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Gary J. Buehler  
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Document Control Room, Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855

**RE: OGD NO. 2007N-0123: AMLODIPINE ABBREVIATED NEW DRUG APPLICATION APPROVALS**

**ANDA NO. 76-846: AMLODIPINE BESYLATE TABLETS (EQUIVALENT TO 2.5 MG, 5 MG, AND 10 MG AMLODIPINE)**

**CP NO. 2007P-0116: STAY ANY ADDITIONAL ABBREVIATED NEW DRUG APPLICATIONS FOR GENERIC AMLODIPINE PRODUCTS UNTIL AFTER THE MYLAN PHARMACEUTICALS INC. 180-DAY EXCLUSIVITY EXPIRES ON SEPTEMBER 23, 2007**

**CP NO. 2007P-0110: TO ENFORCE PEDIATRIC EXCLUSIVITY RIGHTS FOR AMLODIPINE**

**CP NO. 2007P-0111: STAY APPROVAL OF ANY AND ALL SUPPLEMENTS TO LOTREL CONCERNING AMLODIPINE AND PEDIATRIC EXCLUSIVITY**

Dear Mr. Buehler:

This letter is in reference to your March 29, 2007 facsimile, in which you solicited our response to several questions regarding FDA's approval of abbreviated new drug applications ("ANDAs") for generic amlodipine besylate drug products ("amlodipine"). We understand that the Agency has established a unified docket for the amlodipine matters, No. 2007N-0123, and reference is therefore made to that docket. Reference is also made to Teva's ANDA No. 76-846, for which Teva requested final approval by letter dated March 29, 2007, and to the above-referenced Citizen Petitions, in which Mylan Pharmaceuticals, Inc. ("Mylan") has requested that FDA stay the approval of any other generic amlodipine ANDA pending the expiration of a 180-day first-filer exclusivity period, and Pfizer Inc. has requested that FDA stay its approval of any amlodipine products—including Novartis' Lotrel®—pending the expiration of a 180-day pediatric exclusivity period for its Norvasc®-branded drug products.

The questions raised in your facsimile and implicated by the above-referenced Citizen Petitions fall into two general categories. One set of questions essentially seeks to determine whether Mylan is entitled to a 180-day period of exclusivity for its generic amlodipine products, despite the fact that the patent upon which Mylan purports to base such exclusivity—Pfizer's U.S. Patent No. 4,879,303 ("the '303 patent")—expired on March 25, 2007. The other set of questions seeks to determine whether Pfizer is entitled to a six-month period of pediatric exclusivity for its Norvasc®-branded drug products despite the fact that a three-judge panel of the U.S. Court of Appeals for the Federal Circuit now has determined that every asserted claim of the '303 patent is invalid.

The answer to both inquiries is "No." With respect to the former, FDA has long held that the expiration of a patent subject to a first-filer's paragraph IV certification divests the first-filer of any entitlement to 180-day exclusivity. *See, e.g., Abbreviated New Drug Applications: Patent And Exclusivity Provisions*, 59 Fed. Reg. 50338, 50348 (Oct. 3, 1994) ("[A] patent is deemed relevant until the end of the term of the patent or applicable 180-day period, *whichever occurs first.*") (emphasis added). That interpretation is consistent with the plain language and policies of the statutory scheme, and every court that has addressed this issue has deemed FDA's interpretation a reasonable one. *See, e.g., Dr. Reddy's Labs. v. Thompson*, 302 F. Supp. 2d 340 (D.N.J. 2003); *see also Ranbaxy Labs. Ltd. v. Leavitt [Simvastatin]*, 469 F.3d 120, 126 n.\* (D.C. Cir. 2006) ("[T]he first generic applicant may no longer retain exclusivity when the patent has expired."). There is no basis for departing from that settled interpretation here, and the Agency should rule that Mylan is not entitled to continued marketing exclusivity following the March 25, 2007 expiration of the '303 patent.

With respect to the latter inquiry, the plain language of the statute requires the brand manufacturer to *prevail* in post-paragraph IV litigation in order to remain eligible for pediatric exclusivity. *See* 21 U.S.C. § 355a(c)(2)(B) (requiring "the court [to] determine[] that the patent is valid and would be infringed" in post-paragraph IV litigation in order for the brand manufacturer to maintain eligibility for pediatric exclusivity). FDA therefore has interpreted the statute to divest the brand manufacturer of any entitlement to pediatric exclusivity "where an ANDA applicant submits a paragraph IV certification, and prevails in the patent litigation." *Mylan Laboratories, Inc. v. Thompson [Fentanyl Patch]*, 332 F. Supp. 2d 106, 124 (D.D.C. 2004) (quoting FDA).

Crucially, that interpretation applies to any paragraph IV applicant—not just the applicant that first obtained a court determination of invalidity. That is so because long-settled principles of patent law hold that a determination of invalidity estops the brand manufacturer from pursuing infringement claims against any other defendant. *See Blonder-Tongue Labs., Inc. v. University of Ill. Found.*, 402 U.S. 313, 350 (1971). As a result, a brand manufacturer that loses its post-paragraph IV litigation against one applicant cannot possibly prevail in post-paragraph IV litigation against any other defendant—and therefore cannot satisfy the key requirement for obtaining pediatric exclusivity: that it prevail in post-paragraph IV patent litigation.

Those principles control the outcome in this case. Pfizer sued Apotex for infringement, and on March 22, 2007, the Federal Circuit issued its determination that Pfizer's patent claims were "invalid for obviousness." *Pfizer Inc. v. Apotex, Inc.*, No. 2006-1261, 2007 WL 851203, at \*20 (Fed. Cir. Mar. 22, 2007). That decision prevents Pfizer from asserting pediatric exclusivity as to *any* ANDA filer that maintained a paragraph IV certification at the time of expiration,

because Pfizer could not realistically hope to prevail in such litigation. It is of no moment that the Federal Circuit has not yet issued its mandate; nothing in the text of the pediatric exclusivity statute remotely requires the issuance of a mandate, and the policies underlying the Hatch-Waxman Act weigh heavily against adopting any such interpretation of the statute. Indeed, such an interpretation of the statute would permit brand manufacturers to indefinitely delay generic market entry despite the fact that there is no realistic chance of further appellate review. As a result, the Agency should rule that Pfizer is not entitled to pediatric exclusivity for sales of its Norvasc®-branded amlodipine drug products.

For these reasons, and as set forth in greater detail below, final approval of Teva's ANDA is neither barred by Mylan's 180-day exclusivity nor blocked by Pfizer's pediatric exclusivity. The Agency should therefore grant Teva's ANDA No. 76-846 immediate final approval.

## FACTUAL BACKGROUND

### A. Pfizer's Amlodipine Besylate Products

Pfizer Inc. ("Pfizer") manufactures amlodipine besylate ("amlodipine"), a high-blood pressure medication that it markets in 2.5, 5, and 10mg dosage tablets under the trade name Norvasc®. *Apotex*, 2007 WL 851203, \*1. Pfizer has listed two patents as claiming amlodipine in FDA's official register of patents claiming approved pharmaceutical products (the "Orange Book"): US Patent Nos. 4,572,909 ("the '909 patent") and 4,879,303 ("the '303 patent"). See Orange Book at 887-88, available at <http://www.fda.gov/cder/orange/obannual.pdf> (27th ed. 2007) (last visited April 1, 2007). Each of those patents has expired: the former on July 31, 2006, and the latter on March 25, 2007. See *id.*

### B. Mylan's ANDA

On May 22, 2002, Mylan filed the first ANDA seeking approval to sell generic amlodipine in 2.5, 5, and 10-mg dosage tablets. See *Pfizer Inc. v. Mylan Labs., Inc.*, No. 02-cv-1628, 2007 WL 654274, \*2-\*3 (W.D. Pa. Feb. 22, 2007). Mylan's ANDA contained paragraph IV certifications asserting that the '909 and '303 patents were invalid or would not be infringed by its proposed generic amlodipine drug products. *Id.* As a result, Mylan became eligible for a period of 180-day exclusivity for sales of its generic amlodipine products. 21 U.S.C. §§ 355(j)(5)(B)(iv).

Mylan notified Pfizer of its paragraph IV certifications on July 23, 2002, and on September 20, 2002, Pfizer sued Mylan for infringement of both patents pursuant to 35 U.S.C. § 271(e)(2)(A). *Pfizer Inc. v. Mylan Labs., Inc.*, 2007 WL 654274, \*3. That lawsuit did not trigger a 30-month stay of FDA's authority to grant Mylan final marketing approval because it was filed more than 45 days after Pfizer received Mylan's paragraph IV notice. On October 3, 2005, the Agency therefore granted Mylan final approval to begin marketing its generic amlodipine drug products. *Id.* Nonetheless, Mylan chose not to immediately launch its generic amlodipine products into the market.

On October 18, 2006, the *Mylan* district court dismissed Pfizer's infringement claims arising from the '909 patent as moot, noting that the '909 patent had expired on July 31, 2006 and thus could not ground a continuing case or controversy between the parties. *Id.* On

February 27, 2007, however, the court held that Mylan's amlodipine drug products infringed Pfizer's '303 patent and that the '303 patent was valid and enforceable. *Id.* at \*26-31, \*31-35. The district court therefore enjoined FDA from approving Mylan's ANDA until "a date which is not earlier than the date of expiration of the '303 patent (March 25, 2007)." *See Pfizer Inc. v. Mylan Labs., Inc.*, No. 02-cv-1628, Amended Judgment at 2 (Mar. 16, 2007) (Attachment 1). Mylan has since appealed the district court's decision to the U.S. Court of Appeals for the Federal Circuit, which temporarily stayed the district court's injunction on March 23, 2007 but has not yet issued a decision in Mylan's case. *See Pfizer Inc. v. Mylan Labs, Inc.*, No. 2007-1194, Order at 2 (Mar. 23, 2007) (Attachment 2).

### C. Apotex's ANDA

After Mylan had submitted its ANDA for generic amlodipine drug products, Apotex, Inc. ("Apotex," which then was known as Torpharm, Inc.) filed its own ANDA for generic amlodipine drug products. Like Mylan's ANDA, Apotex's ANDA contained a paragraph IV certification to the '303 patent. *See Complaint, Pfizer Inc. v. Torpharm, Inc.*, No. 03-5289 (N.D. Ill., filed Aug. 1, 2003), at 3 (Attachment 3). On June 23, 2003, Apotex notified Pfizer of its paragraph IV certification, and on July 30, 2003, Pfizer filed a patent infringement action against Apotex. *Id.* In contrast to the *Mylan* case, that lawsuit did trigger a 30-month stay of approval for Apotex's products because it was filed within 45 days of Pfizer's receipt of Apotex's paragraph IV notice.

Apotex eventually counterclaimed for a declaratory judgment of patent invalidity or unenforceability, but on January 18, 2006, the district court issued an oral decision holding that Apotex infringed Pfizer's '303 patent and that the '303 patent was valid and enforceable. *See Apotex*, 2007 WL 851203, \*5-\*7. The district court then entered an order enjoining the Agency from approving Apotex's ANDA until patent expiration and any period of pediatric exclusivity to which Pfizer might be entitled. *Id.* Apotex appealed the district court's decision to the Federal Circuit, and on March 22, 2007, the Federal Circuit reversed the district court's decision, holding in a published decision that the asserted claims of the '303 patent were "invalid for obviousness." *See id.*

### D. Teva's ANDA

On September 9, 2003, Teva filed its own ANDA for sales of generic amlodipine products. As filed, that ANDA contained paragraph III certifications to the '909 and '303 patents. On March 23, 2007, Teva amended its ANDA. First, to reflect the fact that the '909 patent expired in July 2006, Teva revised its paragraph III certification with respect to that patent to a paragraph II certification. Second, in order to reflect its belief that the '303 was invalid or otherwise unenforceable, Teva revised its paragraph III certification with respect to that patent to a paragraph IV certification. Teva simultaneously notified Pfizer of its paragraph IV certification, but Pfizer did not file an infringement action against Teva prior to the expiration of the '303 patent. On March 28, 2007, based on FDA's longstanding rule compelling ANDA applicants to convert extant paragraph IV certifications to paragraph II certifications following patent expiration, Teva converted its paragraph IV certification on the '303 patent to a paragraph II certification. It then moved for immediate final approval of its ANDA.

### **E. Post *Pfizer v. Apotex* Proceedings**

On March 22, 2007, Pfizer filed a Citizen Petition seeking to enforce pediatric exclusivity rights against Novartis's Lotrel®, a combination product containing amlodipine. See CP No. 07-p-0110.

On March 23, 2007, following the Federal Circuit's decision in *Pfizer v. Apotex*, Mylan simultaneously moved the district court in its litigation and the Federal Circuit to vacate the district court's prior injunction precluding Mylan from marketing its generic amlodipine drug products until the expiration of the '303 patent. The district court refused to do so, see *Pfizer Inc. v. Mylan, Inc.*, No. 02-CV-1628, Order at 1 (Mar. 23, 2007) (Attachment 4), but Judge Prost, presiding over a motions panel of the Federal Circuit, entered an order "temporarily stay[ing]" the district court's order pending further briefing by the parties. See *Pfizer Inc. v. Mylan, Inc.*, No. 2007-1194 (Fed. Cir. Mar. 23, 2007) (single-judge order) (Attachment 5). With the injunction lifted, Mylan launched its generic amlodipine drug products into the market on the afternoon of March 23, 2007. See Mylan Press Release, Mar. 23, 2007 (Attachment 6).

At almost the same time, Mylan filed an emergency application to the United States District Court for the District of Columbia for a Temporary Restraining Order ("TRO") that would preclude FDA from approving any other generic ANDAs for amlodipine. See *Mylan Pharmaceuticals, Inc. v. Thompson*, No. 07-579 (D.D.C. filed Mar. 26, 2007). On March 26, 2007, the district court (Urbina, J.) partially granted Mylan's TRO application. See *id.*, Order at 1-2 (filed Mar. 26, 2007) (Attachment 7). In particular, based on FDA's representation to the Court that it would solicit comments from all affected parties and issue a decision with respect to Mylan's exclusivity on April 11, 2007, the Court declined to enjoin FDA from approving subsequent ANDAs prior to April 11, but entered a temporary injunction that would preclude the Agency from making those approvals effective between April 11 and April 13, so that TRO proceedings could unfold. See *id.*

On March 26, 2007, Mylan filed a Citizen Petition seeking to preclude FDA from approving any other generic amlodipine products pending the expiration of a 180-day first-filer exclusivity period.

On March 29, 2007, Teva intervened to protect its interests in the *Mylan v. Thompson* TRO action. See *id.*, Order Granting Teva's Motion to Intervene (filed Mar. 29, 2007) (Attachment 8). Later that afternoon, Teva received FDA's request to respond to the questions addressed in this letter.

## **ARGUMENT**

### **I. MYLAN IS NOT ENTITLED TO 180-DAY EXCLUSIVITY.**

For more than a decade, FDA has squarely held that the expiration of a patent subject to a first filer's paragraph IV certification divests the first filer of any entitlement to 180-day exclusivity. That interpretation is consistent with the plain language of the statute; longstanding FDA regulations on 180-day exclusivity; the existing case law on 180-day exclusivity; and the policies underlying the statute. Mylan has not identified any basis for departing from FDA's settled practice, and there is none. As a result, Mylan is not entitled to continued marketing exclusivity for generic amlodipine drug products, and the Agency may not lawfully rely upon

Mylan's first-filer status to withhold the approval of any pending ANDA that otherwise is eligible for final approval.

**A. The Plain Language Of The Statute And Longstanding FDA Regulations Compel The Conclusion That Patent Expiration Divests The First Filer Of Any Remaining 180-Day Exclusivity.**

On its face, the plain language of the Hatch-Waxman Act distinguishes between cases where a patent has expired and cases where the patent has not. In the former circumstance, the statute permits the Agency to grant an applicant final approval "effective immediately." 21 U.S.C. § 355(j)(5)(B)(i). In the latter circumstance, by contrast, the statute precludes the Agency from granting final approval for "one hundred and eighty days after" either (1) the first paragraph IV applicant commercially markets its product or (2) the date of a court decision holding the patent invalid or not infringed. *Id.* § 355(j)(5)(B)(iv).

The statute implements this sharp dichotomy between expired and unexpired patents by tying the effective date of an applicant's final approval to the type of patent certification contained in the applicant's ANDA. To that end, the statute provides that the approval of an ANDA "shall be made effective" on the latest of four possible dates, and each of those dates depends on the applicant's patent certification at the time it seeks final approval from the Agency. 21 U.S.C. § 355(j)(5)(B).

- First, where an applicant has submitted a paragraph I or paragraph II certification, the statute provides that "the approval [of the applicant's ANDA] may be made effective immediately." 21 U.S.C. § 355(j)(5)(B)(i).
- Second, where an applicant has submitted a paragraph III certification, "the approval [of the applicant's ANDA] may be made effective on the [certified] date [of patent expiration]." *Id.* § 355(j)(5)(B)(ii).
- Third, where an applicant has submitted a paragraph IV certification and was sued by the brand manufacturer within 45 days, "the approval [of the applicant's ANDA] shall be made effective upon the expiration of the thirty-month [stay]" or, depending on the outcome of such litigation, upon the date of a court decision holding the patent invalid or not infringed, or the date a patent injunction is lifted following a court decision that the patent is valid and would be infringed. *Id.* § 355(j)(5)(B)(iii).
- Finally, where an applicant has submitted a paragraph IV certification and filed its ANDA subsequent to another manufacturer's ANDA containing a paragraph IV certification, "the application shall be made effective not earlier than one hundred and eighty days after" either the prior applicant's first commercial marketing or a court decision holding the patent invalid, not infringed, or otherwise unenforceable. *Id.* § 355(j)(5)(B)(iv).

Thus, where a blocking patent expires and the applicant submits a paragraph II certification, the first-filer's exclusivity no longer bars final approval of the applicant's ANDA. Instead, under the plain terms of the statute, "the approval may be made effective immediately." *Id.* § 355(j)(5)(B)(i).

To effectuate that aspect of the statutory scheme, FDA regulations have long required applicants to amend their earlier patent certifications upon patent expiration (or otherwise permit the Agency to deem all extant certifications to be paragraph II certifications). *See, e.g.*, 21 C.F.R. § 314.94(a)(12)(viii)(C)(1) (2002) (“[A]n applicant shall amend a submitted certification if, at any time before the effective date of the approval of the application, the applicant learns that the submitted certification is no longer accurate.”); *id.* § 314.94(a)(12)(viii) (2002) (addressing certification amendments for cases where “the patent expires before [a post-paragraph IV] lawsuit is resolved or expires after the suit is resolved but before the end of the 180-day exclusivity period.”); *see also Abbreviated New Drug Applications: Patent And Exclusivity Provisions*, 59 Fed. Reg. 50,338, 50,348 (Oct. 3, 1994) (“[A] patent is deemed to be relevant ... 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.**”) (emphasis added).

That is precisely what happened in this case. Prior to the ‘303 patent’s expiration, Teva filed a paragraph IV certification to that patent. Following the patent’s expiration, and pursuant to the mandate of § 314.94(a)(12)(viii)(C)(1), Teva amended its ANDA to include a paragraph II certification to the ‘303 patent. As a result, Teva’s ANDA no longer contains a paragraph IV certification, and the plain language of the statute divests Mylan of any exclusivity it previously held against Teva, by requiring the Agency to grant Teva’s otherwise eligible ANDA final approval “effective immediately.” 21 U.S.C. § 355(j)(5)(B)(i).

Mylan’s Citizen Petition neither addresses 21 U.S.C. § 355(j)(5)(B)(i) nor challenges FDA’s longstanding regulations with respect to amended patent certifications. Indeed, the petition specifically represents that “Mylan does not request that the FDA reverse any position that it has publicly announced with respect to the effect of the 180-day exclusivity after patent expiration.” *See* Mylan Petition at 3. That should be the beginning and end of this matter. FDA’s longstanding regulations compel the conversion of paragraph IV certifications to paragraph II certifications upon patent expiration, and FDA has “publicly announced” on multiple occasions that the expiration of a patent divests the first-filer of its exclusivity—even after the first-filer’s 180-day period has commenced.

Nonetheless, Mylan insists that it remains entitled to exclusivity under 21 U.S.C. 355(j)(5)(B)(iv), because “Mylan’s Paragraph IV certification did not change when the patent expired [and] fully complies with the language of § 355(j)(5)(B)(iv), as it ‘is for a drug for which a previous application has been submitted under this subsection [containing] a [subclause IV] certification.’” *Id.* (underscore and alterations in original). But that argument is not only wrong on the facts—it completely misses the point of the statute.

It is wrong on the facts, because Mylan’s application is **not** an application ““for a drug **for which a previous application has been submitted** ... containing a subclause IV certification.”” *Id.* (alterations omitted; emphasis added). Instead, Mylan’s application—which contained the first paragraph IV certification filed by any generic applicant—**is** the “previous application containing a paragraph IV certification” to which the statute refers. And Mylan’s argument misses the point of the statute, because 21 U.S.C. § 355(j)(5)(B)(iv) does not hinge only on the previous applicant’s paragraph IV certification, but on the subsequent applicant’s certification.

By its plain terms, 21 U.S.C. § 355(j)(5)(B)(iv) applies *only* where the subsequent applicant—here, Teva (and not Mylan)—has a paragraph IV certification at the time it moves for final approval. See 21 U.S.C. § 355(j)(5)(B)(iv) (“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...”). It therefore is irrelevant that “Mylan’s Paragraph IV certification did not change when the patent expired.” Mylan Petition at 3. Teva’s certification did change at that time, and by its plain terms, 21 U.S.C. § 355(j)(5)(B)(iv) no longer bars the Agency from granting immediate final approval to Teva’s ANDA. Instead, now that Teva has a paragraph II certification on file, 21 U.S.C. § 355(j)(5)(B)(i) is the appropriate provision to apply, and that provision mandates that the Agency approve Teva’s ANDA “effective immediately.” 21 U.S.C. § 355(j)(5)(B)(i).

**B. Existing Case Law Supports Holding That Patent Expiration Divests A First-Filer Of 180-Day Exclusivity.**

Every court that has addressed the impact of patent expiration on a first-filer’s 180-day exclusivity supports the view that patent expiration divests the first filer of its exclusivity period, even after that period has commenced. See, e.g., *Ranbaxy Labs. Ltd. v. Leavitt [Simvastatin]*, 469 F.3d 120, 126 n.\* (D.C. Cir. 2006); *Dr. Reddy’s Labs., Inc. v. Thompson*, 302 F. Supp. 2d 340, 354-55 (D.N.J. 2003). For instance, in *Dr. Reddy’s*, the court specifically upheld FDA’s determination that the expiration of a patent divests the first-filer of its eligibility for exclusivity as a reasonable interpretation of the statute. 302 F. Supp. 2d at 354-55.

To be sure, *Dr. Reddy’s* involved a case where the underlying patent expired before the Agency granted final approval to the first filer, rather than after it did so. But the court’s rationale applies equally on the facts of this case. As *Dr. Reddy’s* explains, a rule maintaining exclusivity after patent expiration would lead to perverse results, because it would allow an applicant to file the first paragraph IV certification immediately prior to patent expiration and then delay the onset of full market competition even after the only patent barrier to full generic competition has fallen. *Dr. Reddy’s*, 302 F. Supp. 2d at 354. As the court noted, that would be inconsistent with the purpose of the statutory scheme, which is intended to encourage patent challenges in order to remove “listed patents that prevent final ANDA approval,” *id.*, and thereby facilitate early generic market entry. Once there are no remaining listed patents that prevent final ANDA approval, however, there is no reason to erect another barrier to full generic market entry; all subsequent applicants should be permitted to enter the market without regard to their status as subsequent filers. *Id.* (“Once a listed patent expires, there is no longer a need to provide an incentive to challenge it in court. Consistent with this statutory purpose, the FDA construes the statute to award 180-day exclusivity based only upon paragraph IV certifications to unexpired patents.”) (citing 59 Fed. Reg. 50338, 50348)). Moreover, *Dr. Reddy’s* squarely upheld FDA’s determination that all applicants (and not just first filers) must convert to paragraph II certifications following patent expiration. *Id.* at 354-55; see also *id.* at 355-56 (upholding FDA’s interpretation of 21 C.F.R. § 314.94(a)(12)(viii)). That, of course, is precisely what Teva did, and Mylan neither challenges Teva’s conversion to a paragraph II certification nor addresses its consequences.

More recently, the D.C. Circuit built on *Dr. Reddy’s* holding by explaining that “the text and structure of the statute suggest ... that the first generic applicant may no longer *retain* exclusivity when the patent has expired.” *Ranbaxy*, 469 F.3d at 126 n.\* (emphasis added). That

is so, the court suggested, because of 21 U.S.C. § 355(j)(5)(B)(i), which provides that an application containing a paragraph II certification may be approved “effective immediately.” *Id.* As the D.C. Circuit thus has recognized, the statute plainly suggests that there is no basis for continuing first-filer exclusivity after patent expiration, because the statute unambiguously permits subsequent ANDAs to be approved as soon as they contain post-expiration paragraph II certifications. *See supra* at 6-7.

**C. Divesting The First Filer Of Exclusivity Upon Patent Expiration Is Consistent With FDA’s Interpretation Of The Court-Decision Trigger.**

Finally, interpreting the statute to divest a first filer of its remaining 180-day exclusivity is consistent with FDA’s longstanding interpretation of the pre-MMA court-decision trigger. By now, it is well-settled that the first filer effectively may be deprived of its exclusivity where a subsequent applicant prevails in its own paragraph IV litigation, and thereby triggers the first-filer’s 180-day exclusivity period, before the first filer can market its product. *See, e.g., Minnesota Mining & Mfg. Co. v. Barr Labs.*, 289 F.3d 775, 780 (Fed. Cir. 2002) (“The District of Columbia Circuit has explicitly held that § 355(j)(5)(B)(iv)(II) [can be] triggered by the termination of an action commenced by the second ANDA filer, and we agree.”) (citing *Teva Pharms. USA, Inc. v. FDA*, 182 F.3d 1003, 1010 (D.C. Cir. 1999)). Thus, if a subsequent applicant obtains a court decision of invalidity, non-infringement, or unenforceability through its own post-paragraph IV litigation with the patentee, the first filer’s exclusivity will begin to run—whether or not the first filer is eligible to market its product at that time.

As a result, the first filer’s 180-day exclusivity period may run out entirely before the first filer can market its product for a single day. *See, e.g., SmithKline Beecham Corp. v. Geneva Pharms., Inc.*, 210 F.R.D. 547, 553 (E.D. Pa. 2002). In such cases, all applicants—regardless of their patent certification—are entitled to market their drug products on the 181st day after the triggering court decision, and that is so whether or not the first applicant has enjoyed a moment of its exclusivity period. It goes without saying that if the first filer’s exclusivity period can **begin and end** before the first filer can ever use it, that period cannot be extended past the 180th day simply because the manufacturer began its commercial marketing at some point **during** the period. In other words, it is well-settled that the mere triggering of a 180-day exclusivity period does not necessarily entitle the first filer to its full 180 days of exclusive marketing.

The same is true of patent expiration: the mere fact that Mylan finally triggered its 180-day exclusivity period two days before patent expiration does not entitle Mylan to the full measure of its exclusivity now that the final patent obstacle has expired. Instead, permitting Mylan to do so would be flatly inconsistent with the fundamental goal of the statutory scheme, which aims to “get generic drugs into the hands of patients at reasonable prices—fast.” *Andrx Pharms., Inc. v. Biovail Corp. Int’l*, 256 F.3d 799, 809 (D.C. Cir. 2001) (quoting *In re Barr Labs., Inc.*, 930 F.2d 72, 76 (D.C. Cir. 1991)). That policy assumes a paramount importance once the expiration of a listed patent opens the pathway to full generic market entry, and there is no basis for depriving consumers of broader competition and increased price relief now that the ‘303 patent has expired.

## II. PFIZER IS NOT ENTITLED TO PEDIATRIC EXCLUSIVITY.

Likewise, the plain language of the statute, longstanding Agency regulations, existing judicial precedent, and the policies underlying Hatch-Waxman divest Pfizer of any pediatric exclusivity associated with its Norvasc®-branded amlodipine products. That is so because the Agency consistently has held that the NDA holder must prevail in its post-paragraph IV patent litigation in order to qualify for pediatric exclusivity against generic applicants holding paragraph IV certifications at the time of patent expiration—and Pfizer has now lost its post-paragraph IV patent litigation. Pfizer identifies no compelling basis for departing from that interpretation of the pediatric exclusivity statute, and there is none. As a result, Pfizer is not entitled to pediatric exclusivity for its Norvasc®-branded drug products against generic applicants that held paragraph IV certifications at the time of patent expiration.

### A. **The Plain Language Of The Statute And Existing Judicial Precedent Compel The Conclusion That Pfizer's Patent Loss Divests Pfizer Of Its Entitlement To Pediatric Exclusivity Against Applicants That Held Paragraph IV Certifications At The Time Of Patent Expiration.**

As with 180-day first filer exclusivity, a brand manufacturer's eligibility for pediatric exclusivity depends in part on the kind of certification that a generic applicant submits with respect to the brand manufacturer's listed patents. Specifically, the statute provides that where a brand manufacturer submits studies demonstrating the effectiveness of its drug product in the pediatric population, it may be entitled to a six-month period of post-expiration marketing exclusivity in three certification-related circumstances:

- First, where the branded manufacturer's drug product claims "a listed patent for which a [paragraph II] certification has been submitted ... the period during which an application 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." 21 U.S.C. § 355a(c)(2)(A)(i).
- Second, where the branded manufacturer's drug product claims "a listed patent for which a [paragraph III] certification has been submitted ... the period during which an application 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." 21 U.S.C. § 355a(c)(2)(A)(ii).
- Finally, where the branded manufacturer's drug product claims "a listed patent for which a [paragraph IV] certification has been submitted..., and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application 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." 21 U.S.C. § 355a(c)(2)(B).

Read in isolation, each of these provisions seems to be clear. On one hand, if a generic applicant has submitted a paragraph II or paragraph III certification, the brand manufacturer appears to be entitled to a six-month period of pediatric exclusivity. On the other, if a generic applicant has submitted a paragraph IV certification, the brand manufacturer is not entitled for

pediatric exclusivity against that applicant unless “litigation result[s] from the certification” and “the court determines that the patent is valid and would be infringed” by the applicant.

Nonetheless, significant problems can arise at the intersection of these statutory provisions. In particular, both FDA and the courts have struggled to determine which provision to apply where an applicant submitted a paragraph IV certification prior to patent expiration. In a series of decisions, the Agency has attempted to solve this dilemma by holding that extant paragraph IV certifications are converted to paragraph II certifications at the time of patent expiration, and that the brand manufacturer is therefore entitled to pediatric exclusivity against those applicants under the statutory provision regarding pediatric exclusivity for paragraph II filers—21 U.S.C. § 355a(c)(2)(A). See *Mylan Labs., Inc. v. Thompson [Fentanyl Patch]*, 332 F. Supp. 2d 106 (D.D.C. 2004), *aff’d* 389 F.3d 1272 (D.C. Cir. 2004); *Ranbaxy Labs. Ltd. v. FDA [Fluconazole]*, 307 F. Supp. 2d 15 (D.D.C. 2004), *aff’d* 2004 WL 886333 (D.C. Cir. Apr. 26, 2004) (unpublished disposition); *Barr Labs., Inc. v. Thompson [Tamoxifen]*, 238 F. Supp. 2d 236 (D.D.C. 2002)).<sup>1</sup>

At the same time, however, the Agency has always made clear that there is an exception to that rule in cases where “an ANDA applicant submits a paragraph IV certification, and prevails in the patent litigation.” *Mylan Labs., Inc. v. Thompson [Fentanyl Patch]*, 332 F. Supp. 2d 106, 124 (D.D.C. 2004) (quoting Federal Defendants’ Memorandum In Opposition To Plaintiffs’ Motions For Preliminary Injunction And Summary Judgment And In Support Of Cross-Motion For Summary Judgment at 38 (July 8, 2004)).<sup>2</sup> In that circumstance, FDA has determined that it is appropriate to apply the statutory provision regarding pediatric exclusivity for paragraph IV filers. See *id.* (citing 21 U.S.C. § 355a(c)(2)(B)). That is so because in such cases, the court has *not* determined “that the patent is valid and would be infringed,” 21 U.S.C. § 355a(c)(2)(B), but rather that the blocking patent is invalid, not infringed, or otherwise unenforceable. As FDA thus recognizes, it makes no sense in those circumstances to block paragraph IV applicants behind the brand manufacturer’s pediatric exclusivity simply because the challenged patent has expired: there is no basis for rewarding a brand manufacturer with an extended monopoly simply because it successfully ran out the clock on a patent it never should have obtained (or which otherwise is unenforceable against generic applicants). To prevent that perverse result, the plain language of 21 U.S.C. § 355a(c)(2)(B) must apply where the blocking patent has been held invalid or unenforceable, regardless of the post-expiration conversion (whether *de facto* or *de jure*) of an applicant’s paragraph IV certification to a paragraph II certification.

<sup>1</sup> Notably, no such problem arises where the manufacturer has a paragraph III certification on file at the time of patent expiration, because the pediatric exclusivity statute subjects both paragraph II and paragraph III filers to pediatric exclusivity. In other words, whether the applicant’s paragraph III certification is converted *de facto* or *de jure* to a paragraph II certification, the applicant’s final approval is subject to the brand manufacturer’s pediatric exclusivity.

<sup>2</sup> Pfizer itself has conceded the legitimacy of that approach. In post-*Apotex* briefing, Pfizer specifically conceded that if “the Federal Circuit reverse[s] and find[s] that [the] patent was invalid or unenforceable, the [pediatric] exclusivity period would end immediately.” See Pfizer Inc.’s Opposition To Mylan’s Motion For A Stay Of The Court’s Amended Judgment, *Pfizer Inc. v. Mylan Labs., Inc.*, No 02-CV-1628 (E.D. Pa., filed Mar. 19, 2007), at 5 (Attachment 9).

Indeed, § 355a(c)(2)(B) must apply not only to the ANDA filer that was successful in obtaining a judgment of invalidity, but also to all other applicants holding a paragraph IV certification at the time of patent expiration. That is so because a decision of patent invalidity or unenforceability collaterally estops a patentee or brand manufacturer from asserting infringement claims based on that patent against additional defendants. *See, e.g., Blonder-Tongue Labs., Inc. v. University of Ill. Found.*, 402 U.S. 313, 350 (1971); *see also Mendenhall v. Barber-Greene Co.*, 26 F.3d 1573, 1577 (Fed. Cir. 1994) (“[O]nce the claims of a patent are held invalid in a suit involving one alleged infringer, an unrelated party who is sued for infringement of those claims may reap the benefit of the invalidity decision under the principles of collateral estoppel.”); *General Electro Music Corp. v. Samick Music Corp.*, 19 F.3d 1405, 1413 (Fed. Cir. 1994) (“The principle of *Blonder-Tongue* ... respecting collateral estoppel also applies to unenforceability.”).

As a result, once the Federal Circuit invalidates an asserted patent or declares the patent unenforceable in one paragraph IV applicant’s litigation, that judgment precludes the patentee or brand manufacturer from prevailing in patent litigation filed against any other paragraph IV applicant. It therefore would be absurd to interpret the statute to require each generic applicant that submitted a paragraph IV certification prior to patent expiration to await both the onset of patent litigation and its inevitable victory over the brand manufacturer in order to defeat pediatric exclusivity. In other words, while pediatric exclusivity is generally determined on an applicant-by-applicant basis, there is no ground for adopting that approach in cases where there has been a judicial determination that the patent is invalid or unenforceable, because that determination precludes the brand manufacturer from fulfilling the essential precondition to pediatric exclusivity—that it obtain a “court determin[ation] that the patent is valid and infringed,” 21 U.S.C. § 355a(c)(2)(B)—in any case involving any applicant that had a paragraph IV certification on file at the time of patent expiration.

That is precisely the case here. As Pfizer itself has recognized, the Federal Circuit did *not* determine that the ‘303 patent was “valid and infringed,” 21 U.S.C. § 355a(2)(B), but rather (to quote Pfizer) “issued [a] Decision, holding that ... the only claims Pfizer asserted in its Hatch-Waxman patent infringement action ... are invalid as obvious.” *See Response of Plaintiff-Appellee Pfizer Inc. Pursuant To The Court’s March 23, 2007 Order, Pfizer Inc. v. Mylan Labs., Inc.*, No 2007-1194 (Fed. Cir., filed Mar. 26, 2007), at 3 (capitalization in original) (Attachment 10). Under these circumstances, the appropriate provision of the statute to apply is 21 U.S.C. 355a(c)(2)(B), which by its plain terms and pursuant to longstanding patent law principles precludes Pfizer from triggering its pediatric exclusivity against any applicant that had submitted a paragraph IV certification at the time of patent expiration—including Teva.

Despite all of this, Pfizer argues that the *Fentanyl Patch*, *Fluconazole*, and *Tamoxifen* decisions control this case, because they demonstrate that “[t]he agency has .. repeatedly rejected attempts by generic applicants to manipulate the statutory regime in such a way as to deprive innovators who have invested the extensive time and resources required for pediatric studies of their exclusivity.” *See, e.g., Pfizer Petition For Stay Of Action*, No. 07P-0111, at 3; *Pfizer Citizen Petition*, No. 07P-0110, at 6 (same). But that simply is not so. While each of those decisions did hold that the expiration of a patent and corresponding conversion of an extant paragraph IV certification to a paragraph II certification entitles the brand manufacturer to a six-month period of pediatric exclusivity, none arose after the brand manufacturer lost its litigation.

Thus, in the *Fentanyl Patch* litigation, the brand manufacturer won its post-paragraph IV litigation in the district court, and the Federal Circuit had not issued any decision on the merits of the ensuing appeal at the time the Agency assessed the brand manufacturer's entitlement to pediatric exclusivity. See 389 F.3d at 1277; 332 F. Supp. 2d at 114. In the *Fluconazole* litigation, the parties stipulated to the dismissal of their case prior to trial in the district court. 307 F. Supp. 2d at 17. And in the *Tamoxifen* case, the generic applicant settled its patent litigation with the brand manufacturer, entered the market as an authorized generic, and withdrew its paragraph IV certification before the court issued any decision on the patent merits. 238 F. Supp. 2d at 242. As a result, each of these cases is perfectly consistent with FDA's longstanding position—which specifically has been relied upon by the courts, see *Fentanyl Patch*, 332 F. Supp. 2d at 124—that a brand manufacturer is not entitled to pediatric exclusivity against any applicant holding a paragraph IV application at the time of patent expiration where the brand manufacturer has lost a patent infringement case. Put simply, none of those cases involved a patent loss by the brand manufacturer—much less one based on patent invalidity.

**B. There Is No Basis For Delaying Generic Entry Until The Federal Circuit's Mandate Issues.**

As if to concede that its patent loss at the Federal Circuit prevents the assertion of pediatric exclusivity against any generic manufacturer that submitted a paragraph IV certification prior to the expiration of the '303 patent, Pfizer ultimately resorts to arguing that the Federal Circuit's decision is ineffective until the Federal Circuit issues its mandate to the district court. See Letter from Peter Safir to Sheldon Bradshaw ("Safir Letter"), Mar. 25, 2007, at 2-3 (Attachment 11). But that argument has no basis in the text of the pediatric exclusivity statute—which speaks only to the "court[s] determin[ation] that the patent is valid and infringed"—and it reflects a fundamental misunderstanding of appellate procedure.

That is so because an appellate court "determines" the merits of a case in its opinions and orders, and those opinions and orders constitute the court's "judgment" under Rule 36 of the Federal Rules of Appellate Procedure. That rule directs the clerk of the court to "prepare, sign, and enter the judgment ... after receiving the court's *opinion*," and requires the clerk "[o]n the date when judgment is entered [to] serve on all parties a copy of *the opinion* ... and a notice of the date when the judgment was entered." Fed. R. App. P. 36 (emphasis added). Here, the clerk entered the court's judgment in this case—"Disposition: Reversed"—on March 22, 2007, and the opinion on which that judgment was based reflected the court's square "determin[ation]" that Pfizer's patent was invalid as obvious. See Docket, *Pfizer Inc. v. Apotex, Inc.*, No. 2006-1261 (Attachment 12); see also Fed. R. App. P. 36 ("A judgment is entered when it is noted on the docket."). That, after all, is why Pfizer itself has referred to the Federal Circuit's opinion and judgment in the *Apotex* case as a "**Decision**" with a "**holding** that ... the only claims Pfizer asserted in its Hatch-Waxman patent infringement action ... are invalid as obvious." See Response of Plaintiff-Appellee Pfizer Inc. Pursuant To The Court's March 23, 2007 Order, *Pfizer Inc. v. Mylan Labs., Inc.*, No. 2007-1194 (Fed. Cir., filed Mar. 26, 2007), at 3 (capitalization in original; emphasis added). It simply defies credulity to think that the Federal Circuit's opinion and judgment were anything other than a "determin[ation]" of patent invalidity.

In sharp contrast to the court's opinion and judgment, the appellate court's mandate merely "consists of a certified *copy* of the judgment, a *copy* of the court's opinion, if any, and any direction about costs." Fed. R. App. P. 41(a). By definition, however, those "*copies*" do

not represent any independent legal “determination” of the patent merits. To the contrary, it is well understood that the scope of a mandate is circumscribed by the content of the court’s judgment, as reflected in its opinion on the merits. *See, e.g., Exxon Chem. Patents, Inc. v. Lubrizol Corp.*, 137 F.3d 1475, 1483-84 (Fed. Cir. 1998).

That, presumably, is why the pediatric exclusivity statute focuses on the merits of the court’s “determin[ation],” as opposed to the court’s eventual issuance of a mandate. In that respect, the pediatric exclusivity statute stands in marked contrast to the many federal statutes which do focus on the court’s issuance of a mandate (as opposed to the judgment embodied in its opinion and order). *See, e.g.,* 26 U.S.C. § 7481(a) (finality is determined “upon mandate” issued by Court of Appeals or Supreme Court); 15 U.S.C. § 21(g) (finality determined *inter alia* “upon the expiration of thirty days from the date of issuance of the mandate of the Supreme Court”); 15 U.S.C. § 45 (same). These statutes thus demonstrate that Congress knows how to time events from the issuance of an appellate “mandate” when it wants to—and it did not do so here.

Moreover, delaying generic market entry until the issuance of the mandate would be flatly inconsistent with the structure and purposes of the Hatch-Waxman Act. The whole point of the statutory scheme is to “get generic drugs into the hands of patients at reasonable prices—fast.” *Andrx Pharms.*, 256 F.3d at 809 (quoting *Barr Labs.*, 930 F.2d at 76). Once it is reasonably clear that a patent is invalid or otherwise unenforceable, as it is when the Federal Circuit issues a published opinion invalidating the asserted claims of a patent, there is simply no sound basis for delaying the onset of market competition—not least of all because the prospect of further appellate proceedings resulting in a reversal of the court’s opinion and judgment is virtually nonexistent. *See* Judicial Business of the United States Courts: 2006 at 50 Table S.1 (Attachment 13) (showing that of 34,580 dispositions in the various courts of appeals, just 65—less than 1 in 500—were issued by *en banc* courts); *id.* at 101 Table A-1 (Attachment 14) (showing that of approximately 9600 petitions for *certiorari*, fewer than 90—less than 1 in 100—were granted by the Supreme Court).<sup>3</sup>

Those slim prospects for further appellate review thus stand in marked contrast to the high likelihood that a losing brand manufacturer can run out the clock on its pediatric exclusivity before the mandate issues. As Pfizer is quick to note, losing litigants have 14 days to file a petition for rehearing *en banc*, and the filing of such a petition indefinitely stays the mandate pending the court’s disposition of such a motion. Even after a petition is denied, the mandate is generally delayed another 7 days—and during that period the losing litigant can move to stay issuance of the mandate pending further review by the Supreme Court. *See* Safir Letter at 2. Suffice it to say, that process can take months, because litigants have 90 days to file a petition for *certiorari* (and can seek an extension of up to 60 days), and respondents have 30 days to respond to such a petition. *See* Sup. Ct. RR. 13.1, 13.5, 15.3, 30.4. As a result, it should come as no

<sup>3</sup> Though the judicial conference does not track *en banc* review by the Federal Circuit, there is good reason to believe that the prospects of such review in that court are far lower than the national average. In contrast to virtually every other appellate court in the country, the Federal Circuit pre-circulates its opinions to every active member of the court prior to issuing them, and in connection with that process has established a formal mechanism for the court’s judges to request revisions and even formal *en banc* review of an opinion prior to its issuance. *See, e.g.,* Federal Circuit Internal Operating Procedure 14. As a result, *en banc* review is especially rare in that court because all active judges of the court have an opportunity to review, comment on, and effectuate changes to opinions before they are finalized—significantly minimizing the possibility that a three-judge panel will issue a decision with which a court majority disagrees.

surprise that Pfizer has informed the Agency that it intends to file a petition for rehearing *en banc* at the Federal Circuit (and has foreshadowed subsequent efforts to delay the mandate even longer by seeking a stay pending Supreme Court review). *See* Safir Letter at 2-3 & n.1. At bottom, then, forestalling market competition until the mandate issues will all but guarantee that manufacturers can block market competition for the duration of a pediatric exclusivity period, despite the fact that there is no reasonable possibility that the Federal Circuit's decision of patent invalidity will be reviewed—much less reversed.

Pfizer's only response to these arguments is that the Agency has issued a preliminary, procedural Guidance that in certain cases allegedly precludes the agency from "approving the pending ANDA until 'the date the district court issues a judgment that the patent is invalid, unenforceable, or not infringed pursuant to a mandate issued by a court of appeals.'" FDA Guidance, *Court Decisions, ANDA Approvals, and 180-Day Exclusivity Under The Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act*, ¶ IV.A (Mar. 2000). But contrary to Pfizer's representations, that Guidance has nothing to do with the pediatric exclusivity provisions at issue in this case. Instead, it addresses how to determine the date of a triggering court decision for purposes of establishing when the first generic applicant's 180-day exclusivity begins to run, and by its own terms, is expressly restricted to a narrow set of circumstances not remotely present here. *See id.* at 4 (stating that the Guidance is intended to interpret the first-filer exclusivity provisions of the Act, and will apply only "for approval and exclusivity determinations for ANDAs containing a paragraph IV certification where the ANDA cites a reference listed drug *for which no other ANDA containing a paragraph IV certification has been submitted.*") (emphasis added).<sup>4</sup>

## CONCLUSION

Consistent with the analysis set forth above, Teva therefore responds to the questions presented in your March 29, 2007 facsimile as follows:

- (1) The Federal Circuit's *Apotex* decision should be given effect as of the date of the court's judgment, and FDA need not await the issuance of the Federal Circuit's mandate. Entry of the Federal Circuit's judgment divested Pfizer of its eligibility for pediatric exclusivity against any manufacturer that had submitted a paragraph IV certification prior to the expiration of the '303 patent, and the subsequent

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<sup>4</sup> Even if that Guidance were relevant, however, it provides no support for Pfizer's position in this case. The court-decision provisions of 21 U.S.C. § 355(j)(5)(B) are *timing* provisions, and the Agency has interpreted the statute to delay the court-decision trigger pending issuance of the mandate where a district court decision of patent validity is reversed on appeal. That interpretation has the salutary effect of helping prevent subsequent applicants from prematurely triggering a first filer's exclusivity—and that is especially important where the first applicant's approval is subject either to a 30-month stay or to a patent injunction based on a determination of patent validity in the first-filer's litigation. In that respect, the Agency's interpretation of the court-decision trigger benefits generic applicants by maintaining the core incentive structure of the Hatch-Waxman Act.

By contrast, the "court determin[ation]" requirement of 21 U.S.C. § 355a(c)(2)(B) is an *eligibility* provision, and thus focuses on the substance of the court's determination—not its timing. After all, the commencement of pediatric exclusivity is already fixed as the date of patent expiration, and the issuance of a mandate thus has no impact on the timing of pediatric exclusivity or the core incentive structure of the Hatch-Waxman Act. Indeed, requiring generic applicants to await the issuance of the mandate would undermine the statute's incentive structure by minimizing the incentive to challenge pharmaceutical patents.

expiration of that patent both divested Mylan of its 180-day exclusivity and entitled all applicants holding paragraph IV certifications at the time of patent expiration to immediate final approval.

- (2) If FDA must await the issuance of the mandate, all unapproved ANDAs are subject to Pfizer's pediatric exclusivity pending issuance of that mandate.
- (3) Now that the '303 patent has expired, longstanding FDA regulations either require all unapproved ANDA applicants to convert to paragraph II certifications or permit the Agency to deem all extant certifications to be paragraph II certifications.
- (4) As a result of the *Apotex* decision and following the expiration of the '303 patent, pediatric exclusivity attaches only to those applicants that held paragraph III certifications at the time of patent expiration. Applicants that held paragraph IV certifications at that time are eligible for immediate final approval, whether or not the Agency subsequently deemed the applicant's certification to be a paragraph II certification or the applicant subsequently filed a paragraph II certification.
- (5) 180-day exclusivity triggered before patent expiration no longer bars the approval of otherwise eligible ANDAs following patent expiration.

For the foregoing reasons, final approval of Teva's ANDA is neither barred by Mylan's 180-day exclusivity nor blocked by Pfizer's pediatric exclusivity. The Agency should therefore grant Teva's ANDA No. 76-846 immediate final approval.

Sincerely,  
Teva Pharmaceuticals USA, Inc.



Deborah A. Jaskot  
Vice-President, Regulatory Affairs