IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

APOTEX INC. 150 Signet Drive Weston, Ontario M9L 1T9 and APOTEX CORP. 2400 North Commerce Parkway, Suite 400, Weston, Florida 33326 *Plaintiffs*, v. MICHAEL O. LEAVITT, in his official capacity as Secretary of Health and Human Services, 200 Independence Avenue, SW Washington, DC 20204, ANDREW C. VON ESCHENBACH, M.D., in his official capacity as Commissioner of Food and Drugs, 5600 Fishers Lane Rockville, MD 20857 and UNITED STATES FOOD AND DRUG ADMINISTRATION, 5600 Fishers Lane Rockville, MD 20857 *Defendants*.	Civil Action No.

APOTEX'S COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF

Plaintiffs Apotex Inc. and Apotex Corp. ("Apotex") bring this complaint for declaratory and injunctive relief against Defendants Michael O. Leavitt, in his official capacity as Secretary of Health and Human Services ("HHS"), Andrew C. von Eschenbach, in his official capacity as

Commissioner of Food and Drugs, and the United States Food and Drug Administration (collectively, "FDA"). In support thereof, Apotex states as follows:

NATURE OF THE ACTION

1. Apotex brings this suit to set aside FDA's refusal to stay the effectiveness of Abbreviated New Drug Application ("ANDA") 76-273 filed by Dr. Reddy's Laboratories, Inc. Absent a stay, Dr. Reddy's will be permitted to distribute generic clopidogrel bisulfate tablets during the remainder of the 180 days during which Apotex is entitled to be the sole generic manufacturer of that drug under the Drug Price Competition and Patent Term Restoration Act of 1984 ("Hatch-Waxman Amendments"), which amended the Federal Food, Drug, and Cosmetic Act ("FDCA"). FDA's action violates the FDCA and must be set aside by this Court under Section 706 of the Administrative Procedure Act ("APA").

2. Apotex filed the first ANDA for clopidogrel bisulfate tablets containing a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) ("paragraph IV certification") that U.S. Patent No. 4,847,265 ("the '265 patent"), listed as covering clopidogrel bisulfate tablets, was invalid. Under the Hatch-Waxman Amendments to the FDCA, that certification permitted the patent holder and New Drug Application ("NDA") holder, Sanofi-Synthelabo ("Sanofi"), to claim a technical act of patent infringement and initiate suit. *See* 35 U.S.C. § 271(e)(2). Certification also entitled Apotex to 180 days of generic marketing exclusivity. 21 U.S.C. § 355(j)(5)(B)(iv) (2002).

3. Apotex and Sanofi have been engaged in patent litigation regarding the validity of the '265 patent since 2002. The litigation is now before the United States Court of Appeals for the Federal Circuit ("CAFC") and has been argued and submitted.

4. Apotex commenced marketing generic clopidogrel bisulfate tablets on August 8, 2006, relying upon the 180 days of generic marketing exclusivity provided under the FDCA. Sanofi moved to enjoin Apotex's marketing as infringing, and a preliminary injunction was entered 23 days into Apotex's exclusivity. Apotex remains under injunction pending the outcome of the CAFC proceedings and has not enjoyed the benefit of the remaining 156 days of the exclusivity period to which it is entitled under FDCA.

5. Apotex sought to protect its remaining 156 days of exclusivity by promptly notifying FDA of the injunction entered against Apotex and requesting that FDA process additional ANDAs for clopidogrel bisulfate tablets in a manner that would protect Apotex's 180 days of generic marketing exclusivity. Notwithstanding this request, FDA approved Dr. Reddy's ANDA 76-273 on January 14, 2008 without any effectiveness condition that would protect Apotex's remaining generic exclusivity.

6. On February 13, 2008, Apotex filed a Petition with FDA seeking a stay of the effective date of ANDA 76-273 pursuant to 21 C.F.R. § 10.35. Apotex sought only to stay the effective date of Dr. Reddy's formal approval in a manner that would protect Apotex's remaining 156 days of generic exclusivity but would permit unrestricted generic competition at the end of that exclusivity period. Despite the fact that the CAFC decision may issue imminently, FDA has not responded to Apotex's Stay Petition.

7. FDA's action with respect to ANDA 76-273 deprives Apotex of the full benefit of the 180 days of generic marketing exclusivity to which the FDCA entitles it as the first ANDA applicant to file a paragraph IV certification for the '265 patent. Should Dr. Reddy's commence marketing under ANDA 76-273, as FDA has authorized, Apotex will suffer substantial and

irreparable losses of market share, sales and profits. Apotex thus is entitled to relief from this Court:

(a) Declaring that Apotex is entitled to the full benefit of 180 days of marketing exclusivity for clopidogrel bisulfate tablets, to which Apotex became entitled when it became the first filer of an ANDA for clopidogrel bisulfate tablets containing a paragraph IV certification for the '265 patent; and

(b) Preliminarily and permanently enjoining FDA from making ANDA 76-273, or any other ANDA relating to clopidogrel bisulfate tablets, effective until the earlier of (i) 156 days after Apotex's entitlement to market clopidogrel bisulfate tablets is restored by action of the CAFC; or (ii) the expiration of the '265 patent.

PARTIES

8. Plaintiff Apotex Inc. is a corporation organized and existing under the laws of Canada and has its principal place of business at 150 Signet Drive, Weston, Ontario, Canada M9L 1T9. Apotex, Inc. develops and manufactures quality, lower-priced generic drugs.

9. Plaintiff Apotex Corp. is a corporation organized and existing under the laws of the State of Delaware, and has its principal place of business at 2400 North Commerce Parkway, Suite 400, Weston, Florida 33326. Apotex Corp. is the United States marketing and sales affiliate for Apotex Inc.

10. Defendant Michael O. Leavitt is the Secretary of HHS, and the official charged by law with administering the FDCA. He is sued in his official capacity. Secretary Leavitt maintains offices at 200 Independence Avenue, S.W., Washington, D.C. 20201.

11. Defendant Andrew von Eschenbach is the Commissioner of Food and Drugs. He has been delegated the authority to administer the drug approval provisions of the FDCA through

FDA. He is sued in his official capacity. Commissioner von Eschenbach maintains offices at 5600 Fishers Lane, Rockville, MD 20857.

12. Defendant FDA is an agency within HHS and an "agency" within the meaning of the APA. FDA maintains offices at 5600 Fishers Lane, Rockville, MD 20857.

JURISDICTION AND VENUE

13. This action arises under the FDCA, 21 U.S.C. § 301, *et seq.*, the APA, 5 U.S.C. § 551, *et seq.*, and the Declaratory Judgment Act, 28 U.S.C. §§ 2201-2202. This Court has subject matter jurisdiction under 28 U.S.C. §§ 1331, 1361.

14. This Court has personal jurisdiction over the Defendants because they are either located and/or conduct substantial business in, or have regular and systematic contact with, this District.

15. Venue is proper in this District under 28 U.S.C. § 1391(e).

16. FDA's agency action or inaction creates an actual controversy for which Apotex is entitled to review and relief under 5 U.S.C. §§ 702, 704-06. Apotex is a legal entity that has suffered a legal wrong and has been adversely affected by final agency action and/or agency action wrongly withheld and thus has standing to maintain this action pursuant to the APA.

17. There exists an actual, substantial, and continuing controversy between the parties regarding FDA's decision to make Dr. Reddy's ANDA 76-273 effective prior to the exhaustion of Apotex's 180 days of marketing exclusivity under the FDCA. FDA's refusal to safeguard Apotex's remaining exclusivity is an abuse of discretion, arbitrary, capricious, and contrary to law.

FACTUAL ALLEGATIONS

Statutory Framework for Approval of New and Generic Drugs

18. The Hatch-Waxman Amendments to the FDCA govern the approval of generic drugs. Although the applicable provisions of the FDCA have subsequently been amended by the Medicare Prescription Drug, Improvement and Modernization Act of 2003 ("MMA"), Pub. L. No. 108-173 § 1101(c)(1), those revisions do not apply to the ANDAs at issue in this case, which were pending prior to the MMA's enactment. Unless otherwise noted, all references to the FDCA are to the pre-2003 version of the statute.

19. A person seeking to sell a new chemical entity as a drug must file and gain approval of a New Drug Application ("NDA"). That NDA must provide data on the composition of the drug, clinical trial results establishing the safety and efficacy of the drug, the means of manufacturing it, labeling for the intended uses of the drug, and information with respect to any relevant patents that might be asserted as protecting the drug from competition. *See* 21 U.S.C. §§ 355(b)(1), (c)(2).

20. Generic drugs contain the same active ingredient, and provide the same therapeutic benefit, as NDA-approved drugs. They are, however, generally sold at a lower price than NDA-approved drugs. Congress enacted the Hatch-Waxman Amendments to streamline and expedite the process of bringing generic drugs to market.

21. A company seeking FDA approval to market a generic version of a drug previously approved through an NDA may file an ANDA without repeating the safety and efficacy studies conducted for the NDA-approved product. The ANDA applicant must establish that its proposed product is bioequivalent to the NDA-approved drug and, with some exceptions,

that it has the same active ingredient, dosage form, dosage strength, route of administration and labeling as the NDA-approved version. 21 U.S.C. § 355(j)(2)(A).

22. The ANDA applicant must also provide one of four certifications with respect to each of the patents listed in the NDA (and subsequently published by FDA). Among those certifications is a "paragraph IV certification," in which the ANDA applicant declares that the listed patent is invalid or will not be infringed by the product contemplated by the ANDA. *See* 21 U.S.C. § 355(j)(2)(B). A paragraph IV certification signals the ANDA applicant's intent to market its product prior to the expiration of the patent or patents listed as claiming the NDA-approved drug and constitutes a technical act of infringement permitting the NDA holder to commence a patent action under 35 U.S.C. § 271.

23. If the owner of a listed patent that is the subject of a paragraph IV certification then sues the ANDA applicant within 45 days after receiving notice of the paragraph IV certification, the applicable statute generally forbids FDA from making the ANDA approval effective until at least 30 months after the patent owner's receipt of that notice unless certain specified conditions are met. *See* 21 U.S.C. § 355(j)(5)(B)(iii) (2002).

24. The Hatch-Waxman Amendments encourage generic companies to challenge pharmaceutical patents by filing paragraph IV certifications in order to get generic products to market prior to patent expiration. The first applicant to submit an ANDA containing a paragraph IV certification and challenge the validity of a listed patent almost inevitably bears the litigation costs and risks inherent in protracted patent litigation.

25. In order to encourage companies to bear those costs and risks, Congress, through the Hatch-Waxman Amendments, granted 180 days of generic marketing exclusivity as an

incentive for generic manufacturers to file ANDAs on drugs covered by listed patents. The relevant statutory provision, as it existed prior to the MMA, provides:

> (iv) If the [ANDA] contains a [paragraph IV certification] and is for a drug for which a previous application has been submitted under this subsection [containing] such a certification, the application **shall be made effective not earlier than one hundred and eighty days after**—
>
> > (I) the date the Secretary receives notice from the applicant under the previous [ANDA] of the first commercial marketing of the drug under the previous application, or
> >
> > (II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed, whichever is earlier.

21 U.S.C. § 355(j)(5)(B)(iv) (2002) (emphasis added). This language demonstrates a clear congressional intent to provide the first ANDA applicant to file a paragraph IV certification for a listed patent with the economic benefit of 180 days of generic marketing exclusivity to encourage prompt challenges to questionable or inapplicable patents. The "not earlier than" language provides a safety valve to ensure that the 180-day period will not be unfairly curtailed by, for example, an improvidently granted injunction issued during the period of marketing exclusivity against a first filer who commences commercial marketing prior to a determination that a listed patent is invalid or not infringed.

Apotex's Development of Generic Clopidogrel Bisulfate Tablets and Challenge to Existing Patents

26. Clopidogrel bisulfate is a drug used to reduce heart attacks and strokes. Sanofi-Synthelabo and other Sanofi entities (collectively "Sanofi") markets clopidogrel bisulfate tablets under the brand name Plavix®. Plavix® was approved by FDA on November 17, 1997 under NDA 20-839. Sanofi listed the '265 patent with FDA, along with another, now-expired, patent. The '265 patent expires on November 17, 2011.

27. In November 2001, Apotex filed an ANDA for clopidogrel bisulfate containing a paragraph IV certification challenging the validity of the '265 patent. Apotex's ANDA was the first-filed ANDA relating to clopidogrel bisulfate tablets with a paragraph IV certification.. On March 21, 2002, Sanofi sued Apotex for patent infringement in the United States District Court for the Southern District of New York. *Sanofi-Synthelabo v. Apotex, Inc.*, No. 02-CIV-2255 (S.D.N.Y.).

28. The statutory 30-month stay triggered by the lawsuit under 21 U.S.C. § 355(j)(5)(B) expired on May 17, 2005, and on January 20, 2006, FDA approved Apotex's ANDA 76-274.

29. Apotex launched its generic clopidogrel bisulfate product on August 8, 2006, over five years before expiration of the '265 patent. Twenty-three days later, the U.S. District Court for the Southern District of New York preliminarily enjoined Apotex from selling clopidogrel bisulfate product pending the outcome of the patent case. *Sanofi-Synthelabo v. Apotex, Inc.*, 488 F. Supp. 2d 317 (S.D.N.Y. 2006), *aff'd,* 470 F.3d 1368 (Fed. Cir. 2006).

30. After a bench trial, the district court determined that Apotex had not proven the invalidity of the `265 patent by clear and convincing evidence and entered a permanent injunction. *Sanofi-Synthelabo v. Apotex, Inc.*, 492 F. Supp. 2d 353 (S.D.N.Y. 2007), *appeal pending.* Apotex has appealed the issuance of the permanent injunction to the Federal Circuit, arguing that the '265 patent claims are invalid for anticipation and obviousness. Oral argument was held on March 3, 2008.

31. If Apotex is successful on appeal, the Federal Circuit will issue a mandate requiring the district court to lift the injunction seven days after its opinion is announced. Fed. R. App. Proc. 41(b). This will permit Apotex to resume selling; however, a timely request by

Sanofi for rehearing and/or rehearing *en banc* will defer the issuance of mandate until Sanofi's request is decided. Thus, Apotex's resumption of sales after a favorable Federal Circuit decision may be deferred for some time.

32. At least three other manufacturers have filed paragraph IV certifications for the '265 patent in connection with ANDAs for clopidogrel bisulfate and have been sued by Sanofi: Dr. Reddy's Laboratories, Teva Pharmaceuticals and Cobalt Pharmaceuticals.

33. The district court entered permanent injunctions against both Teva and Cobalt soon after entry of the injunction against Apotex. Both Teva and Cobalt have appealed to the Federal Circuit; however, both cases have been stayed pending the outcome of Apotex's appeal. *Sanofi-Aventis v. Teva Pharms.*, No. 07-1521 (Fed. Cir. Nov. 21, 2007); *Sanofi-Aventis v. Cobalt Pharms.*, No. 07-1522 (Fed. Cir. Dec. 6, 2007) (docket entries staying cases pending issuance of mandate in *Sanofi-Synthelabo v. Apotex, Inc.*, No. 07-1438 (Fed. Cir.)).

34. Upon information and belief, no injunction was entered against Dr. Reddy's. Instead, Sanofi and Dr. Reddy's entered a stipulated order that requires Dr. Reddy's to provide Sanofi with 10 business days' notice before manufacturing, using, offering to sell, or selling any product claimed under the '265 patent. The stipulation also allows Dr. Reddy's to import clopidogrel bisulfate for sale in the United States immediately upon Apotex's obtaining a favorable result in the appeal pending before the CAFC.

35. Upon information and belief, FDA has subsequently granted tentative approval to two other ANDAs for clopidogrel bisulfate tablets: ANDA 77-665 (Mylan Pharmaceuticals, tentative approval granted June 18, 2007), and ANDA 78-004 (Roxane Laboratories, tentative approval granted September 26, 2007). "Tentative approval" means that a drug product meets

FDA standards for U.S. marketing, but existing patents and/or exclusivity prevent the drug from being marketed. *See, e.g.*, 21 C.F.R. §§ 314.105, 314.107.

36. Upon information and belief, on January 14, 2008, FDA gave final approval to Dr. Reddy's ANDA 76-273 for clopidogrel bisulfate tablets without conditioning its effective date to protect Apotex's remaining exclusivity.

37. On February 13, 2008, Apotex filed a Petition for Stay of Action with FDA requesting that FDA stay the effective date of final approval of Dr. Reddy's ANDA 76-273 and any other pending ANDA for clopidogrel bisulfate tablets until resolution of the patent litigation and the expiration of Apotex's remaining exclusivity should the '265 patent be deemed invalid.

38. Apotex requested that FDA respond no later than March 15, 2008. To date, FDA has not responded.

39. Unless this Court grants the relief sought, Dr. Reddy's would be able to commence marketing almost immediately in the event of a CAFC decision of invalidity, while Apotex would remain bound by injunction until the mandate issues. Not only would Apotex be denied its remaining 156 days of exclusivity, but Dr. Reddy's would have a significant head start over Apotex in the marketplace, a marketplace that would be made available only by Apotex's challenge to the '265 patent.

FIRST CAUSE OF ACTION
(Violation of the FDCA and the APA)

40. FDA's grant of unconditional final approval to Dr. Reddy's ANDA and its refusal to allow Apotex to enjoy the remaining 156 days of exclusivity for its generic clopidogrel bisulfate tablets violates the exclusivity regime of the Hatch-Waxman Amendments. FDA's actions are thus in excess of its statutory authority, arbitrary, capricious, an abuse of discretion and otherwise not in accordance with law, in violation of 5 U.S.C. § 706.

41. FDA's grant of an unconditional final approval to Dr. Reddy's ANDA, thus eliminating Apotex's remaining exclusivity, is final agency action that is subject to judicial review. Apotex has no adequate remedy at law.

42. Apotex will suffer substantial and irreparable harm absent the requested relief in the form of lost sales and good will and decreased market share that can never be recovered.

43. Neither Defendants nor any other entity will suffer cognizable harm if the relief requested herein is granted, and the public interest will be served by such relief.

PRAYER FOR RELIEF

Wherefore, Apotex prays that this Court:

A. Set aside FDA's action denying a stay of ANDA 76-273 as contrary to law, an abuse of discretion, and arbitrary and capricious;

B. Preliminarily and permanently enjoin FDA from making effective the approval of ANDA 76-273, or any other ANDA for clopidogrel bisulfate tablets, until the earlier of

(i) 156 days after Apotex's entitlement to market clopidogrel bisulfate tablets is restored by action of the CAFC, or

(ii) the expiration of the '265 patent; and

C. Provide such other and further relief as the Court may deem just and proper.

Dated: April 23, 2008

Respectfully submitted,

By: _____

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