

NAPM



NATIONAL ASSOCIATION OF PHARMACEUTICAL MANUFACTURERS

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Food and Drug Administration
Dockets Management Branch (HFA-305)
Department of Health and Human Services
Room 1061
5630 Fishers Lane
Rockville, Maryland 20852

Re: Docket No. 00P-0499

Dear Food and Drug Administration:

The National Association of Pharmaceutical Manufacturers (NAPM) is a national, not for profit trade association representing manufacturers of generic pharmaceutical products, as well as suppliers of goods and services to the generic drug industry. NAPM submits this comment in connection with the citizen petition submitted by Lord, Bissell & Brook, on behalf of Apotex, Inc., the TorPharm division of Apotex, Inc., and Apotex Corporation (collectively "Apotex"). In that petition, Apotex asked the Agency to remove two patents from the "Orange Book." While NAPM takes no position on whether those two patents are properly listed in the "Orange Book," NAPM supports some of Apotex's underlying positions. NAPM's views are set forth in an amicus curiae brief submitted to the court in Apotex, Inc. v. Shalala, Civ. No. 1:00CV00729(TPJ) (D.D.C.). A copy of that amicus brief is enclosed. NAPM respectfully requests that the Agency consider the views set forth in its amicus brief in connection with Apotex's citizen petition.

NAPM appreciates the Agency's consideration of its views.

Sincerely yours,

Robert S. Milanese ₂₁₇

Robert S. Milanese
President

Enclosure

00P-0499

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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

APOTEX, INC.,)
)
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 Plaintiff,)
)
 v.) Civ. No. 1:00CV00729 (TPJ)
)
 DONNA E. SHALALA, et al.,)
)
)
 Defendants.)

**AMICUS CURIAE BRIEF OF
NATIONAL ASSOCIATION OF PHARMACEUTICAL MANUFACTURERS
SUPPORTING PLAINTIFF**

PRELIMINARY STATEMENT

The National Association of Pharmaceutical Manufacturers (NAPM) submits this *amicus curiae* brief supporting plaintiff Apotex, Inc. (Apotex). The parties -- Apotex; defendants Food and Drug Administration (FDA), Donna E. Shalala, and Jane E. Henney (collectively "federal defendants"); and defendant-intervenor SmithKline Beecham Corporation (SmithKline) -- do not object to the filing of this *amicus* brief.

NAPM is a national, not-for-profit, trade association representing manufacturers and distributors of generic drugs, as well as manufacturers and suppliers of bulk pharmaceutical chemicals and suppliers of services to the U.S. generic drug industry. Because a generic drug product cannot be lawfully marketed in the U.S. until its sponsor has submitted an Abbreviated New Drug Application (ANDA) and received approval by FDA, NAPM and its members have an obvious and keen interest in the outcome of this case involving the ANDA approval process.

Apotex has filed an ANDA with FDA for permission to market a generic version of the popular drug Paxil®. SmithKline holds an approved New Drug Application (NDA) for Paxil, a prescription drug product with the active ingredient paroxetine hydrochloride hemihydrate, indicated for the treatment of depression, social anxiety, panic, and obsessive compulsive disorders. Between 1992 and 1999, SmithKline notified FDA that three patents claim Paxil, U.S. Patent No. 4,721,723 (the '723 patent), U.S. Patent No. 5,872,132 (the '132 patent), and U.S. Patent No. 5,900,423 (the '423 patent). FDA has listed those patents, pursuant to its interpretation of its statutory mandate, in the Patent and Exclusivity Addendum to the agency's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the "Orange Book."

Apotex alleges that the '132 patent and the '423 patent do not meet the statutory criteria for Orange Book listing and that these unlawful patent listings in the Orange Book are a significant impediment to Apotex's ability to bring a generic version of Paxil to market. Among other relief, as sought by Apotex, this Court should order FDA to remove the '132 and '423 patents from the Orange Book.

This *amicus* brief first describes the statutory and regulatory scheme in which this matter arises. To effectuate congressional intent, FDA is obligated under the Federal Food, Drug and Cosmetic Act (FDC Act), 21 U.S.C. §§ 301-397, to "look behind" the patents submitted to FDA by "brand name" drug applicants for listing in the Orange Book, in order to determine whether those patents in fact meet the statutory criteria for being listed. This brief also addresses how FDA's ceding to the large brand name segment of the pharmaceutical industry of this part of its regulatory responsibility to approve drugs is an unlawful delegation of authority and contravenes

the public interest. Last, this brief explains why FDA's implementation of the patent listing provisions of the FDC Act is unlawful, as applied.

STATUTORY BACKGROUND

Congress amended the FDC Act in 1984 to address the approval process for generic drug products by enacting the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984). That law is commonly known as the "Hatch-Waxman Amendments." Under these provisions, FDA is empowered to approve an ANDA, which allows the lawful marketing of a generic drug product for human use. See generally, 21 U.S.C. § 355(j). An ANDA for a generic drug must be based on, and reference, the appropriate FDA-approved "listed drug." 21 U.S.C. § 355(j)(2)(A). That listed drug is the brand name or innovator drug product that the generic drug intends to copy.

The holder of each NDA for a brand name drug product is required to submit to FDA information concerning all U.S. patents that claim the drug or a method of using the drug.¹ 21 U.S.C. § 355(b)(1) and (c)(2). Specifically, the FDC Act provides that an applicant must file:

the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.

21 U.S.C. § 355(b)(1). Upon approval of the NDA, FDA must publish the appropriate patent information and update it monthly in the Orange Book. See 21 U.S.C. § 355(b)(1) and (j)(7)(A).

¹ Method of use patents are not relevant to this case and will not be discussed further.

The FDC Act includes requirements that are identical in substance and applicable to patents that issue after NDA approval. 21 U.S.C. § 355(c)(2).

An ANDA applicant must file with its application a certification with respect to each patent on the listed drug that is set forth in the Orange Book. With respect to the current controversy, one type of statutory certification is relevant: a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), commonly known as a "Paragraph IV" certification, which states that a listed patent is invalid or will not be infringed by the manufacture, use, or sale of the drug for which the ANDA is submitted.

An ANDA applicant submitting a Paragraph IV certification must give notice to the patent holder and the holder of the NDA for the listed drug that it has filed a Paragraph IV ANDA for the listed drug. 21 U.S.C. § 355(j)(2)(B). Thereafter, assuming that substantive ANDA approval requirements have been satisfied, the effective date of the ANDA approval depends on whether a lawsuit for patent infringement has been filed by the NDA holder or patent holder against the ANDA applicant. If the NDA holder or patent holder files such a patent infringement lawsuit within 45 days from the date of receipt of the notice of the ANDA filing, the effective date of ANDA approval is, except as otherwise ordered by the court, delayed until 30 months after the date of receipt of that notice or the date of a court decision that such patent is invalid or not infringed, whichever is earlier. 21 U.S.C. § 355(j)(5)(B)(iii).

FACTUAL BACKGROUND

The factual circumstances from which this case arises are set out in the papers of Apotex and the federal defendants and are only briefly summarized here. FDA approved SmithKline's NDA for Paxil in December 1992. As part of the NDA approval process, SmithKline submitted

to FDA information about the '723 patent, entitled "Anti-Depressant Crystalline Paroxetine Hydrochloride Hemihydrate," as the only patent covering Paxil. When FDA approved Paxil, it listed the '723 patent in the Orange Book.

Apotex filed an ANDA for a generic version of Paxil on March 31, 1998. With its ANDA, Apotex filed a paragraph IV certification as to the '723 patent, notifying SmithKline that Apotex had filed the ANDA and that Apotex's proposed generic product did not infringe the '723 patent. SmithKline promptly filed suit and by operation of the Hatch-Waxman Amendments, the approval of Apotex's ANDA was automatically stayed by FDA for 30 months. That 30-month stay expires on November 21, 2000.

In 1999, SmithKline submitted information to FDA about two additional patents -- the '132 and '423 patents -- that, SmithKline asserted, claimed Paxil. These two patents are for an anhydrate form of paroxetine hydrochloride -- one which contains no chemically-bound water. (The active ingredient in the marketed and approved Paxil product is paroxetine hydrochloride hemihydrate -- a form of paroxetine that has one molecule of chemically-bound water for every two molecules of paroxetine hydrochloride.) FDA listed both new patents in the Orange Book in connection with Paxil, even though they claim a chemical form of the paroxetine hydrochloride active ingredient not present in Paxil.

By permitting the listings of the '132 and '423 patents, FDA caused Apotex to file additional paragraph IV certifications of non-infringement. Within 45 days of receiving the

certifications, SmithKline sued Apotex again for patent infringement,² resulting in an automatic stay of approval of Apotex's ANDA, until February 2002.

Thus, Apotex contends that these two later patent listings resulted in a 15-month further delay in the approval of its ANDA in question. Apotex argues, in relevant part, that FDA has abrogated its statutory authority under the FDC Act by permitting SmithKline to list in the Orange Book patents that do not, in fact, claim the FDA-approved Paxil drug product. FDA counters, among other things, that its task in listing patents is merely a ministerial one and that it has neither a statutory obligation, nor the resources and expertise, to review patents for their accuracy and relevance to the approved and marketed form of Paxil.

ARGUMENT

I. FDA CAN AND MUST "LOOK BEHIND" A PATENT BEFORE PERMITTING ITS LISTING IN THE ORANGE BOOK

A. FDA's Practice Contravenes The Intent Of The Hatch-Waxman Amendments

In enacting the Hatch-Waxman Amendments, Congress intended to foster competition in the drug industry by expediting the approval of safe and effective generic drugs, thereby lowering the cost of medicines to all consumers. See H.R. Rep. No. 98-857, Part I, 98th Cong., 2d Sess. 14, 16-17 (1984), reprinted in 1984 U.S.C.C.A.N. 2647, 2649-50. "Facing the classic question of the appropriate trade-off between greater incentives for the invention of new products and greater affordability of those products, Congress struck a balance between expediting generic drug applications and protecting the interests of the original drug manufacturers." Abbott Laboratories

² NAPM takes no position on the question of whether SmithKline's patents are in fact infringed.

v. Young, 920 F.2d 984, 985 (D.C. Cir. 1990), cert. denied, 502 U.S. 819 (1991). See also Mead Johnson Pharm. Group v. Bowen, 838 F.2d 1332, 1333 (D.C. Cir. 1988) ("purpose of this legislation was to increase competition in the drug industry by facilitating the approval of generic copies of drugs"). Congress spoke clearly in its passage of the Hatch-Waxman Amendments, to reduce health care costs through generic competition and make "more low cost generic drugs" available to consumers. H.R. Rep. No. 857 at 14, 1984 U.S.C.C.A.N. at 2647. The Court of Appeals for this Circuit has recognized that the availability of affordable, safe and effective medicines is an important public health matter:

[F]or poorer people -- the users for whom access to generic drugs is most important -- a pecuniary savings on drugs may have important health benefits. The difference between sinking, say, 3% and 20% of one's income into pharmaceuticals spells a large difference in the range of economically accessible food and shelter.

In re: Barr Labs., Inc., 930 F.2d 72, 75 (D.C. Cir. 1991).

FDA contravenes this congressional intent when it lists in the Orange Book patents which, as with SmithKline's two patents for paroxetine hydrochloride anhydrate, on their face do not claim the approved listed drug.³ That the patents at issue do not "claim" the listed drug Paxil is

³ SmithKline argues that the patents at issue were properly listed. In support of its view that FDA properly listed the '132 and '423 patents in the Orange Book, SmithKline cites Ben Venue Lab., Inc. v. Novartis Pharm. Corp., 10 F. Supp. 2d 446 (D.N.J. 1998). SmithKline Brief at 7-8. Although SmithKline contends that the Ben Venue decision stands for the proposition "that patents on drug substances are properly listed regardless of differences in hydration between what is claimed in the patent and what appears in the specific product," that assertion is incorrect. In Ben Venue, the court concluded that a patent regarding the pentahydrate form of the active drug ingredient (five chemically bound molecules of water with each molecule of the active drug ingredient) was properly listed in the Orange Book in connection with an approved drug product in lyophilized (freeze-dried, containing no water of hydration) form, because "[t]here is no dispute that the patented pentahydrate form of the Aredia drug substance is used in the manufacture of the

(continued...)

clear. In the Hatch-Waxman Amendments, Congress intended to define the word "claim" as the term is widely meant and applied in patent law. Hoechst-Roussel Pharmaceuticals, Inc. v. Lehman, 109 F.3d 756, 758 (Fed. Cir. 1997); H.R. Rep. No. 98-857, pt. I, 98th Cong., 2d Sess. 37 (1984), reprinted in 1984 U.S.C.C.A.N. 2647, 2670. Patent law has defined the term "claim" consistently since the Patent Act of 1836 to describe the invention that an applicant believes is patentable and the patent owner's property rights in that invention. Hoechst-Roussel, 109 F.3d at 758; Corning Glass Works v. Sumitomo Elec. U.S.A., Inc., 868 F.2d 1251, 1257-58 (Fed. Cir. 1989). "Claims" within a patent define the invention that the patent owner or its assignees may prevent others from making, using, or selling for the life of the patent. Hoechst-Roussel, 109 F.3d at 760.

The Patent and Trademark Act was amended by the Hatch-Waxman Amendments to include language identical to the "claims" language added to the FDC Act. 35 U.S.C. § 156. Specifically, pursuant to those provisions, "[t]he term of a patent which claims a product, a method of using a product, or a method of manufacturing a product shall be extended" from the original expiration date of the patent if, among other things, the product had been subject to a

³(...continued)

Aredia drug-product." 10 F. Supp.2d at 458. The court concluded that the patented drug substance was properly listed in the Orange Book because it was used as a component during the manufacturing process of the brand product. 10 F. Supp.2d at 456-57. On that basis, the Ben Venue decision is readily distinguishable. Here, there is no contention that the anhydrate form of paroxetine hydrochloride, which is the subject of the '132 and '423 patents, was ever used as a component in the manufacture of Paxil, which contains the hemihydrate form of paroxetine hydrochloride.

regulatory review period before its commercial marketing or use.⁴ 35 U.S.C. § 156(a). The Patent and Trademark Office (PTO) has therefore had occasion to apply its well-established principles regarding the scope of a "claim" to the question of whether a patent on a chemical can be said to "claim" a drug containing a related form of that chemical within the meaning of the Hatch-Waxman Amendments. The PTO determined that it cannot. In Hoechst-Roussel, the Federal Circuit reviewed this determination and agreed with the PTO. Id. at 757.

In Hoechst-Roussel, the patent holder argued that it was entitled to an extension of its patent for the compound 1-hydroxy-tacrine, to compensate for the time during which FDA was reviewing the drug COGNEX®. The active ingredient in COGNEX, however, is tacrine hydrochloride. Although tacrine hydrochloride is metabolized into 1-hydroxy-tacrine in the body, the active ingredient in the drug product is tacrine hydrochloride, not 1-hydroxy-tacrine. Thus, the Hoechst-Roussel patent at issue did not claim the active ingredient that FDA had approved in COGNEX. 109 F.3d at 757-59.

The PTO and, ultimately the Federal Circuit, held that Hoechst-Roussel was not entitled to extend the life of its patent because the company had not claimed in its patent either the active ingredient that received FDA approval, tacrine hydrochloride, or a method of using tacrine hydrochloride. Instead, Hoechst-Roussel claimed the "chemically distinct" compound 1-hydroxy-tacrine. Because 1-hydroxy-tacrine, described in the patent, was chemically distinct from the active ingredient in the approved drug COGNEX, Hoechst-Roussel's patent did not "claim" the

⁴ The patent extension provisions thus give back to a patent holder time lost in the NDA process during which FDA reviews a drug for regulatory approval. Hoechst-Roussel, 109 F.3d at 757.

drug that FDA had approved, and the company was not entitled to an extension of its patent under Hatch-Waxman. 109 F.3d at 759.

The Hoechst-Roussel case demonstrates that a patent does not "claim" a listed drug for purposes of the Hatch-Waxman Amendments if its subject is an ingredient that is chemically distinct from the active ingredient in the listed product. While the Federal Circuit was interpreting a different part of the Waxman-Hatch Amendments than is at issue here, it is a fundamental principle of statutory construction that identical words or terms used in different parts of the same act are intended to have the same meaning. Estate of Cowart v. Nicklow Drilling Co., 505 U.S. 469, 479 (1992); Sorenson v. Dept. of Treasury, 475 U.S. 851, 860 (1986). Consequently, the terms "claim" and "claims" can be inferred to have the same meaning in Title II, Section 201(a) of the Hatch-Waxman Amendments (codified at 35 U.S.C. § 156) and Title I, Section 102(a)(1) and (2) of the Hatch-Waxman Amendments (codified at 21 U.S.C. § 355(b)(1) and (c)(2)).

The Federal Circuit determined that Hoechst-Roussel's patent could not "claim" COGNEX because the patent described a compound which was chemically distinct from the approved active ingredient. Similarly, the Paxil drug that FDA approved contains paroxetine hydrochloride hemihydrate, a chemical which is, unquestionably, chemically distinct from the anhydrate forms of paroxetine hydrochloride claimed in SmithKline's '132 and the '423 patents. Because paroxetine hydrochloride anhydrate is chemically distinct from paroxetine hydrochloride hemihydrate, the '132 and '423 patents do not "claim" Paxil and FDA should not have been listed the patents in the Orange Book.

B. FDA Is Obligated Under The FDC Act To Look Behind The Patent Information SmithKline Submitted For Orange Book Listing

As discussed above, section 355 sets forth substantive requirements for the type of patent information that is properly submitted to FDA for listing in the Orange Book. These provisions do not on their face require FDA to "rubber stamp" a patent listing sought by a brand name drug company. Congress has given FDA ample authority to police patent listing submissions, by giving it the statutory authority to refuse to approve, or to withdraw approval of, an NDA for which inappropriate patent information is submitted. For example, 21 U.S.C. § 355(d)(6) provides that FDA shall refuse to approve an NDA for a brand name product if "the application failed to contain the patent information prescribed by [21 U.S.C. § 355(b)]." Similarly, section 355(e) provides that FDA shall withdraw approval of an NDA if "the patent information prescribed by [section 355(c)] was not filed" in a timely fashion. Moreover, section 355(e)(5) allows FDA to withdraw approval of an NDA if "the application contains any untrue statement of a material fact." (There can be no doubt that the patent information submitted to FDA is "material.") Finally, the submission of false information not only gives FDA the authority to withdraw approval (discussed above), it can also result in criminal prosecution. See 18 U.S.C. § 1001. These provisions demonstrate that FDA does indeed have extensive authority to police the accuracy of patent listings.

Not only does FDA have the authority to look behind submitted patent information, FDA is obligated to do so before listing it in the Orange Book. The FDC Act requires NDA applicants to submit to FDA only those patents that claim the drug for which the applicant submitted the application. 21 U.S.C. § 355(b)(1) and (c)(2). FDA itself acknowledged this statutory directive,

stating that “[f]or patents that claim a drug substance or drug product, the applicant shall submit information only on those patents that claim a drug product that is the subject of a pending or approved application, or that claim a drug substance that is a component of such a product.” 21 C.F.R. § 314.53(b).

As explained above, the Hatch-Waxman Amendments impose an obligation on FDA to ascertain that patent information submitted to FDA is relevant to the NDA being referenced.

Contrary to this obligation, however, FDA has taken the position that it:

does not have the resources or the expertise to review patent information for its accuracy and relevance to an NDA. Therefore, the agency declines . . . to ensure that patent information is complete and relevant to an NDA The agency believes that the . . . applicant’s potential liability if it submits an untrue statement of material fact, will help ensure that accurate patent information is submitted.

59 Fed. Reg. 50,338, 50,345 (1994).

FDA’s reading of the statute as providing the agency with the authority to accept, without verifying, any patent information submitted by an NDA applicant and to publish such unverified information in the Orange Book, and then to refuse to examine a patent listing even when challenged,⁵ is an unlawful reading of the statute. Under established canons of statutory construction, a statute must be read in such a way as to give effect to all of its provisions. See United States v. McGoff, 831 F.2d 1071, 1080 (D.C. Cir. 1987). FDA’s reading of the statute does not accomplish this objective because it allows an NDA holder to submit and have listed patents which are simply not relevant to the NDA drug product and the statutory standard for

⁵ 21 C.F.R. § 314.53(f) provides that FDA will not change challenged patent information without the NDA sponsor’s agreement.

Orange Book listing. This interpretation thus ignores the phrase, in section 355(b) (and substantially identical language in section 355(c)), that sets forth the substantive limitation for Orange Book listing: "patent which claims the drug for which the applicant submitted the application."

It is well-established that the provisions of the FDC Act are to be construed liberally so as to promote the public health. United States v. Rutherford, 442 U.S. 544, 553 (1979). This goal, as discussed above, is directly fostered by the availability of lower cost, but safe and effective, generic drugs. Serono Laboratories, Inc. v. Shalala, 158 F.3d 1313, 1326 (D.C. Cir. 1998) (public interest aided by Hatch-Waxman Amendments which increase availability of lower cost drugs and enable some consumers to afford drug products where, previously, they could not); H.R. Rep. No. 98-857 at 14, 1984 U.S.C.C.A.N. at 2647. To effectuate these goals, FDA has wide authority under the FDC Act to look behind the bald assertions of NDA patent submissions to determine whether the applicant has complied with the FDC Act and whether the patent in question actually claims the drug FDA approved.

The provisions of the FDC Act that require the submission and subsequent publishing of patent information serve the very specific purpose of identifying those patents which claim the NDA-approved drug. The statutory scheme Congress envisioned can work only if read to impose upon FDA an obligation to verify that patent information that is submitted to it for publication is relevant to the NDA for which it is submitted, in the sense that the patent in fact claims the drug FDA is reviewing and approves.

FDA, on the other hand, reads the statute as providing it with the authority to accept and publish patent information that it has not verified as relevant. See 59 Fed. Reg. at 50,345 (1994).

Although normally an agency's interpretation of its organic statute is entitled to significant deference, Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc., 467 U.S. 837, 842-45 (1984), that deference is not to be applied to alter the clearly expressed intent of Congress. K Mart Corp. v. Cartier, Inc., 486 U.S. 281, 291 (1988); Chevron, 467 U.S. at 842-43. See also FDA v. Brown & Williamson, ___ U.S. ___, 120 S.Ct. 1291, 1297 (2000) ("although agencies are generally entitled to deference in the interpretation of statutes that they administer, a reviewing court, as well as the agency, must give effect to the unambiguously expressed intent of Congress"). Thus, "if employment of an accepted canon of construction illustrates that Congress had a *specific* intent on the issue in question, then the case can be disposed of" by rejecting any interpretation of the statute that is contrary to that intent. Halverson v. Slater, 129 F.3d 180, 184 (D.C. Cir. 1997) (citations omitted) (emphasis in original). Employing these principles, FDA's policy of refusing to look behind a patent submission is contrary to Congress' intent and must be rejected.

II. FDA HAS UNLAWFULLY DELEGATED ITS OBLIGATIONS UNDER THE FDC ACT TO PRIVATE INDUSTRY

Because FDA has announced its refusal to "look behind" the patent information submitted by an NDA holder to determine whether the information was properly submitted, the policy effectively delegates to the NDA holder FDA's duty to verify the relevancy of patent information submitted by that NDA holder. This policy is, thus, improper because, contrary to established principles of constitutional and administrative law, it delegates a public duty to a private entity. See Carter v. Carter Coal Co., 298 U.S. 238, 310-11 (1936); Sierra Club v. Lynn, 502 F.2d 43, 59 (5th Cir. 1974). This unlawful delegation is particularly noxious because of the large market incentives for NDA holders to submit questionable patent information. See Sierra Club v. Sigler,

695 F.2d 957, 963 n.3 (5th Cir. 1983) ("an agency may not delegate its public duties to private entities . . . particularly private entities whose objectivity may be questioned on grounds of conflict of interest"). Accord Pistachio Group of the Ass'n of Food Industries v. United States, 671 F. Supp. 31, 35 (Ct. Int'l Trade 1987). In fact, the policy amounts to ceding to the regulated industry control over entry into the market of competitive products, contrary to the clear intention of Congress. See National Ass'n of Regulatory Utility Comm'rs v. FCC, 737 F.2d 1095, 1143-44 (D.C. Cir. 1984) (an agency cannot "cede to private parties . . . the right to decide contests between themselves").

This improper delegation is enough to invalidate FDA's policy. As the United States Court of Appeals for the Fifth Circuit has explained, although an agency is not expected to ignore useful and relevant information merely because it emanates from an applicant, "[t]his does not mean it may substitute the applicant's efforts and analysis for its own." Lynn, 502 F.2d at 59. Decisions that alter agency outcomes "cannot be abandoned to [private entities] and isolated from all types of review, administrative or judicial, merely for reasons of convenience." Pistachio Group, 671 F. Supp. at 35.

FDA interprets the FDC Act to give it the authority to accept patent information for publication in the Orange Book without first verifying that the information received from the NDA applicant meets the statutory criteria for such submission. Responsibility for ensuring that the information being published meets the statutory criteria is thus, inappropriately, left entirely to the submitter of the information. As discussed above, this position amounts to an unconstitutional delegation of FDA's own statutory obligations to police the patent certification requirements of the

Waxman-Hatch Amendments. FDA's interpretation must therefore be rejected because, if accepted, it would render the patent listing provisions of the FDC Act themselves unconstitutional.

Federal statutes are, however, "to be construed to avoid serious doubts as to their constitutionality." Communications Workers of America v. Beck, 487 U.S. 735, 762 (1988). When faced with such doubts, courts first look to "whether it is fairly possible to interpret the statute in a manner that renders it constitutionally valid." Id. In this instance, a constitutionally valid interpretation of the patent and certification provisions of 21 U.S.C. § 355(b)(1) and (c)(2) is readily available. To avoid an improper and unconstitutional delegation to private industry, FDA need only interpret the language of section 355(b)(1) and (c)(2) as carrying with it an obligation that FDA confirm that the applicant has complied with the statutory criteria and has submitted only patents that actually claim the drug. Such an interpretation is not only in accord with the stated intent of Congress to speed lower cost, safe, and efficacious drugs to the public, but also saves these provisions of the FDC Act from what would otherwise be a constitutional infirmity.

III. FDA'S POLICY AS APPLIED, IS INVALID BECAUSE IT IS ARBITRARY AND CAPRICIOUS AND OTHERWISE CONTRARY TO LAW

A. FDA Has Articulated No Reasonable Basis For Listing A Patent Where The Agency Is On Notice That The Patent Does Not Claim The Approved Drug

As noted, the agency defends its policy by claiming an inability to take any other course because of limitations on its resources. This explanation is, however, untenable. FDA has more than sixty attorneys in its Office of General Counsel alone. In addition, the agency has hundreds of technical and scientific personnel who do nothing but assess the composition, formulation, and use of pharmaceutical products. The agency thus clearly has the scientific and legal capacity to

determine whether a particular patent claims a particular drug. Moreover, a lack of resources by itself cannot constitute a sufficient reason for refusing to give effect to portions of an agency's organic statute, particularly where there is no evidence that the agency sought the required resources. "A member of the President's Cabinet, charged with executing the law should not be . . . allowed to argue that his own failure to request funding to comply with an Act of Congress is a proper excuse for his failure to pursue his statutory obligations." Animal Legal Defense Fund v. Madigan, 781 F. Supp. 797, 805 n.5 (D.D.C. 1992).

In many cases, moreover, FDA will be able to make a determination that a patent should not be listed without expending additional resources or without requiring expertise that it does not already possess. In the case of Paxil, for example, the agency was on notice that the '132 and '423 patents should not have been listed because SmithKline's patent submissions stated on their face that the patents claimed a different form of the active ingredient than that present in the approved product. No additional resources or expertise would have been needed to determine whether the patents claim the approved drug. It is well settled that an agency must articulate a satisfactory explanation for its actions, including a rational connection between the facts found and the choice made. Motor Vehicles Mfrs. Ass'n v. State Farm Mut. Ins., 463 U.S. 29, 43 (1983). Because the articulated rationale does not provide any reasonable basis for FDA's policy, particularly as applied in situations where no additional resources or expertise are required, the policy is arbitrary and capricious and must be overturned. 5 U.S.C. § 706 (2)(A).

B. FDA's Policy, As Applied, Is Contrary To Law Because It Constitutes A Failure To Enforce A Clear Statutory Mandate

A court must reject an agency's interpretation of its organic statute if the interpretation is "inconsistent with the statutory mandate or [would] frustrate the policy that Congress sought to implement." FEC v. Democratic Senatorial Campaign Comm., 454 U.S. 27, 32 (1981). See also Public Service Comm'n of New York v. Mid-Louisiana Gas Co., 463 U.S. 319, 339 (1983) (overturning the Federal Energy Regulatory Commission's interpretation of the Natural Gas Policy Act of 1978 because the interpretation was "contrary to the history, structure, and basic philosophy of the [Act]"). The District of Columbia Circuit has re-affirmed this principle on numerous occasions. Commonwealth of Massachusetts v. DOT, 93 F.3d 890, 892 (D.C. Cir. 1996); Kerr-McGee v. NRC, 903 F.2d 1, 6 (D.C. Cir. 1990); United Food and Commercial Workers Int'l. Union Local No. 576, AFL-CIO v. N L R B, 675 F.2d 346, 351 (D.C. Cir. 1982).

It was the clear intention of Congress that only patents that claim the drug for which an NDA was submitted be listed in the Orange Book as relevant to that NDA. Moreover, as explained in detail above, Congress, in enacting the Hatch-Waxman Amendments, intended to make lower cost pharmaceutical products available to the public as quickly as possible. See e.g., Barr, 930 F.2d at 79. FDA's interpretation of the statute as not requiring it to verify that patent information submitted by NDA holders is relevant to the referenced NDA is entirely inconsistent with this congressional objective and therefore cannot be allowed to stand.

SmithKline argues that the fact that the statute provides that, upon the submission of patent information by the holder of an approved NDA, FDA "shall" publish it demonstrates an

“unequivocal” decision by Congress to “impose a mandatory duty on FDA to publish the information submitted by the NDA holder.” SmithKline Brief at 6.

As the D.C. Circuit long ago explained, however,

Although . . . the use of the word “shall” in a statute is “normally the language of command,” . . . “shall” may sometimes “be directory only,” and its interpretation “depends upon the background circumstances and context in which [it is] used and the intention of the legislative body . . . which used [it].”

Buckley v. Valeo, 519 F.2d 821, 893 n.191 (D.C. Cir. 1975) (citations omitted), aff’d in part, rev’d in part on other grounds, 424 U.S. 1, 96 (1976). NAPM sees no unequivocal mandatory duty to accept patent information without verifying its relevance, despite the fact that the statute uses the word “shall.” In fact, the existence of such a mandatory duty to publish anything submitted by an NDA holder would allow NDA holders to have FDA list patents that are obviously unlistable under the statutory criteria.

To the contrary, FDA has an unequivocal duty to ensure that patents submitted for publication meet the statutory criteria. FDA’s policy of refusing to carry out this duty is impermissible, as an agency does not have discretion to refrain from enforcing a clear statutory mandate. National Wildlife Fed’n v. EPA, 980 F.2d 765, 770 (D.C. Cir. 1992).⁶

⁶ Concededly, some agency enforcement decisions are committed to agency discretion by law, and therefore unreviewable, absent meaningful standards in the statute for judicial review. Heckler v. Chaney, 470 U.S. 821, 832-33 (1985). Heckler does not, however, preclude this Court from rejecting FDA’s refusal to give effect to the statutory provisions at issue here, because the D.C. Circuit has held that Heckler is not directly applicable where a challenge is to a statutory interpretation, rather than to a particular enforcement decision. National Wildlife Fed’n v. EPA, 980 F.2d at 773. “[W]hen a legal challenge focuses on an announcement of a substantive statutory interpretation, courts are emphatically qualified to decide whether an agency has acted outside the bounds of reason” Int’l Union, United Auto., Aerospace, and Agric. Implement Workers v. Brock, 783 F.2d 237, 245-46 (D.C. Cir. 1986). In any case, unlike the situation in Heckler, here there is a meaningful standard in the statute, which is quite reviewable by the courts. The statute states clearly that patents are to be listed if they claim the drug. Thus, FDA’s interpretation

(continued...)

CONCLUSION

For the foregoing reasons, NAPM urges this Court to adopt Apotex's position that FDA is required to review patent information to ensure it meets statutory requirements before Orange Book listing.

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Respectfully submitted,

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⁶(...continued)
of the statute as providing it with the authority to list patents in the Orange Book without verifying that the patents are relevant to the NDA for which they are listed is not the type of discretionary judgement concerning the allocation of enforcement resources that Heckler shields from review.