IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

MYLAN LABORATORIES INC., AND MYLAN PHARMACEUTICALS INC.,

Plaintiffs,

and

MUTUAL PHARMACEUTICAL CO.,

Intervenor-Plaintiff

v.

MICHAEL O. LEAVITT, et al.,

Defendants, *Cross-Defendants*

and

TEVA PHARMACEUTICALS USA, INC.,

Intervenor-Defendant

and

APOTEX INC.,

Intervenor-Defendant,Cross claimant

Civil Action No. 07-579 (RMU)

Judge Ricardo M. Urbina

APOTEX'S MOTION FOR A PRELIMINARY INJUNCTION

Intervenor-Defendant, Cross-Claimant Apotex, Inc. ("Apotex"), hereby moves for a preliminary injunction on its Cross Claim for injunctive relief against Michael O. Leavitt, in his official capacity as Secretary of Health and Human Services, Andrew C. von Eschenbach, in his official capacity as Commissioner of Food and Drugs, and the United States Food and Drug Administration ("FDA").

For the reasons stated in its accompanying Memorandum of Points and Authorities and exhibits thereto, Apotex respectfully requests that this Court enter a preliminary injunction:

A. directing FDA to immediately grant Apotex final approval of its ANDA for the sale and marketing of amlodipine besylate tablets.

B. directing FDA to immediately convert Mylan's final ANDA approval for amlodipine besylate tablets to a tentative approval as of March 16, 2007.

C. directing FDA to immediately convert Mylan's Paragraph IV ANDA certification to a paragraph II ANDA certification as of March 23, 2007.

D. directing FDA to immediately order Mylan to stop interstate distribution of its amlodipine besylate tablets.

E. directing FDA to order Mylan to recall all its amlodipine besylate tablets in the marketplace.

April 23, 2007

Respectfully submitted,

/s/Arthur Y. Tsien

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APOTEX'S MEMORANDUM OF POINTS AND AUTHORITIES IN SUPPORT OF ITS MOTION FOR PRELIMINARY INJUNCTION TO ORDER THE FDA TO IMMEDIATELY GRANT APPROVAL TO APOTEX'S ANDA FOR AMLODIPINE AND REQUIRE FDA TO ORDER MYLAN TO STOP MARKETING ITS GENERIC AMLODIPINE AND FOR OTHER RELIEF

INTRODUCTION

Apotex, Inc. ("Apotex") is entitled to an injunction ordering the United States Food and Drug Administration's ("FDA") to approve Apotex's Abbreviated New Drug Application ("ANDA") for generic amlodipine. The injunction is appropriate because:

(1) Apotex has a substantial likelihood of success on the merits because the FDA's decision to not approve Apotex's ANDA until after the mandate of the United States Court of Appeals for the Federal Circuit has issued is arbitrary, capricious, an abuse of discretion or otherwise not in accordance with law under the Administrative Procedure Act ("APA"), 5 U.S.C. § 706(2)(A).

(2) Apotex will suffer irreparable harm if it is not permitted to enter the market for amlodipine immediately.

(3) The public interest in acquiring reduced pricing of prescription drugs is substantial and favors issuing the injunction.

(4) The balance of harms favors Apotex.

Apotex is also entitled to an injunction ordering the FDA to notify Mylan that it does not have final approval for its ANDA for generic amlodipine. The injunction is appropriate because:

(1) Apotex has a substantial likelihood of success on the merits that the FDA's continuing acquiescence in the purported final approval of Mylan's ANDA despite agency policy and judicial precedents to the contrary is arbitrary, capricious, an abuse of discretion or otherwise not in accordance with law under the APA, 5 U.S.C. § 706(2)(A).

(2) Apotex will suffer irreparable harm if Mylan remains on the market when Apotex is not on the market.

(3) The public interest favors the faithful application of the laws.

(4) The balance of harms is neutral.

ARGUMENT

I. THE COURT HAS THE POWER TO GRANT APOTEX'S REQUESTED INJUNCTIONS

The court may issue the preliminary injunctions requested by Apotex if Apotex demonstrates that:

(1) there is a substantial likelihood it will succeed on the merits;

(2) it will be irreparably injured if an injunction is not granted;

(3) an injunction will not substantially injure the other party; and

(4) the public interest will be furthered by an injunction.

Davenport v. International Bhd. of Teamsters, 166 F.3d 356, 361 (D.C. Cir. 1999); *see also World Duty Free Americas, Inc. v. Summers*, 94 F. Supp. 2d 61, 64 (D.D.C. 2000).

The court does not consider the factors in isolation from one another, and no one factor is necessarily dispositive as to whether preliminary injunctive relief is warranted. *See CityFed Fin. Corp. v. Office of Thrift Supervision*, 58 F.3d 738, 746 (D.C. Cir. 1995).

A particularly strong showing on one factor may compensate for a weak showing on one or more of the other factors. *Serono Labs. v. Shalala,* 158 F.3d 1313, 1318 (D.C. Cir. 1998)*, on remand,* 35 F. Supp. 2d 1 (D.D.C. 1999)*,* For instance, as to the first factor, "the court is not required to find that ultimate success by the movant is a mathematical probability, and indeed, [the court] may grant [an injunction] even though its own approach may be contrary to [the movants'] view of the merits. The necessary 'level' or 'degree' of possibility of success will vary according to the court's assessment of the other factors." *New Mexico v. Richardson*, 39 F. Supp. 2d 48, 50 (D.D.C. 1999) (quoting *Holiday Tours*, 559 F.2d at 843).

A strong showing of likely success on the merits may warrant issuance of preliminary injunctive relief even if the plaintiff makes a less compelling showing on the other three factors. *See Virginia Petroleum Jobbers Ass'n v. Federal Power Comm'n*, 259 F.2d 921, 925 (D.C. Cir. 1958) ("injury held insufficient to justify a stay in one case may well be sufficient to justify it in another, where the applicant has demonstrated a higher probability of success on the merits"); *National Wildlife Fed'n v. Andrus*, 440 F. Supp. 1245, 1256 (D.D.C. 1977) (enjoining further construction on dam power plant, despite dispute over irreparable injury, because "the court is convinced by plaintiffs' argument on the merits and therefore finds it sufficient on the question of irreparable injury . . .").

II, THE FDA SHOULD BE ORDERED TO APPROVE APOTEX'S ANDA FOR AMLODIPINE

B. Apotex Has A Substantial Likelihood Of Success On The Merits Because The FDA's Interpretation Of The Statute Is Clearly Wrong

1. The FDA Is Entitled To No Deference Because The Statutory Language Is Unambiguous

"If the intent of Congress is clear, that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress." *Chevron USA Inc. v NRDC*, 467 U.S. 837, 842-43 (1984). The FDA has adopted the view of several of the commentators who urged the FDA to accept the view that a judgment of a United States Court of Appeals is not final until mandate issues.[1] Because the FDA's view is not consistent with clear

[1] *See* Letter from Gary J. Buehler, Director, Office of Generic Drugs, to ANDA Holder/Applicant for Amlodipine Besylate Tablets (Apr. 18 2007) (FDA Decision); Letter from John W. Ongman, Attorney for Mutual Pharmaceutical Company to Gary J. Buehler, Director, Office of Generic Drugs (Apr. 4, 2007) (Mutual Comment); Letter from David J. Harth, Attorney for Mylan Pharmaceuticals to Gary J. Buehler, Director, Office of Generic Drugs (Apr. 4, 2007) (First Mylan Comment); Letter from Peter O. Safir, Attorney for Pfizer, Inc. to Gary J. Buehler, Director, Office of Generic Drugs (Mar. 25, 2007) (Second Mylan Comment); Letter from Peter O. Safir, Attorney for Pfizer, Inc. to Gary J. Buehler, Director, Office of Generic Drugs (Apr. 5, 2007) (Pfizer Comment); Letter from Michael H. Hinckle, Vice President and General Counsel, Synthon Pharmaceuticals, Inc. to Gary J. Buehler, Director, Office of Generic Drugs (Apr. 3, 2007) (Synthon Comment); Letter from G. Srinivas, Drug

statutory language, supported by unambiguous Supreme Court precedent and the Advisory Committee Notes to the Federal Rules of Appellate Procedure regarding the finality of the judgments of United States Courts of Appeal, it must be reversed.

2. The FDA's Interpretation Is Not Consistent With The Statutory Language

The FDA has refused to approve Apotex's ANDA because of Pfizer's pediatric exclusivity under 21 U.S.C. § 355a (c)(2)(B), which reads (emphasis supplied):

> if the drug is the subject of a listed patent for which a certification has been submitted under subsection … (j)(2)(A)(vii)(IV) of section 505, 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 … section 505(j)(5)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions.)

In the present case the Federal Circuit was the "court [that] determine[d]" that all the relevant claims of Pfizer's patent were not "valid" on March 22, 2007. The Federal Circuit's judgment was final because under Federal Rule of Appellate Procedure 36 an appellate court "determines" the merits of the case in its opinion and that opinion constitutes the "judgment." Rule 36 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 supplied).

In the present case, the clerk for the Federal Circuit entered the judgment "Reversed" on March 22, 2007. The opinion on which that judgment was based "determine[d]" that the claims of Pfizer's patent that were asserted against Apotex were invalid. *See* Judgment and Opinion,

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Regulatory Affairs, Zydus Pharmaceuticals (USA) Inc. to Gary J. Buehler, Director, Office of Generic Drugs (Mar. 30, 2007) (Zydus Comment).

attached as Exhibit A. The Federal Circuit's judgment was served on the District Court for the Northern District of Illinois and was entered into that court's docket for this case. This is in accordance with Federal Rule of Appellate Procedure 36 ("A judgment is entered when it is noted on the docket"). On the day Exhibit A was entered in the Federal Circuit, that opinion and judgment could have been the subject of a petition for certiorari under the Rules of the Supreme Court. *See* Supreme Court Rules 14(1)(i)(i)&(iv). The judgment was final.

3. The FDA's Decision Is Not Consistent With Supreme Court Case Law

The Supreme Court recognizes that the entry of judgment is "an appellate court's final adjudication." *Hibbs v. Winn*, 542 U.S. 88, 96-97 (2004). The Supreme Court pays attention to the difference between the date of entry of judgment and the issuance of the mandate – it knows and observes the difference. *See id., citing and quoting* Supreme Court Rule 13(3) ("The time to file a petition for a writ of certiorari runs from the date of entry of the judgment or order sought to be reviewed, and not from the issuance date of the mandate (or its equivalent under local practice).").

4. In Deciding Petitions for Panel Rehearing, Rehearing En Banc, And Certiorari, The Courts Of Appeal And The Supreme Court Are Not "Determining"

A petition for rehearing or rehearing *en banc* does not vacate the opinion or the judgment of the Court of Appeals issued by the three-judge panel, even under the Federal Rules of Appellate Procedure. Charles Alan Wright, Arthur R. Miller and Edward H. Cooper, 16A Fed. Prac. & Proc. Juris.3d § 3981.2. (2007) (Courts of Appeal are split between those that automatically vacate the panel decision, and those that require a specific order to withdraw it). The Federal Circuit does not have an express rule on the matter, but in practice vacates panel decisions that are to be reheard.

"Granting hearing or rehearing en banc is always discretionary with the court of appeals." *Id.* at § 3981.1. In deciding whether to rehear *Apotex v. Pfizer*, the Federal Circuit would *not* be "determining" whether the Pfizer's patent is valid or infringed – it would be determining whether the panel decision needs to be revisited for reasons of consistency with prior cases, or because it presents an issue of exceptional importance. *Id.*

Similarly, the Supreme Court's certiorari procedure is discretionary. Supreme Court Rule 10. The principal considerations are whether there is conflict among the United States Courts of Appeal, the appellate court has seriously departed from accepted or usual proceedings, the appellate court has sanctioned such a departure by a lower court, the appellate court has decided an important issue of federal law that should be decided by the Supreme Court, or the appellate court has decided a case in a way that conflicts with Supreme Court precedent. *Id.*

Both of these mechanisms involve courts deciding *whether they will re-determine* the issue, not whether the Court of Appeals *has made a determination*. Accordingly, applications for these later events do not make the initial judgment any less a "determination" by an Article III Court.

5. The FDA Has Long Drawn The Line Based On Whether Appeal Was Available Or Not, Excluding The Possibility of Rehearing Or Certiorari

The FDA's analysis regarding the meaning of the phrase "the court determines" is wrong, and entitled to no deference. First, the FDA has long construed a "decision of a court" or "court decision" as a "final decision of a court from which no appeal can or has been taken." Court Decisions, ANDA Approvals, and 180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act, at 2 (Mar. 2000) (hereinafter "Court Decisions Guidance"). This is the definition the FDA used for years. *Id.* Once the judgment of the appellate

court is entered, it is not subject to any more *appeals* as a matter of right, only discretionary petitions and certiorari.

The statutory construction question posed is *when* the Federal Circuit has "determined" that Pfizer's patent is invalid as against Apotex. The FDA says it has not done so until the mandate issues. It is not within the FDA's purview to tell Article III Courts what they have "determined" and what they have not, and the FDA is not entitled to any deference on that issue.

6. The FDA's Reliance On The Advisory Committee Notes To Federal Rule of Appellate Procedure 41(c), Without Reading The Notes To 41(d), Is Not Reasonable and Not Entitled To Deference

The seeds for the error in the FDA's analysis appear to have arisen from a misunderstanding of the distinction between judgment and mandate. As *Hibbs* teaches, finality is determined by the judgment, not the mandate. *Hibbs*, 542 U.S. at 96-97. FDA relies on the comment to Fed. R. App. P. 41(c) for the proposition that an appellate judgment does not become final until mandate issues. However, it is wrong to read the comment for Rule 41(c) in isolation and not read it along with the comment for Rule 41(d). The Advisory Committee Notes to Federal Rule of Appellate Procedure 41(d) read (emphasis supplied):

> The Committee's objective is to treat a request for rehearing en banc like a petition for panel rehearing so that a request for a rehearing en banc will *suspend the finality* of the court of appeals' judgment and *delay the running of the period for filing a petition of certiorari*.

The Advisory Committee also knew that the judgment was final as of the date of entry, and *suspended* by the petition procedure for the purpose of making sure that it did not reach the Supreme Court too soon.

7. The FDA's Reliance On Statutes That Use Mandate To Set Finality Is Misplaced

In drafting the pediatric exclusivity statute, Congress focused on the court's "determination," not when it relinquishes jurisdiction to another court. The FDA has relied on statutes that say that the orders of administrative agencies become final a certain time after the mandate of a reviewing court issues. *E.g.,* 26 U.S.C. § 7481(a) (finality of a Tax Court decision – not the appellate court or Supreme Court decision – remanded to the Tax Court from the Supreme Court or a Court of Appeals is 30 days after mandate); 15 U.S.C. § 21(g) (the orders of the Commission, Board, or Secretary – not a court – vest with jurisdiction become final 30 days after the issuance of mandate from the Supreme Court); 15 U.S.C. § 45 (same). These are not apposite – the Federal Circuit here is reviewing a district court, not an administrative agency. Further, all that these statutes prove is that when Congress wants to specify something other than the otherwise clear general rule – that a court has made a "determination" when it enters a judgment – it can pass a statute to obtain its alternative desired outcome. This in no way lends ambiguity to the present statute or supports the FDA's interpretation. Just because interested parties disagree as to an interpretation of statutory language, this does not make that language ambiguous. In the present case, Congress could have used the word "mandate" if it wanted to do so. Instead it used the words "court determines," which in the appellate context is the Federal Circuit's judgment of invalidity or noninfringement.

8. Congress Wanted The Courts To Get Generic Drugs To Consumers If Possible, Not Enable Brand Manufacturers To Use Delaying Tactics To Keep Generic Drugs Off The Market

The FDA's interpretation puts the finality of the judgment of the Federal Circuit in the hands of Pfizer, not the hands of the Federal Circuit. The congressional policy was to put the "determination" in the hands of the courts, not aggrieved parties. The FDA's interpretation is directly contrary Congress' intent that the court make the determination.

The FDA has apparently concluded that Congress' intended effect was to make controlling the unlikely discretionary events of rehearing and certiorari so that a brand manufacturer such as Pfizer could maintain its pediatric exclusivity in the face of an adverse appellate decision. Losing litigants have 14 days to file petitions for rehearing, and that petition *indefinitely* stays the mandate. Fed. R. App. P. 41(d)(1). Even if the petition for rehearing is denied *immediately*, there is another 7 days for the mandate to issue. Fed. R. App. P. 41(b). Petitions for rehearing are exceedingly rare – they are granted only in a few cases.[2]

This can be further extended because, as noted earlier, parties have 90 days to petition for certiorari. The Supreme Court takes fewer than 100 cases a year, and "paid cases" like Pfizer's (cases not filed *in forma pauperis*) would have less than a 4% chance of receiving certiorari. Timothy S. Bishop & Jeffrey W. Sarles, *Petitioning and Opposing Certiorari in the U.S. Supreme Court*, http://library.findlaw.com/1999/Jan/1/241457.html. Permitting the filing of discretionary applications that have a low likelihood of success to extend the brand company monopoly is contrary to the central purpose of the Hatch-Waxman Act of getting generic drugs to consumers as soon as possible.

B. Apotex Will Be Irreparably Harmed Without A Preliminary Injunction

A decision not to order the FDA to approve Apotex's ANDA for generic amlodipine would seriously disadvantage Apotex. If the preliminary injunction is not granted, and Mylan continues to sell its generic drug, Apotex will lose its opportunity to fight for a leadership

[2] A review of petitions for rehearing submitted to the Federal Circuit over a 16-month period demonstrated that the Federal Circuit grants petitions for rehearing by the panel less than 3% of the time, while petitions for rehearing en banc are granted only about 0.6% of the time. See George Quillin & Jacqueline Wright, Rare Success Upon Filing Petitions for Rehearing by the Panel or En Banc at the Federal Circuit vs. Certiorari at the Supreme Court, CORPORATE COUNSEL OUTSIDE PERSPECTIVES, July 2004, at A6, http:www.foley.com/files/tbls31Publications/ FileUploadl37/2090/Quillin - Wright FINAL.pdf. Further, the Federal Circuit itself has expressed this view, stating in official guidance documents that "Rehearings are rarely granted." See Guide-for Pro Se Petitioners and Appellants, p. 7, available at http://fedcir.gov/pdf/guide.pdf.

position in the marketplace as an early entrant. Having that leadership position is essential to capture a sizable portion of the amlodipine market and associated annual sales that are forecasted to reach the hundreds of millions of dollars – harms for which there is no legal redress.

Loss of market share in a highly competitive industry is irreparable harm because of the difficulty of recovering from a loss of market share. As the court in *Novartis Consumer Health, Inc. v. Johnson & Johnson-Merck Consumer Pharms. Co.*, 290 F.3d 578, 595-96 (3d Cir. 2002), explained (emphasis supplied):

> Nonetheless, we conclude that the District Court's error in citing the wrong standard was harmless because there is sufficient evidence in the record to support a finding of irreparable harm necessary to issue a preliminary injunction. The District Court observed that the promotion and sale of MNTS had already had a measurable effect on Maalox's market share as reflected by a decrease in sales of Maalox that corresponds to the increased sales for MNTS. 129 F. Supp. 2d at 369. **We are satisfied that this loss of market share constitutes irreparable harm**. *See Moltan Co. v. Eagle-Picher Indus., Inc.*, 55 F.3d 1171, 1175 (6th Cir. 1995) (affirming decision to grant preliminary injunction where manufacturer's false claims were causing irreparable injury to a competitor in the form of lost sales and market share); *Cordis Corp. v. Medtronic, Inc.,* 835 F.2d 859, 864 (Fed. Cir. 1987) ("a loss in market share caused by an injunction could result in irreparable harm"); see also *Pappan Enters., Inc. v. Hardee's Food Sys., Inc.*, 143 F.3d 800, 805 (3d Cir. 1998) ("Grounds for irreparable injury include loss of control of reputation, loss of trade, and loss of goodwill."); *Opticians Ass'n v. Indep. Opticians*, 920 F.2d 187, 195 (3d Cir. 1990) (same). **In a competitive industry where consumers are brand-loyal, we believe that loss of market share is a "potential harm which cannot be redressed by a legal or an equitable remedy following a trial."** *Instant Air Freight*, 882 F.2d at 801.

Representatives from both parties that are seeking to establish a leadership position in the market for generic amlodipine tablets have offered declarations supporting the proposition that irreparable harm is caused by being kept out of the generic drug market during this crucial period. *See* McIntire Decl. (for Apotex) (attached as Exhibit B); Roman Decl. (for Mylan) (attached as Exhibit C). The existence of irreparable harm is undisputed by the parties with economic interests in the matter.

FDA's refusal to approve Apotex's ANDA has prevented Apotex from getting a fair start in this race to market. Mylan is obtaining a head start against Apotex that it is not entitled to. That head start will permit Mylan to secure distribution channels, favorable positioning in customer supply programs, and access to customers, thereby enabling Mylan to retain a greater market share in the long term. *See* Roman Decl., ¶6 at 2. Without an injunction, if, as Apotex expects, it is found that the Federal Circuit's "determin[ation]" that the asserted claims of Pfizer's patent were invalid as of in the date of the court's opinion and judgment of March 22, 2007, Apotex will never be able to recover for its lost market share from FDA or anyone else.

Based on its experience in the industry, Apotex calculates that if it receives final FDA approval for its ANDA in April 2007, a best case scenario would give Apotex a 30% market share of the generic sales, which would result in Apotex sales of $83,718,851 for the first 12 months post-launch. McIntire Decl., ¶14, Exhibit B.

Even in a worst case scenario, for an April launch, Apotex would have 20% of the market at approximately $55,673,036 in sales for the first 12 months post-launch. (*Id.*) However, if Apotex is prohibited from launching until September 2007, it would be lucky to obtain a 10% market share with yearly revenues of approximately $5,244,000. (*Id.*)

Mylan itself recognizes the value of the market for generic Norvasc® tablets. Mylan's Vice President and General Counsel, Brian S. Roman, filed a declaration to support Mylan's emergency application for a temporary restraining order, stating that Mylan "has forecasted that its revenues would reach several million dollars per day" (Exhibit C, ¶ 6), and he further stated that by being the first to launch into the generic marketplace, Mylan will be able to gain favorable positioning in customer supply programs and access to additional customers, thereby obtaining and retaining a greater market share in the long term. (*Id.*) Mr. Roman also claimed

that FDA approval of other ANDAs would mean that "Mylan would lose a portion of the amlodipine market and associated sales that are forecasted to reach the hundreds of millions of dollars. . . ." (*Id.*) FDA should be ordered to immediately grant Apotex final approval to sell generic amlodipine besylate to mitigate this irreparable harm, which will continue to grow until Apotex's products reach the market.

C. The Public Interest Is Served By The Issuance Of a Preliminary Injunction

The public has a well-recognized interest in "receiving generic competition to brand-name drugs as soon as is possible," *Boehringer Ingelheim Corp. v. Shalala*, 993 F. Supp. 1, 3 (D.D.C. 1997), and a "delay in the marketing of [the generic] drug could easily be against the public interest in reduced prices," *Schering Corp. v. Sullivan*, 782 F. Supp. 645, 652 (D.D.C. 1992). Accordingly, the public interest is in having Apotex on the market with its generic drug.

D. The Balance Of Harms Favors Apotex

Presently, Mylan is on the market. If this Court orders the FDA to permit Apotex to enter the market, Mylan will have to compete for market share with Apotex as opposed to being the only true generic on the market. If it were to turn out that the preliminary injunction was issued erroneously, and Apotex was forced to leave the market, Mylan could seize the market share that Apotex had been holding. In other words, in the event of an erroneous preliminary injunction, Mylan is not harmed. However, if the Court erroneously withholds the injunction, Apotex will never be able to recover its market share in this highly competitive market as recognized in *Cordis*. Accordingly, allowing Apotex to enter the market minimizes the prospect of irreparable harm all around, while the risk of economic harms is equal.

III. THE FDA SHOULD BE ORDERED TO RECOGNIZE THAT MYLAN'S ANDA FOR AMLODIPINE HAS NOT HAD FINAL APPROVAL SINCE MYLAN LOST IN THE DISTRICT COURT, AND SEND A LETTER TO THAT EFFECT

A. Apotex Is Likely To Succeed On Its Claim That Mylan Has No Legal Right To Market Its Generic Amlodipine Besylate Tablets At This Time

For the reasons discussed below, Mylan was not entitled to begin marketing generic amlodipine besylate tablets on March 23, 2007. Had FDA applied its judicially-sanctioned precedents, Mylan would not have held final ANDA approval, only a "tentative" approval, at that time and at all times since then.

1. When Mylan Lost In Its Patent Infringement Litigation With Pfizer, Its Approval to Market Generic Amlodipine Besylate Became Tentative By Operation Of Law

On February 27, 2007, Mylan lost its patent suit to Pfizer in the Pennsylvania district court. Specifically, the Pennsylvania court entered judgment against Mylan and in favor of Pfizer, concluding that the '303 patent was infringed by Mylan, not unenforceable, and not invalid. On March 16, 2007, the Pennsylvania district court issued an amended judgment, which stated as follows in relevant part:

> **ORDERED, ADJUDGED AND DECREED** that, pursuant to the provisions of 35 U.S.C. § 271(e)(4)(A), the effective date of any approval of Mylan's Abbreviated New Drug Application No. 76-418, seeking FDA approval of amlodipine besylate tablets, 2.5, 5 and 10 mg dosage strengths, shall be a date which is not earlier than the date of expiration of the '303 patent (March 25, 2007)….

Under established FDA practice and judicial precedents, the March 16, 2007 amended judgment pursuant to 35 U.S.C. § 271(e)(4)(A) from the Pennsylvania district court converted Mylan's final approval to a tentative approval by operation of law. The present situation is the same as the situation addressed by the D.C. Circuit in *Mylan Laboratories, Inc. v. Thompson*, 389 F.3d 1272 (D.C. Cir. 2004). In both situations, Mylan had filed a paragraph IV certification,

was sued for patent infringement, and had received final ANDA approval. In both situations, Mylan then lost its patent case before the district court. In both cases, the district court presiding over the patent action ordered, pursuant to 35 U.S.C. § 271(e)(4)(A), that the effective date of ANDA approval be delayed until patent expiration.

In the earlier matter considered by the D.C. Circuit (involving a generic fentanyl "patch" drug product), FDA converted Mylan's final approval to a tentative approval following Mylan's loss in patent litigation. FDA then went on to conclude that at the time the applicable patent expired, Mylan's paragraph IV certification was automatically converted to a paragraph II certification (patent expired). As Mylan then had a tentatively approved paragraph II ANDA on the date of patent expiration, final approval was blocked for an additional six months after patent expiration by 21 U.S.C. § 355a(c)(2)(A)(i). Once its final approval was converted by operation of law to a tentative approval, Mylan did not have any legal right to ship its generic product in interstate commerce. Mylan challenged the legality of FDA's actions, which challenges were rejected by the district court and affirmed by the D.C. Circuit.

There are no meaningful distinctions between the current amlodipine matter and the earlier fentanyl patch matter considered by the D.C. Circuit.[3] FDA's failure to apply the reasoning sanctioned by the D.C. Circuit with regard to the fentanyl patch matter to the current

[3] Mylan may try to argue that one distinguishing feature between the current matter and the fentanyl patch matter is the March 23, 2007 Federal Circuit order that "temporarily stayed" the Pennsylvania district court's March 16, 2007 amended judgment. But that "temporary stay" was intended only to maintain the status quo pending further briefing and the Federal Circuit's consideration, and did not reflect a substantive reversal or vacating of the March 16 amended judgment by the Federal Circuit.

Although the Federal Circuit on March 26, 2007 stayed the Pennsylvania district court's March 16, 2007 amended judgment against Mylan, that Federal Circuit decision had no effect on the applicability of pediatric exclusivity to Mylan. Specifically, the Federal Circuit's March 26, 2007 order did not affect the requirement in 21 U.S.C. § 355a(c)(2)(A) that "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," as the determination as to the applicability of pediatric exclusivity is made at the time of patent expiration (March 23, 2007), not three days later. Simply stated, the Federal Circuit's March 26 order has no effect on whether Mylan was entitled to be on the market at that time, or any time thereafter.

matter constitutes arbitrary and capricious agency action, in violation of the APA, 5 U.S.C. § 706(2)(A). The Agency cannot justify this inconsistent treatment because no lawful reason exists. FDA's failure to convert Mylan's amlodipine ANDA final approval to a tentative approval after Mylan's patent loss is unlawful and cannot stand. *See Indep. Petroleum Ass'n of Am. v. Babbitt*, 92 F.3d 1248, 1258 (D.C. Cir. 1996) (stating that an agency must afford similar treatment to comparable cases); *El Rio Santa Cruz Neighborhood Health Ctr., Inc. v. HHS*, 300 F. Supp. 2d 32, 42 (D.D.C. 2004) (finding HHS's denial of coverage was arbitrary and capricious due to agency's inconsistent treatment of similarly situated parties); *Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 27-28 (D.D.C. 1997) (granting injunctive relief based on FDA's disparate treatment of one product as a device and another product as a drug); *Bush-Quayle '92 Primary Comm. v. FEC*, 104 F.3d 448, 453 (D.C. Cir. 1997) (stating that should an agency change its course, it "must supply a reasoned analysis indicating that prior policies and standards are being deliberately changed, not casually ignored") (quoting *Greater Boston Tel. Corp. v. FCC*, 444 F.2d 841, 852 (D.C. Cir. 1970)); *Transactive Corp. v. United States*, 91 F.3d 232, 237 (D.C. Cir. 1996) (finding Treasury acted arbitrarily for not conforming its electronic benefits transfer policies to its existing regulations nor offering a 'reasoned analysis' for the difference).

2. Because Mylan Only Has Tentative Approval By Operation Of Law, FDA Should Be Ordered To Withdraw Mylan's Final Approval and To Order Mylan To Immediately Cease Interstate Distribution of Amlodipine Besylate Tablets

Once the district court's judgment against Mylan converted Mylan's final approval to a tentative approval by operation of law, Mylan was prohibited from selling its generic product until FDA issued a letter granting final approval to sell. As FDA previously had told Mylan in similar circumstances:

> First, the FDA concluded that the Vermont district court's order that "the effective date of any approval of Mylan's ANDA product shall be no earlier than the date of expiration of the '580 patent family, transformed Mylan's ANDA approval into "an approval with a delayed effective date," which "is a tentative approval that cannot be made effective **until the FDA issues a letter granting final effective approval**."

Mylan v. Thompson, 389 F.3d 1272, 1277 (D.C. Cir. 2004) (citations omitted) (emphasis added). This result was required by the Code of Federal Regulations, 21 C.F.R. 314.107(a) and (b)(3)(v), which states:

> (a) General. …approval of an application or abbreviated application for a drug product becomes effective on the date FDA issues an approval letter … for the application or abbreviated application.
>
> (b)(3)(v)…Tentative approval of an application does not constitute "approval" of an application and cannot, absent a final approval letter from the agency, result in an effective approval under paragraph (b)(3) of this section.

FDA must apply this regulation – and Mylan must obey it - with respect to what is now Mylan's tentative approval.

As previously described, Mylan is in an identical position as it was when FDA ruled an approval letter was required before it was allowed to sell, namely (1) Mylan first obtained final approval of its ANDA; (2) it lost its infringement case in the district court and the district court ordered the effective approval date could be no earlier than the expiration date of the patent; and (3) as a result Mylan's approval was reclassified from a final to a tentative approval by operation of law. Because FDA in *Mylan v. Thompson* concluded an approval letter must issue after a final approval is reclassified as a tentative approval and the D.C. Circuit upheld that ruling, *id.* at 1282 ("…the FDA was bound under the district court's order to treat the status of Mylan's ANDA

under the FDCA 'the same as that of other ANDAs blocked from final approval by patent or exclusivity rights.'"), the same rule must apply here.

In fact, Mylan was again told earlier this year that an injunction of the district court would compel a change in the effective date of an application that had previously been finally approved by FDA. In *Ortho-McNeil Pharmaceutical, Inc. v. Mylan*, 2007 WL 869545 (March 20, 2007 D.N.J.) (unpublished), Mylan argued the district court had no authority to order the effective date of an application to be changed after it had already obtained final approval from FDA. *Id.* at *2. The district court held that "Congress envisioned the factual scenario in which the ANDA had been approved, and intended that the district court then change the effective date." *Id.* (*citing* H. R. Rep. No. 98-857, pt. 1 (1984) ("In the case where an ANDA had been approved, the order would mandate a change in the effective date.")) And controlling precedent requires that once the earliest effective date FDA can issue final approval has changed, only a letter issued by FDA can finally approve the application and allow Mylan to move forward.

Instead, Mylan has ignored two earlier, indistinguishable directives directed at the company that it was **not** finally approved to sell its generic product until FDA issued a letter reclassifying its tentative approval to a final approval. Mylan is now selling its generic product without express FDA authority to do so in direct violation of 21 U.S.C. §355(a) (prohibition against introducing unapproved drugs into interstate commerce and §331(d) (corresponding "prohibited act"). The fact that FDA was required to issue a letter of approval is exemplified in this case because it was necessary, even after the expiration of the patent and the Federal Circuit's March 26 stay of the Pennsylvania district court's order, for FDA to decide whether or not pediatric exclusivity should apply to Mylan because its patent litigation was not resolved

prior to expiration of the patent. *Mylan v. Thompson*, 389 F.3d 1272, 1282-83 (D.C. Cir. 2004)[4]. Not until FDA had decided that issue could it have granted final approval to Mylan. Mylan sold anyway. FDA has still not finally approved Mylan's application after it was converted to a tentative approval by operation of law. Mylan sells anyway, in disregard of the law.

Even if we were to assume FDA's ruling that Apotex is blocked by Pfizer's pediatric exclusivity until the Federal Circuit issues a mandate were correct (it is not), this ruling cannot be reconciled with Mylan's continued selling of its generic product. Apotex continues to be blocked from obtaining final approval due to Pfizer's pediatric exclusivity, but Mylan is not. Once Mylan lost in the district court, it only had tentative approval, and even after the patent expired, it was still bound by Pfizer's pediatric exclusivity. FDA is equating **Apotex's** victory with the Federal Circuit's stay of Mylan's district court injunction pending resolution of Mylan's appeal. Yet inexplicably, Apotex's actual victory is ineffectual while Mylan's purported victory is final. Apotex's case is the only case where a final judgment finding the patent invalid and uninfringed has issued. Mylan, on the other hand, is in the position of a generic defendant whose case is still pending, and who is still bound by a district court's judgment finding the patent valid and infringed. Even if the Federal Circuit's stay of Mylan's injunction freed the way for FDA to finally approve Mylan's application (it did not), the decision certainly didn't constitute a letter issuing final approval.

FDA has simply chosen to ignore Mylan's illegal rush to the market. FDA's failure to act and its condoning Mylan's continued unlawful marketing of a tentatively approved drug are

[4] The FDA's equation of Apotex's victory with a Mylan victory is erroneous. Each decision of the district courts of the United States must be followed. No court has overruled the Pennsylvania district court's order in the Mylan action, and the FDA is bound by that decision and cannot deem Mylan to have won its action.

contrary to law and arbitrary and capricious and harm Apotex. Apotex is entitled to preliminary injunctive relief against FDA to remedy this situation.

B. An Injunction Against Continued Sales of Generic Amlodipine By Mylan Would Further The Public Interest

The public interest is best served by granting the requested injunctive relief, as the public's interest lies in the "faithful application of the laws" (*Mova Pharmaceutical Corp. v. Shalala*, 140 F.3d 1060, 1066 (D.C. Cir. 1998)), which, here, is served by requiring the agency to apply the governing statute in a manner that is consistent with FDA's prior judicially-approved rulings and the controlling statutory language. Injunctive relief comports with the purpose of the statute and, in particular, the need to properly interpret the pediatric exclusivity provisions as well as the need to give proper respect to court judgments. Any other result will undermine the balance struck in Hatch-Waxman and the pediatric exclusivity law.

Granting the requested injunction would mean, in essence, replacing Mylan's illegally marketed generic amlodipine tablets with those of Apotex, which earned the right to market by being the only generic firm to win its patent case against Pfizer. Apotex stands ready to ship once it receives final approval. Pfizer also is presently marketing both a "generic" amlodipine besylate product and its branded drug, Norvasc®. Thus, the public will continue to have generic amlodipine tablets available.

C. Apotex Will Be Irreparable Harmed Without A Preliminary Injunction

A decision not to order the FDA to notify Mylan that Mylan's ANDA for generic amlodipine is not approved would seriously harm Apotex. If the preliminary injunction is not granted, and Mylan continues to sell its generic drug, Apotex will lose its opportunity to fight for a leadership position in the marketplace as an early entrant. Having that leadership position is

essential to capture a sizable portion of the amlodipine market and associated annual sales that are forecasted to reach the hundreds of millions of dollars – harms for which there is no legal redress.

Loss of market share in a highly competitive industry is irreparable harm because of the difficulty of recovering from a loss of market share. *Novartis Consumer Health, Inc. v. Johnson & Johnson-Merck Consumer Pharms. Co.*, 290 F.3d 578, 595-96 (3d Cir. 2002). Representatives from both parties that are seeking to establish a leadership position in the market for generic amlodipine tablets have offered declarations supporting the proposition that irreparable harm is caused not obtaining this leadership position which is otherwise impossible to attain. *See* McIntire Decl. (for Apotex) (attached as Exhibit B); Roman Decl. (for Mylan) (attached as Exhibit C). The existence of irreparable harm arising from not getting the market share that the party is entitled to is undisputed by the parties.

The only thing standing between Apotex and market leadership in the true generic drug market is the FDA's approval of Mylan when Mylan was not entitled to such approval. Apotex's demonstration of likelihood of success on the merits shows that Mylan should be off the market. The head start that Mylan has seized is rightfully Apotex's, and Apotex cannot replace that position with any remedy at law.

The harm to Apotex, coupled with Mylan's disregard of the law (in the form of having been told twice before it could not lawfully market its generic product in essentially identical situations) warrant an injunction to require FDA to order Mylan to recall its illegally distributed product from the marketplace.

D. The Balance Of Harms Is Neutral

Presently, Mylan is on the market. If this Court orders the FDA to notify Mylan to leave the market and to require Mylan to recall its unlawfully marketed generic product from the marketplace, Mylan will have to compete for market share with Apotex when it reenters the market. Each party is seeking the same market share for the same reasons. Neither needs the market share more than the other. The balance of harms is neutral.

CONCLUSION

For the reasons stated herein, Apotex respectfully requests that this Court enter a preliminary injunction:

A. directing FDA to immediately grant Apotex final approval of its ANDA for the sale and marketing of amlodipine besylate tablets.

B. directing FDA to immediately convert Mylan's final ANDA approval for amlodipine besylate tablets to a tentative approval as of March 16, 2007.

C. directing FDA to immediately convert Mylan's Paragraph IV ANDA certification to a paragraph II ANDA certification as of March 23, 2007.

D. directing FDA to immediately order Mylan to stop interstate distribution of its amlodipine besylate tablets.

E. directing FDA to order Mylan to recall all its amlodipine besylate tablets in the marketplace.

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Respectfully submitted,

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