity and unfairness—which Mylan believes it certainly does—but was "merely an unreasonable one plainly at variance with the policy of the legislation as a whole," that still would be sufficient to require this Court to follow the purpose, "rather than the literal words." *United States v. American Trucking Ass'ns*, 310 U.S. 534, 543 (1940) (citations omitted).

B. THE FDA CANNOT DELIST THE '303 PATENT UNTIL MYLAN'S 180-DAY GENERIC EXCLUSIVITY EXPIRES

The Hatch-Waxman Acts states that the first company to file an ANDA containing a paragraph IV certification to a patent listed in the Orange Book "shall be" entitled to 180-days of exclusivity:

> If the application contains a [paragraph IV certification] and is for a drug for which a previous application has been submitted under this subsection, [containing] such a certification, the application *shall be made effective not earlier than one hundred and eighty days after*
>
> > (I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application; or

> (II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed,
>
> whichever is earlier.

21 U.S.C. § 355(j)(5)(B)(iv) (2002) (emphasis added).

Mylan is entitled to 180-day generic exclusivity because it was the first company to file a paragraph IV certification, challenging the validity of the '303 patent, listed as covering Norvasc. *See* 21 U.S.C. § 355(j)(5)(B)(iv) (providing 180-day generic exclusivity only where an ANDA contains a certification "described in" 21 U.S.C. § 355(j)(2)(A)(vii)(IV), which only describes certifications to patents "which claim[] the listed drug . . . or . . . a use for such listed drug. . . ."). Generally, the FDA will delist a patent on the request of the new drug application ("NDA") holder. *See Ranbaxy*, 469 F.3d at 123 ("Merck, however, did not sue Ranbaxy or Teva for patent infringement based upon their paragraph IV certifications. Instead, before their ANDAs were approved, Merck asked the FDA to delist the '481 and '520 Patents from the Orange Book, which the agency did in 2004. Consequently, under 21 C.F.R. § 314.94(a)(12)(viii)(B), Ranbaxy and Teva were required to delete the paragraph IV certifications from their ANDAs and thereby lost their eligibility for a period of marketing exclusivity.").

But the FDA created an exception: it will not delist a patent if doing so would deprive a party of its 180-day generic exclusivity rights. In interpreting its delisting regulation, 21 C.F.R. § 314.94(a)(12)(viii)(B), the FDA has explained that "[i]f a patent were removed from the list immediately upon a court decision that the patent is invalid or unenforceable, an applicant with a subsequently filed application might seek to certify that there is no relevant patent and seek an immediately effective approval." 59 Fed. Reg. at 50348. "To ensure that this does not occur, the agency has required that a patent remain on the list after being declared invalid or unenforceable until the end of any applicable 180-day exclusivity period." *Id*. Thus, the FDA's policy does

not—and cannot—allow an NDA holder, "by delisting its patent, to deprive the generic applicant of a period of marketing exclusivity." *Ranbaxy*, 469 F.3d at 126 (holding unlawful "the FDA's policy requiring that the first filer of a paragraph IV certification be sued in order to preserve its statutory exclusivity when the NDA holder seeks to delist the patent rather than to litigate"). As shown below, because Mylan's "applicable" exclusivity period extends for a full 180 days irrespective of the '303 patent's interim expiration, the '303 patent may not be delisted until that period has fully run.[8]

The FDA has acknowledged that when there is an outstanding claim of 180-day exclusivity it would be unjust to thwart the challenger's incentive by allowing the patent to be de-listed:

> This regulation recognizes a limited exception to this delisting and amendment requirement when the patent is the subject of a lawsuit. . . . The reason for this limited exception is to avoid an unjust result that would occur if an ANDA applicant who is eligible for exclusivity prevails in the patent litigation but lost exclusivity if the NDA holder decided to delist.

Federal Defendants' Memorandum in Support of Motion for Summary Judgment and in Opposition to Plaintiffs' Motions for Summary Judgment, No. 1:05-02180 (RWR) (D.D.C. Dec. 2, 2005) [Dkt. No. 8-1] at 11.

Similarly, the FDA's response to comments regarding the proposed regulation recognized that a first-filer's market exclusivity should not be destroyed by delisting:

> [T]he agency agrees that the protection offered by 180-day exclusivity should not be undermined by changes from paragraph IV certification or by the filing of original certifications other than paragraph IV certifications. If a patent were

[8] 21 C.F.R. § 314.94(a)(12)(viii)(B) provides: "A patent that is the subject of a lawsuit under § 314.107(c) shall not be removed from the list until FDA determines either that no delay in effective dates of approval is required under that section as a result of the lawsuit, *that the patent has expired*, or that any such period of delay in effective dates of approval is ended." Mylan is challenging that portion of the FDA's regulations that condition generic exclusivity on whether or not the patent is expired.

> removed from the list immediately upon a court decision that the patent is invalid or unenforceable, an applicant with a subsequently filed application might seek to certify that there is no relevant patent and seek an immediately effective approval. To ensure that this does not occur, the agency has required that a patent remain on the list after being declared invalid or unenforceable *until the end of any applicable 180-day exclusivity period*.

59 Fed. Reg. at 50,348 (emphasis added). The FDA, however, then continues and, ignoring Congress' clear direction to the contrary, hinges generic exclusivity on the patent's life:

> This means that a patent is deemed to be relevant under §314.94(a)(12)(ii) until the end of the term of the patent or applicable 180-day exclusivity period, whichever occurs first. Thus, where there is a patent that has been challenged by a paragraph IV applicant, a subsequent applicant will not be able to file a certification that there is no relevant patent or seek an immediately effective approval until either the patent or the 180-day exclusivity period expires.

Id. But there is nothing in the subsection (5)(B)(iv) that states that a subsequent paragraph IV filer shall not be approved – unless the patent expires.

II. MYLAN WILL BE IRREPARABLY HARMED IF A TRO IS NOT ENTERED BECAUSE DELISTING OF THE PATENT WOULD DESTROY MYLAN'S 180-DAY EXCLUSIVITY

Until the Court of Appeals has resolved the issue of the expiration date of Mylan's 180-day exclusivity, it would be improper for the FDA to delist the '303 patent, thereby destroying Mylan's 180-day exclusivity and irreparably prejudicing Mylan's right to have the issue decided by the courts.

This Court has recognized that the loss of the 180-day exclusivity period constitutes irreparable harm. *Apotex, Inc. v. Food and Drug Administration*, No. 06-0627, 2006 U.S. Dist. LEXIS 20894, at *58 (D.D.C. Apr. 19, 2006) (finding that the first to file companies "stand to lose a statutory entitlement, which is a harm that has been recognized as sufficiently irreparable[] and that "[o]nce the statutory entitlement has been lost, it cannot be recaptured" (internal citation omitted)), *aff'd*, 449 F.3d 1249 (D.C. Cir. 2006); *Mova Pharmaceutical Corp. v. Shalala*, 955 F.

Supp. 128, 131 (D.D.C. 1997) ("depriving Mova of a 180-day statutory grant of exclusivity and giving Mylan an officially sanctioned head start in the market for generic micronized glyburide products will cause injury to Mova"), *aff'd*, 140 F.3d 1060 (D.C. Cir. 1998).

Mylan has expended tremendous resources on the development and approval of its amlodipine products, including millions of dollars on materials, studies, overhead, and litigation. Roman Decl.[9] ¶3. Mylan anticipates that its revenues will be several million dollars per day for the balance of the 180-day exclusivity period. Roman Decl. ¶ 6. Mylan will irrevocably lose a portion of these revenues if the FDA delists the '303 patent before the issue of Mylan's 180-day exclusivity is resolved by the Court of Appeals. Roman Decl. ¶ 6.

Mylan's harm will be substantial and irreparable. *McGregor Printing Corp. v. Kemp*, No. 91-3255, 1992 U.S. Dist. LEXIS 6717, at *16 (D.D.C. May 14, 1992) (irretrievable monetary loss in combination with loss of employment to plaintiff's employees amounted to irreparable injury), *rev'd on other grounds*, 20 F.3d 1188 (D.C. Cir. 1994); *TorPharm*, 1997 U.S. Dist. LEXIS 21983, at *12-13 (irretrievable monetary losses that have a serious effect on plaintiff constitute irreparable harm) (citing *Gulf Oil Corp. v. Dep't of Energy*, 514 F. Supp. 1019, 1026 (D.D.C. 1981)).

The harm to Mylan would be unrecoverable because there is no remedy at law against FDA. This Court and the D.C. Circuit Court of Appeals have found irreparable harm in situations where there is no one from whom to recover loss. *Bracco Diagnostics Inc. v. Shalala*, 963 F. Supp. 20, 29 (D.D.C. 1997) (when the injury is "admittedly economic" but there is no adequate compensatory or other relief, the balance tips in favor of injunctive relief); *National*

[9] *Declaration of Brian S. Roman in Support of Mylan's Emergency Application for a Temporary Restraining Order* [Dkt. No. 3].

Medical Care, Inc. v. Shalala, No. 95-0860, 1995 U.S. Dist. LEXIS 10074, at *7-8 (D.D.C. June 6, 1995); *Express One Int'l, Inc. v. USPS*, 814 F. Supp. 87, 91 (D.D.C. 1992) (nonrecoverable monetary loss sufficient to justify injunctive relief); *O'Donnell Constr. Co. v. District of Columbia*, 963 F.2d 420, 428-429 (D.C. Cir. 1992).

The kind of injury that Mylan would suffer cannot be compensated by monetary damages. Even if it could, Mylan would have no way to recoup its losses from the government, which has no financial liability for erroneous decisions in circumstances like these. *Collagenex v. Thompson*, No. 03-1405, 2003 U.S. Dist. LEXIS 12523, at *33-34 (D.D.C. July 22, 2003).

Even if this Court disagrees about the level of harm to Mylan, injunctive relief may be granted "[w]here, as here, the likelihood of success on the merits is very high, a much smaller quantum of injury will sustain an application for preliminary injunction." *Mova*, 955 F. Supp. at 131.

III. THE PUBLIC WILL BE HARMED IF A TRO IS NOT ENTERED BECAUSE THE INCENTIVES FOR GENERIC DRUG COMPANIES TO FILE PARAGRAPH IV CHALLENGES WILL BE SIGNIFICANTLY REDUCED

There are sound policy reasons behind the exclusivity provisions of the Hatch-Waxman Amendments, and there are sound bases for not allowing hard-earned exclusivity to be destroyed by the arbitrary delisting of a patent. If the '303 patent is delisted before expiration of Mylan's 180-day exclusivity period, then the incentives for generic drug companies to file paragraph IV challenges will be significantly reduced and the public will be deprived of low cost generic alternatives to brand name drugs that are covered by patents that are invalid, unenforceable, or not infringed.

Mylan relied on the incentives promised by Hatch-Waxman and committed enormous resources to challenging an invalid patent. The FDA should not frustrate the policies of the

statute by delisting the '303 patent prior to judicial resolution of the question of whether 180-day exclusivity ends with patent expiration.

To the extent that Mylan's 180-day exclusivity will limit the number of generic amlodipine products for a short period of time, "the public interest in faithful application of the statutes outweighs . . . a marginal increase in the availability of low-cost generic drug products to American consumers, particularly where, as here, the very statute that was designed with consumers' interests in mind is the statute which so clearly entitles [Mylan] to relief. . ." *Mova*, 955 F. Supp. at 131.

IV. BALANCING THE HARM FAVORS ENTRY OF A TRO

The FDA will suffer no harm as a result of a TRO ordering it not to delist the '303 patent until the issue of Mylan's 180-day exclusivity is resolved by the Court of Appeals. Pfizer likewise will not be harmed by the continued listing of its patent in the Orange Book. In fact, the continued listing of the patent in the Orange Book benefits Pfizer because the entry of additional generic competitors would significantly erode Pfizer's market share.

CONCLUSION

For the foregoing reasons, Mylan respectfully asks this Court enter a temporary restraining order enjoining the FDA from approving any additional ANDAs on amlodipine in derogation of Mylan's right to 180-day exclusivity.

Dated: June 26, 2007

Respectfully submitted,

/s/ David J. Harth

David J. Harth (#474632)
HELLER EHRMAN LLP
One East Main Street, Suite 201
Madison, Wisconsin 53703
(608) 663-7460

Shannon M. Bloodworth (#474925)
HELLER EHRMAN LLP
1717 Rhode Island Avenue, NW
Washington, D.C. 20036
(202) 912-2000

E. Anthony Figg (#345124)
Minaksi Bhatt (#434448)
ROTHWELL, FIGG, ERNST & MANBECK PC
1425 K Street, NW
Suite 800
Washington, DC 20005
(202) 783-6040

Stuart A. Williams
Jill Ondos
MYLAN LABORATORIES INC.
1500 Corporate Drive
Suite 400
Canonsburg, Pennsylvania 15317
(724) 514-1840

Attorneys for Plaintiffs
MYLAN LABORATORIES INC. and
MYLAN PHARMACEUTICALS INC.