UNITED STATES OF AMERICA
FEDERAL TRADE COMMISSION
WASHINGTON, D.C. 20580

Bureau of Competition
Policy Planning

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VIA FEDERAL EXPRESS

Dockets Management Branch
Food and Drug Administration
Department of Health & Human Services
Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

CITIZEN PETITION

The Bureau of Competition and Policy Planning Staff of the Federal Trade Commission ("FTC") submit this Citizen Petition to the Commissioner of Food and Drugs pursuant to 21 C.F.R. §§ 10.25(a) and 10.30 concerning certain issues relating to patent listings in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"). We request that the FDA clarify these issues, on an expedited basis, via industry guidance or other means that the FDA considers appropriate.

In recent years, the FTC has gained significant experience concerning competition in the pharmaceutical industry. In particular, the Commission has brought a number of antitrust enforcement activities affecting both the branded and generic drug industries. Last year, the Commission announced plans to conduct an extensive study – pursuant to Section 6(b) of the FTC Act, 15 U.S.C. § 46(b) – of U.S. generic drug competition (the "Study"). The Study will enable the FTC to provide a more complete picture of how generic drug competition has developed under the Hatch-Waxman Act. *See* 66 Fed. Reg. 12512 (Feb. 27, 2001); 65 Fed. Reg. 61334 (Oct. 17, 2000); "FTC to Study Generic Drug Competition," (Oct. 11, 2000) <http://www.ftc.gov/opa/2000/10/genericdrug.htm>. The Office of Management and Budget ("OMB") cleared the Study on April 6, 2001, following the closure of two public comment periods. The FTC will obtain factual information for the Study from name-brand pharmaceutical and generic drug manufacturers through interrogatories and document requests.

The Study seeks information concerning a variety of practices that may have an impact on competition in the pharmaceutical industry, including the possible improper or untimely listing of patents by name-brand pharmaceutical companies in the Orange Book. In this connection, the Study requests name-brand companies to "[i]dentify all patents that the company has filed in the Orange Book and the date of listing (regardless of whether currently listed in the Orange Book) relating to each Drug Product for which the company has been notified of the filing of an ANDA by another person [, and indicate] if the patent(s) was (were) filed in the Orange Book after the

company received approval of the New Drug Application. . . ." 66 Fed. Reg. at 12520. The Study also requests generic drug companies to "[i]dentify each instance in which the company has asserted before a court or before the FDA that a patent was improperly or untimely listed as defined in 21 U.S.C. § 355(b) or (c)." *Id.* at 12521. This information is crucial to determine how often and when name-brand companies have filed new patents after the FDA has approved the drug product. *Id.* at 12517. The consequences of such filings are significant, because as "long as the patent remains listed, ANDA applicants must still make a paragraph IV certification, potentially triggering the 30-month stay of FDA approval of generic drug applications." *Brief of Federal Trade Commission as Amicus Curiae In American Bioscience, Inc., v. Bristol-Myers Squibb Company* (Sept. 1, 2001) at 10, <http://www./ftc.gov/os/2000/09/amicusbrief.pdf>. Thus, such listings can affect when generic competition starts. 66 Fed. Reg. at 12517.

During the public comment period prior to OMB approval of the Study, the FTC received several comments that supported the Commission's proposed examination of Orange Book patent listing practices. For example, Microbix indicated that generic competition can be delayed on name-brand drug products if name-brand companies newly list "irrelevant and undefendable" patents in the Orange Book near the expiration of the name-brand drug product's original patents. Generic competition is delayed because the FDA is prohibited from approving a generic version of the name-brand product for 30 months in order to resolve litigation over the newly-listed patents. Microbix Comment at 2 (Dec. 18, 2000). *See also* General Motors Comment (Dec. 18, 2000) at 2, NACDS Comment at 1-2 (Dec. 18, 2000). These comments are available on the FTC's website at <http://www.ftc.gov/os/comments/genericdrugstudy/index.htm>.

As the FTC proceeds with the Study and continues to investigate methods of competition in the pharmaceutical industry, it would be helpful if the FDA provided further guidance concerning the proper application of its regulations that require certain patents to be listed in the Orange Book. We describe below our interpretation of the pertinent statutory provisions, regulations, and the FDA statements regarding particular drug products. We seek your views on our interpretations. For example, we seek clarification of the FDA's response to a prior Citizen Petition submitted on behalf of Apotex concerning its pending abbreviated new drug application ("ANDA") for the marketing of a generic form of Paxil, which is marketed by GlaxoSmithKline ("GSK", formerly SmithKline Beecham). The Apotex Citizen Petition was submitted to the FDA on February 3, 2000 in Docket No. 00P-0499/CP1. The FDA responded to that petition on November 21, 2000 (the "Citizen Petition Response" (attached)).

Two-Prong Listing Test

First, we seek guidance concerning the criteria that a patent must meet before it can be listed in the Orange Book. We understand that the governing regulation, 21 C.F.R. § 314.53(b), and the statutes on which it is based, 21 U.S.C. §§ 355(b)(1), (c)(2), require that a patent satisfy both of two independent prongs before qualifying for Orange Book listing. To satisfy the first prong, a patent must claim a drug product[1] or method of using a drug product that is the subject of a new drug application ("NDA") or an amendment or supplement to it. To satisfy the second

[1] The interpretation in this regulation of the term "drug" as meaning the "drug product" is consistent with the FDA's position in *Pfizer v. FDA*. 753 F. Supp. 171 (D. Md. 1989).

prong, the patentee must be able to reasonably assert a claim for infringement of the listed patent against someone who manufactures, uses or sells the drug product that is the subject of the NDA. In addition, we understand that the language in 21 C.F.R. § 314.53(b) that follows the two-prong test (*i.e.*, the text following the first full sentence of that section) is merely explanatory language and does not expand the scope of this regulation. Please comment on whether our understanding comports with the FDA's interpretation of 21 C.F.R. § 314.53(b) and 21 U.S.C. §§ 355(b)(1), (c)(2).

Listing of Patents Claiming an Unapproved Aspect of an Approved Drug

Second, we seek guidance concerning whether under the first prong, an NDA holder can list a patent claiming an unapproved aspect of an approved drug. The regulation requires that a patent must "claim[] the drug or a method of using the drug that is the subject of the new drug application . . . ." 21 C.F.R. § 314.53 (b). We read this provision to require that after a drug is approved, a listed patent must claim the drug product as approved by the FDA *in all respects*. We understand that any patent claiming only an unapproved component, an unapproved formulation, or an unapproved use of a drug product cannot satisfy the first prong. Similarly, we understand that any patent claiming an aspect of an approved drug that would require prior FDA approval (*e.g.*, a supplemental NDA) before incorporation or implementation in a marketed drug product – such as a component of the drug, its formulation, a condition of use, an indication, or labeling information – cannot satisfy the first prong.

We note that the FDA made statements consistent with this position in a recent patent listing dispute in federal court between Biovail (name-brand) and Andrx (generic) concerning Biovail's Tiazac product.[2] In that court proceeding, the FDA stated its preliminary conclusion that Biovail was required to file a supplement to its NDA for a change in manufacturing process and formulation that had not been previously approved. The FDA further clarified that the patent at issue must claim the approved formulation of Tiazac to be properly listed in the Orange Book. According to the FDA, to the extent the patent claimed only the new, unapproved formulation, it was not properly listed.

With respect to the listing of patents on unapproved aspects of an approved drug product, we also are seeking elaboration concerning the statement in the Citizen Petition Response that "[p]atents must be listed if they claim the drug substance, or active ingredient, of an approved drug product, or if they claim a drug substance that is the component of such a product." (Response at 6.) We understand the FDA's statement to be simply a restatement of the first prong and consistent with our understanding of the first prong and the criteria for listing drug substance patents set forth above. We understand that any patent claiming only an unapproved component cannot satisfy prong one. Likewise, we understand that if a drug substance patent claims only a chemical compound which the FDA has not approved as a component of an approved drug product, that patent may not be listed. In particular, we understand this to be the

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[2] *See* "Federal Defendant's Notice of Change in Position," *Andrx Pharmaceuticals, Inc., v. Biovail Corp.* (Case No. 01-6194-CV-DIMITROULEAS) (S.D. Fla.) (pleading filed on Feb. 28, 2001).

case even when the claimed unapproved chemical compound differs only in its water of hydration from an approved component.

Please comment on whether our understanding comports with the FDA's interpretation of 21 C.F.R. § 314.53(b) and 21 U.S.C. §§ 355(b)(1), (c)(2), and the related statements in the Citizen Petition Response.

Definition of "Drug Product"

Third, we seek guidance on the meaning of the term "drug product" as defined in 21 C.F.R. § 314.3(b) and as applied in 21 C.F.R. § 314.53(b), and the effect of that definition on the analysis of the second prong. We understand that the relevant "drug product" is only that product which is the subject of the NDA as approved by the FDA. Consequently, in analyzing "whether a claim of patent infringement can reasonably be asserted" against a drug product, one may only consider the drug product in the form approved by the FDA. We understand that for any aspect of a drug product which is subject to FDA approval – including for instance, a drug product's components, formulation, a condition of use, an indication, or labeling information – only the aspects as approved may be considered in the infringement analysis of the second prong. Please comment on whether our understanding comports with the FDA's interpretation of 21 C.F.R. § 314.53(b) and 21 U.S.C. §§ 355(b)(1), (c)(2).

Listing of Drug Substance Patents

Finally, we seek guidance on whether a patent claiming only a chemical compound that the FDA has not approved for use as the drug substance in an approved drug product may be listed. The regulation requires that in order for a drug substance patent to be listed, it must claim a drug substance that is a component of a drug product that is the subject of a pending or approved NDA. *See* 21 C.F.R. § 314.53(b) and 21 U.S.C. §§ 355(b)(1), (c)(2). We understand that if a drug substance patent claims only a chemical compound which the FDA has not approved as a component of an approved drug product, that patent may not be listed.

For example, the Citizen Petition Response states "[p]lease note that for purposes of the same active ingredient requirement in 505(j), FDA considers anhydrous and hemihydrous forms of drug substances to be pharmaceutical equivalents and to contain the same active ingredient." (Response at 6, n. 16.) We understand the FDA's statement to be limited to the issue of whether a drug product, submitted for approval through an ANDA, satisfies the requirement of 21 U.S.C. § 355(j) that it contain the "same active ingredient" as the reference listed drug, even when the active ingredient of the ANDA product and the listed drug differ by water of hydration. For example, in the case of Paxil, the statement is limited to whether the anhydrate and hemihydrate forms of paroxetine hydrochloride are pharmaceutically equivalent and considered to be the same active ingredient for purposes of 21 U.S.C. § 355(j).

We do not read this statement in the Citizen Petition Response as having any bearing on the requirements for listing patents in the Orange Book as set out in 21 U.S.C. §§ 355(b)(1), (c)(2) and 21 C.F.R. § 314.53 (b). In particular, we understand the fact that the FDA may consider one chemical compound pharmaceutically equivalent to, or the same active ingredient as, another chemical compound for purposes of 21 U.S.C. § 355(j) does not alter the requirement

of 21 C.F.R. § 314.53(b) that a listed drug substance patent must claim a component of an approved drug product. We further understand that it is possible for a chemical compound to be pharmaceutically equivalent to an approved active ingredient and considered the same active ingredient for purposes of 21 U.S.C. § 355(j), but not itself be approved as a component of the drug product. For example, although the FDA considers the anhydrous form of paroxetine hydrochloride to be the same active ingredient as the hemihydrous form of paroxetine hydrochloride for purposes of 21 U.S.C. § 355(j), the anhydrous form is not an approved component of the drug product, Paxil.

Please comment on our understanding of 21 C.F.R. § 314.53(b) and 21 U.S.C. §§ 355(b)(1), (c)(2), and the related statements in the Citizen Petition Response.

We appreciate your consideration of this matter.

Respectfully submitted,

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The Bureau of Competition and Policy Planning Staff of the Federal Trade Commission ("FTC") submitted a Citizen Petition to the Commissioner of Food and Drugs on May 16, 2001 concerning certain issues relating to patent listings in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"). This letter amends that petition to include the environmental impact exclusion and certification required under 21 CFR § 25.30.

Environmental Impact

The action requested by this Petition is subject to a categorical exclusion pursuant to 21 C.F.R. § 25.30.

Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully submitted,

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