UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

MYLAN LABORATORIES, INC., *et al*.,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	Civil Action No. 07-0579 (RMU)
	)	
MICHAEL O. LEAVITT, Secretary, Health and Human Services, *et. al*.,	)	
	)	
Defendants,	)	
	)	
and	)	
	)	
TEVA PHARMACEUTICALS USA, INC.,	)	
	)	
APOTEX INC., and	)	
	)	
MUTUAL PHARMACEUTICAL CO., INC.,	)	
	)	
Intervenors.	)	
	)	

GOVERNMENT DEFENDANTS' OPPOSITION TO MYLAN'S APPLICATION FOR TEMPORARY RESTRAINING ORDER FILED JUNE 26, 2007

INTRODUCTION

In plaintiffs' (hereinafter "Mylan") motion for a temporary restraining order filed yesterday, Mylan's principal argument is based on an issue it raised in its first request for emergency relief, which it filed in this Court in April 2007. That issue was rejected by this Court, Mylan Labs., Inc. v. Leavitt, 484 F. Supp. 2d 109 (D.D.C. 2007), and is now on appeal. Under the law of this Circuit, this Court has no jurisdiction to revisit that issue at this time. For this reason, Mylan's application should be denied. Even if the Court were to examine this issue, however, it has no merit and should be rejected.

What precipitated Mylan's latest attempt to restrict competition for amlodipine besylate tablets ("amlodipine") is Pfizer's request to remove the only remaining patent for this product, United States Patent No. 4,879,303 ("'303 patent"), from the "Approved Drug Products With Therapeutic Equivalence Evaluations" (the "Orange Book"). On June 22, 2007, FDA removed the patent from the Orange Book and sent a letter to the drug manufacturers who had submitted ANDAs for amlodipine (including Mylan), notifying them of this event and explaining why FDA took this action. (FDA's June 22, 2007, letter is attached to Mylan's motion as Exhibit A). FDA explained that Pfizer requested the removal of the patent because it no longer met the criteria for listing in the Orange Book, and FDA generally defers to the NDA holder's judgment about whether a patent should be listed. Although there are exceptions to that practice, FDA examined those exceptions and determined they did not apply. Thus, there was no barrier to delisting the patent. See Mylan Ex. A.

As the Court is aware, it was this patent to which Pfizer's six-month pediatric exclusivity for amlodipine attached and which precluded FDA approval of all generic products other than those of Mylan and Apotex. The removal of this patent now opens the way for FDA approval of other generics. In the prior round of litigation on this matter, Mylan relied principally on Pfizer's pediatric exclusivity to argue that other generics should not be approved. With the delisting of the patent, however, Pfizer has waived its claim to any remaining pediatric exclusivity. Recognizing this, Mylan has apparently abandoned its reliance on Pfizer's pediatric exclusivity to shield itself from competition. Mylan is now relying on an alleged 180 days of exclusivity to preclude FDA approval of other generics and the delisting of the '303 patent.

Although not in the context of delisting, Mylan presented its 180-day marketing exclusivity argument to this Court in its first request for emergency relief and the Court squarely

rejected it on the ground that the '303 patent had expired. Pfizer's request to delist the patent does not change this Court's prior analysis (and rejection) of Mylan's claim to 180 days of marketing exclusivity. Mylan did not have 180 days of exclusivity then because the patent was expired, and the delisting of the patent did not change that. This Court rejected Mylan's argument because the patent had expired, not because it was or was not "listed." Thus, Pfizer's delisting of the patent did not change the analysis of the 180-day issue (although delisting serves to moot the pediatric exclusivity issue). Hence, whether or not the '303 patent were delisted, Mylan would not have 180 days of exclusivity. Rather, Mylan is seeking to use FDA's decision to delist the patent to resurrect the 180-day issue.

Because Mylan has already lost this issue in this Court and has appealed it, it cannot reargue the issue now and, in fact, this Court lacks jurisdiction to hear it. Even in the absence of the jurisdictional defect, however, Mylan has no claim to exclusivity because the patent has expired. Pfizer's delisting of the patent does not change this result; in fact, FDA's decision to remove the patent from the Orange Book involved a clearly appropriate application of established law. For all of these reasons, Mylan has little likelihood of success on the merits.

Mylan cannot establish the other requirements for emergency relief. Now that Mylan shares the generic amlodipine market with a Pfizer affiliate as well as Apotex, its claims of irreparable harm from the addition of each new competitor can only be diminishing. Further, any harm to Mylan is offset by the benefit to these other manufacturers. Finally, additional competition brought on by more manufacturers will benefit the public, and the public will benefit from the faithful and proper application of the law.

BACKGROUND

Because this Court has already issued two decisions on the merits in this case over the last few months, the government will not describe at length the legal and factual background to this case. To briefly summarize the issues relevant to the instant motion, Mylan has claimed in this litigation that FDA approvals of its competitors' ANDAs are blocked by Pfizer's "pediatric exclusivity," an award of six months of exclusivity beyond the expiration date of a patent for new drug manufacturers who complete pediatric studies pursuant to a request from FDA, and by Mylan's "180-day marketing exclusivity," an incentive for the first applicant for the generic version of a new drug to challenge the innovator's patent for that drug. Pfizer's decision to delist the patent is in essence a waiver of any remaining claim to pediatric exclusivity that it still had because a listed patent is a "threshold requirement for pediatric exclusivity." Mylan Ex. A at 2. Accordingly, with the delisting of the patent, all other ANDA applicants may seek final approval from FDA now, rather than waiting for the expiration of pediatric exclusivity on September 25, 2007. See id.

I. Pediatric Exclusivity

By the terms of the relevant statutory provisions, pediatric exclusivity applies only to the extent there is a patent listed in the Orange Book to which unapproved ANDAs have submitted patent certifications. 21 U.S.C. § 355a(c). Patents are required to be listed in FDA's Orange Book if they claim the approved drug substance, approved drug product, or an approved method of use. 21 U.S.C. § 355(b)(1); 21 C.F.R. § 314.53. If certain claims of a patent are declared invalid, but one or more of the remaining patent claims claims the approved drug substance,

approved drug product, or approved method of use, the patent can remain properly listed until the expiration of pediatric exclusivity.

The Federal Circuit determined that three claims in the '303 patent that Pfizer asserted that Apotex infringed were invalid as obvious, Pfizer Inc. v. Apotex, Inc., No. 2006-1261, 2007 U.S. App. LEXIS 6623 (Fed. Cir. March 22, 2007), mandate issued, (Fed. Cir. May 21, 2007). However, that litigation did not resolve whether the '303 patent had continued vitality with respect to other ANDAs. The '303 patent could remain in the Orange Book if the remaining claims continued to satisfy the requirements for listing. Although some ANDA applicants asserted that the claims did not meet those requirements, FDA concluded that it lacked the information and expertise to resolve that issue, and therefore could not declare that the other ANDAs were no longer barred by pediatric exclusivity or that the patent should be delisted. See FDA Letter Decision of April 18, 2007, at 10 (submitted to the Court on April 18, 2007) (hereinafter "FDA Decision"). However, FDA did not foreclose the possibility that other information may come to light that would allow FDA to conclude that the patent is invalid: FDA stated that "*in the absence of further judicial or other action clarifying the status of the patent*, FDA will assume the '303 patent remains validly listed." Id. at 10 (emphasis added).

Now Pfizer has resolved that question by delisting the patent. By letter dated June 14, 2007, Pfizer informed FDA that the '303 patent no longer meets the requirements for listing. Mylan Ex. A at 1. FDA delisted the patent on June 22, 2007. Id. As FDA explained in its letter to the ANDA applicants, FDA's role in patent listing is ministerial, and FDA defers to the NDA holder's judgment regarding the listing of patents. Id. Pfizer has waived any remaining claim it

had to pediatric exclusivity, and ANDA applicants lack standing to challenge that waiver. Id. at 2 n.3. Mylan does not raise any arguments about pediatric exclusivity in its current motion.[1]

II. 180-Day Marketing Exclusivity

With respect to 180-day exclusivity, this Court correctly held as follows:

> The FDA ruled that Mylan's 180-day market exclusivity does not extend beyond patent expiration. FDA Decision at 10. Mylan challenges this ruling, arguing that once triggered, the 180-day market exclusivity period remains regardless of the status of the patent. Mylan's Mot. at 12.
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> The genesis of the 180-day exclusivity period is that the statute prevents the FDA from granting paragraph IV certification ANDAs for 180 days. 21 U.S.C. § 355(j)(5)(B)(iv). Mylan contends that "nothing in the text or legislative history of the Hatch-Waxman Act indicates that generic exclusivity is forfeited upon patent expiration." Mylan's Mot. at 12. This is not correct.
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> Under Hatch-Waxman, paragraph IV certifications are no longer valid upon patent expiration. 21 U.S.C. § 355(j)(2)(A)(vii)(II), (IV). Under applicable regulations, ANDA applicants must change their paragraph IV certifications to paragraph II certifications when the certification becomes invalid. 21 C.F.R. § 314.94(a)(12)(viii)(C). When a patent has expired, those applications with paragraph II certifications (including those converted from paragraph IV certifications) are eligible for immediate drug approval. 21 U.S.C. § 355(j)(5)(B)(I).
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> In this case, when Pfizer's Norvasc patent expired on March 25, 2007, all paragraph IV certifications converted to paragraph II certifications and became eligible for approval. Id. The statutory provision cited by Mylan which entitles it to market exclusivity, by its terms, applies only to paragraph IV certifications, which cease to exist upon patent expiration. 21 U.S.C. § 355 (j)(5)(B)(iv). Accordingly, the FDA's conclusion that Mylan's 180-exclusivity does not survive patent expiration constitutes a reasonable interpretation of the statute. And for this reason, Mylan fails to convince the court that it has a substantial likelihood of success on this claim.

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[1] Because the patent is delisted, Mylan's challenge regarding FDA's pediatric exclusivity determination is now moot. Although Mylan does not explicitly concede that point, Mylan states "[n]ow that the FDA has delisted the Pfizer patent, Mylan's claim to 180-day exclusivity has moved to the forefront." Mylan Br. at 2. Because the pediatric exclusivity issue is currently before the D.C. Circuit, this Court need not resolve the mootness issue.

Mylan Labs., Inc. v. Leavitt, 484 F. Supp. 2d at 122-23 (citations omitted). Mylan appealed the entirety of this Court's decision, and it also raised this issue in its motion for injunction pending appeal filed with the Court of Appeals.

Mylan is now attempting to bring the 180-day exclusivity issue back to the forefront. However, the patent's expiration should be the end of the matter. As FDA explained in its June 22 letter, an exception to delisting is set forth in 21 C.F.R. § 314.94(a)(12)(viii), which provides:

> A patent that is the subject of a lawsuit under § 314.107(c)[2] 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.

Thus, under section 314.94(a)(12)(viii), FDA can refuse to remove a patent from the Orange Book when an otherwise valid 180-day exclusivity claim would be prematurely extinguished by the delisting of the patent. However, under the terms of the regulation, the 180-day exclusivity claim ceases to be a barrier to delisting after "the patent has expired" or the exclusivity period no longer operates to delay the approval of other ANDAs. 21 C.F.R. § 314.94(a)(12)(viii). Here, because Mylan's exclusivity expired with the patent on March 25, 2007, FDA determined that there is no barrier to patent delisting under this regulation. FDA Letter at 2. Similarly, FDA considered whether the exception to delisting recognized by the D.C. Circuit in Ranbaxy Labs. v. Leavitt, 469 F.2d 120, 126 (D.C. Cir. 2006), applied, and determined that it did not apply to these

facts.

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[2] Section 314.107(c), 21 C.F.R., is the regulation that describes the operation of 180-day exclusivity.

ARGUMENT

I. THE COURT LACKS JURISDICTION TO REVIEW MYLAN'S CLAIM OF CONTINUED ENTITLEMENT TO 180-DAY MARKETING EXCLUSIVITY

Mylan admits that it is rearguing the 180-day exclusivity issue already decided by this Court, but claims that it is entitled to do so because the Court "got it wrong." Mylan Br. at 2. Mylan, however, is not making this argument in the context of a motion for reconsideration. In fact, it moved for reconsideration and failed to raise this issue. Following reconsideration, it appealed this Court's decision to the D.C. Circuit. The filing of an appeal, even an interlocutory appeal such as in the instant case, deprives the Court of jurisdiction over issues involved in the appeal. "The filing of a notice of appeal, including an interlocutory appeal, 'confers jurisdiction on the court of appeals and divests the district court of control over those aspects of the case involved in the appeal.' The district court does not regain jurisdiction over those issues until the court of appeals issues its mandate." United States v. DeFries, 129 F.3d 1293, 1302 (D.C. Cir. 1997), quoting in part Griggs v. Provident Consumer Discount Co., 459 U.S. 56, 58 (1982). See also Fundicao Tupy S.A. v. United States, 841 F.2d 1101, 1103-04 (Fed. Cir. 1988) (on appeal of a preliminary injunction, "[t]he filing of a timely and sufficient notice of appeal has the effect of immediately transferring jurisdiction from the district court to the court of appeals with respect to any matters involved in the appeal. It divests the district court of authority to proceed further with respect to such matters . . . .") (citation omitted); Decatur Liquors, Inc. v. District of Columbia, 384 F.Supp.2d 58, 60 n.1 (D.D.C. 2005) ("On January 7, 2005, Defendants filed a motion to dissolve the preliminary injunction, which the Court denied because Defendants had appealed and the Court was without jurisdiction. See Decatur Liquors v. District of Columbia, 2005 WL 607881, 2005 U.S. Dist. LEXIS 4246 (D.D.C. Mar. 16, 2005)." Here, Mylan's appeal

raises the very issue raised in its preliminary injunction motion – whether it has a probability of success in showing that FDA's rejection of its request for 180 days of marketing exclusivity is arbitrary and capricious – and this Court lacks jurisdiction over the instant motion.

In addition, the law-of-the-case doctrine should prevent this Court from revisiting an issue it has already decided. "[T]he same issue presented a second time in the same case in the same court should lead to the same result." LaShawn v. Barry, 87 F.3d 1389, 1393 (D.C. Cir. 1996) (emphasis in original). See also Kimberlin v. Quinlan, 199 F.3d 496, 500 (D.C. Cir. 1999); Feirson v. District of Columbia, 362 F. Supp. 2d 244, 247 (D.D.C. 2005). Mylan has not presented "extraordinary circumstances" that warrant reconsideration of this issue by the court. See LaShawn, 87 F.3d at 1393.

II. FDA PROPERLY DETERMINED, AND THIS COURT PROPERLY HELD, THAT 180-DAY MARKETING EXCLUSIVITY EXPIRES WITH THE PATENT

Even if the Court had jurisdiction to review its earlier determination and even if that holding were not the law of the case, the Court's finding that 180-day marketing exclusivity does not extend beyond patent exclusivity was clearly correct. As the Court recognized, the statutory mechanism for the application of 180-day exclusivity, by its terms, can only operate before the patent expires. Because an application containing the first paragraph IV certification blocks only other applications containing paragraph IV certifications, once the patent expires, and ANDAs no longer need to maintain their paragraph IV certifications, 180-day exclusivity is no longer a barrier to approval.

Mylan argues that the rule should apply differently on these facts because its exclusivity "vested" before the patent expired. Mylan Br. at 8. However, the statute does not mention "vesting," and Mylan cannot make a plain language argument in support of its "vesting" distinction. Instead, it argues that, under the plain language of the statute, there is no explicit

provision that mandates that exclusivity terminate with patent expiration. See Mylan Br. at 9-11. The Court has already rejected that argument; in its first motion emergency relief, Mylan argued "that once triggered, the 180-day market exclusivity period remains regardless of the status of the patent." See 484 F. Supp. 2d at 122.[3]

Mylan further asserts that policy arguments favor permitting it to maintain its exclusivity. Mylan Br. at 11-13. However, the enactment of the Hatch-Waxman amendments involved the balancing of conflicting policy interests. See Tri-Bio Labs, Inc. v. United States, 836 F.2d 135, 139 (3d Cir. 1987), cert. denied, 488 U.S. 818 (1988). There is nothing sacrosanct about 180-day exclusivity that deserves protection above all other interests. Moreover, policy arguments cannot trump the clear statutory provisions.

Mylan argues that FDA's interpretation produces "absurd results." Mylan Br. at 15-17. To reach this "absurd result," it misrepresents FDA's analysis in the context of its pediatric exclusivity decision. Mylan Br. at 15. Mylan asserts that "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. . . . FDA's interpretation would lead to the absurd result that filers that certified under paragraph IV, and thus took on the risk of litigation (such as Apotex), were blocked by Mylan's 180-day exclusivity, while the FDA would be free to approve those who merely certified under paragraph II and III and took no risk at all." Mylan Br. at 15-16. However, FDA did not conclude that Apotex maintained a paragraph IV certification. It found that all of the paragraph IV certifications, including Apotex's, converted to paragraph II

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[3] Mylan also attempts to distinguish the cases that have recognized that 180-day exclusivity expires with the patent on the ground that the cases did not involve a "vested" exclusivity. See Mylan Br. at 13-14. This is a distinction without a difference: Mylan fails to explain anything in those decision that would support a different finding for "vested" exclusivity.

certifications on patent expiration. FDA Letter at 9 ("When the '303 patent expired on March 25, 2007, all of the unapproved ANDAs were required to change (or deemed to have changed) to paragraph II certifications and became subject to Pfizer's pediatric exclusivity at that time. That is their status during the period before the mandate issues."); see also Government Appellees' Corrected Opposition to Mylan's Motion for Injunction Pending Appeal, No. 07-5156 at 14 (May 23, 2007) (After patent expiration, "Apotex's ANDA was deemed to have a paragraph II certification and was subject to Pfizer's pediatric exclusivity. If the mandate did not issue before the pediatric exclusivity expired, or if the Federal Circuit reconsidered and reversed the panel decision, pediatric exclusivity would have continued to bar the approval of Apotex's ANDA until the pediatric exclusivity period expired."). Mylan's "absurd results" argument should be rejected because it is based on an erroneous premise.

Accordingly, Mylan offers no compelling reason for the Court to question its previous holding on 180-day exclusivity.

III. FDA PROPERLY DELISTED THE '303 PATENT

Mylan has no basis to challenge the delisting of the patent. FDA's June 22, 2007, decision to remove the '303 patent from the Orange Book represents a clear application of the law. It is well established, and Mylan does not dispute, that FDA's role in listing patents is ministerial. See Apotex, Inc. v. Thompson, 347 F.3d 1335, 1348-49 (Fed. Cir. 2003); aaiPharma, Inc. v. Thompson, 296 F.3d 227, 243 (4th Cir. 2002), cert. denied, 538 U.S. 923 (2003); Alphapharm Pty Ltd. v. Thompson, 330 F. Supp. 2d 1, 7-8 (D.D.C. 2004). FDA generally defers to the NDA holder's assessment of whether a patent should be delisted, particularly when, as here, the NDA holder requests that the patent be removed from the Orange Book because it no

longer meets the requirements for listing. Thus, the only question for the Court is whether there is an exception to delisting that requires that the patent stay in the Orange Book.

The answer is no. FDA has established through regulation an exception to delisting when an ANDA applicant has filed a paragraph IV certification to that patent and is engaged in litigation related to that certification. However, the exception set forth in 21 C.F.R. § 314.94(a)(12)(viii) by its very terms does not apply when "the patent has expired." Mylan Ex. A at 2. Mylan relies heavily on Ranbaxy Labs. v. Leavitt, 469 F.2d 120, 126 (D.C. Cir. 2006), to argue that FDA may not delist patents when a paragraph IV certification has been filed. Ranbaxy, however, did not involve an expired patent and, in fact, the Court noted that the result would in all likelihood be different if the patent had expired. Id. at 126 n.*. In addition, the court cited and did not question the holding in Dr. Reddy Labs. v. Thompson, 302 F. Supp. 2d 340, 354-55 (D.N.J. 2003), that 180-day exclusivity does not extend beyond patent expiration. See 469 F.2d at 124-25. Further, because Pfizer sued Mylan on its paragraph IV certification, Ranbaxy Labs. is factually inapposite.

To argue on these facts that the patent should not be removed from the Orange Book, Mylan resorts to urging the Court to apply 21 C.F.R. § 314.94(a)(12)(viii) in part and strike it down in part. That is, Mylan seeks to have the Court require that FDA apply an exception to delisting to preserve Mylan's 180-day exclusivity claim, but, at the same time, strike down the language of the regulation that provides that the exception does not apply to expired patents. Mylan Br. at 8 ("The portion of the FDA's regulations . . . is arbitrary, capricious and contrary to law."); see also Mylan Br. at 18-20. And, to achieve this result, Mylan asks the Court to reverse its own holding that Mylan's entitlement to 180-day exclusivity terminated when the patent expired. The Court should not do so for two reasons. First, as discussed above, reconsideration

of this Court's earlier decision is improper at this time. Second, this Court's holding on 180-day exclusivity was clearly correct, and Mylan has not offered any compelling reason to question it. Accordingly, once the patent was delisted, there can be no exclusivity on that patent and Mylan's application should be denied.

IV. IRREPARABLE INJURY, THE BALANCE OF HARMS, AND THE PUBLIC INTEREST

In its April 30 decision on Mylan's first motion for emergency relief, this Court rejected Mylan's claim that it would suffer irreparable injury absent a preliminary injunction. 484 F.Supp.2d at 123. Mylan makes no further showing in this second attempt at emergency relief that it will suffer a loss that "would threaten the continued existence of [its] business." Id. In fact, inasmuch as Mylan already has competition from generic products (Apotex and Pfizer's generic), its claim is even weaker than it was previously.

Additionally, this Court found that a "faithful and coherent interpretation of the FDCA and Hatch-Waxman outweighs the purely financial harm to these drug companies." Id. at 124. The Court also held: "The public interest does not favor a distortion of the principles of the Hatch-Waxman Act. . . . By ensuring that the FDA follows its mandate under Hatch-Waxman while at the same time ensuring that the FDA's management of ambiguities created by the statute and its regulations are reasonable, the court best protects the public's interest." Id. (citation omitted). Mylan has made no better showing in this round of briefing that the public interest or the balance of harms weigh in its favor.

CONCLUSION

For the foregoing reasons, Mylan's application for a temporary restraining order should be denied.

Of Counsel:

DANIEL MERON
General Counsel

SHELDON T. BRADSHAW
Associate General Counsel
Food and Drug Division

ERIC M. BLUMBERG
Deputy Chief Counsel, Litigation

KAREN E. SCHIFTER
Associate Chief Counsel, Litigation
U.S. Dept. of Health & Human Services
Office of the General Counsel
5600 Fishers Lane
Rockville, MD 20857
301-827-1152

Respectfully submitted,

PETER D. KEISLER
Assistant Attorney General

C. FREDERICK BECKNER III
Deputy Assistant Attorney General

EUGENE M. THIROLF
Director

/s/
DRAKE CUTINI
Attorney
Office of Consumer Litigation
U.S. Department of Justice
PO. Box 386
Washington, D.C. 20044
Tel: 202-307-0044
Fax: 202-514-8742
drake.cutini@usdoj.gov