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May 3, 2002

By Hand Delivery

Dockets Management Branch
Food and Drug Administration
Room 1061
5630 Fishers Lane
Rockville, MD 20857

Re: Docket No. 01P-0248/00P-0499

The undersigned, on behalf of GlaxoSmithKline Corporation ("GSK"), submits this response to Apotex's April 9, 2002, letter from Hugh Moore to Daniel Troy requesting that FDA expedite its response to the citizen petition filed by the Federal Trade Commission (Docket No. 01P-0248). That petition seeks "further guidance" on the requirements for listing patents in FDA's Approved Drug Products with Therapeutic Equivalence Evaluations ("Orange Book") through "clarification" of FDA's denial, dated November 21, 2000, of a citizen petition submitted by Apotex (Docket No. 00P-0499) that asked FDA to remove from the Orange Book information on certain GSK patents covering paroxetine hydrochloride.[1]

GSK takes this opportunity to make two brief points. First, the case law continues to develop in a manner entirely consistent with GSK's prior stated positions on patent listings. In particular, the Federal Circuit recently made clear that "whether the patent

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[1] On July 19, 2001, GSK responded to FTC's citizen petition, demonstrating, first, that the listing issues raised by the Apotex and FTC petitions have been raised in litigation and that FDA should defer resolution of these issues to the courts presently adjudicating them and, second, that the challenged listing are proper in any event. Since then, the district court hearing Apotex's case against FDA and GSK in Washington ruled in FDA's favor on the claims against the Agency and transferred the claims against GSK to the district court hearing the patent cases in Philadelphia. Apotex has appealed the decision in FDA's favor.

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claims the drug product that is being actually marketed has nothing to do with the propriety of the listing of the patent in the Orange Book" – thus rejecting the entire basis on which Apotex filed its initial citizen petition and on which it has pursued its litigation.[2] FDA previously refused to delist the GSK patents in a well-reasoned decision denying Apotex's citizen petition, and it continues to defend that decision in court. There is no need for FDA to devote further resources to "clarifying" its views by way of responding to yet another citizen petition. If any additional guidance is necessary, it can come from the appellate and district courts that are currently addressing the issues.[3] Indeed, any modification of FDA's

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[2] *Andrx Pharmaceuticals, Inc. v. Biovail Corp.*, 276 F.3d 1368, 1376 (Fed. Cir. 2002). "Rather," the court continued, " the critical question is the relationship of the patent to the drug products and drug substances covered by the NDA." *Id.* Here, for reasons already explored at length by both GSK and FDA (in its denial of the Apotex citizen petition), the drug substance is paroxetine hydrochloride. The patents at issue claim paroxetine hydrochloride. Indeed, the basis for Apotex's ANDA is that the various forms of paroxetine hydrochloride (anhydrous, hemihydrate) are all identical. That should be the end of the matter. *See* FDA Response to Apotex Citizen Petition at 6 n.16; *see also* Orange Book at xv, vii ("[a]nhydrous and hydrated entities, as well as the different polymorphs [i.e., different crystalline forms], are considered pharmaceutical equivalents"); *Zenith Laboratories, Inc. v. Abbott Laboratories*, No. 96-1661, 1996 U.S. Dist. LEXIS 22567 (D.N.J. Aug. 5, 1996) (patent claiming terazosin hydrochloride anhydrate listable where terazosin hydrochloride dihydrate used in the approved drug product); *Ben Venue Laboratories, Inc. v. Novartis Pharmaceutical Corp.*, 10 F. Supp.2d 446, 456 (D.N.J. 1998) (following *Zenith* and rejecting argument that patent directed to an approved active ingredient cannot be listed if the finished drug product does not contain the same form of active ingredient claimed in the patent as "contrary to FDA's regulatory interpretation, as well as contrary to common sense").

[3] See footnote 1 regarding the current litigation. Apotex has complained that it is foreclosed from raising its listing arguments in the infringement litigation, but it has studiously refused to dismiss its claims in this regard. As the Federal Circuit has stated, "as part of its inherent power to give effect to a judgment, a court may order delisting of a patent in the context of a properly filed patent-infringement suit." *Mylan Pharmaceuticals, Inc. v. Thompson*, 268 F.3d 1323, 1333 (Fed. Cir. 2001), citing *Abbott Laboratories v. Novopharm Ltd.*, 104 F.3d 1305, 1309 (Fed. Cir. 1997). In addition, the FTC has proceeded with its own enforcement work based on patent listing allegations even without additional "clarification" from FDA. *See In re Biovail Corp.*, File No. 011-0094 (Apr. 23, 2002), available at http://www.ftc.gov/os/caselist/0110094.htm. (That proceeding is irrelevant to the Paxil® situation because it involved the listing of a drug product (formulation) patent allegedly known by the NDA holder not to cover the approved drug product and the submission of an allegedly "misleading" declaration to the contrary. Here, by contrast, Apotex challenges the (continued...)

previously-stated position would be contrary to the legislative compromise of Hatch-Waxman.

Even if FDA were at liberty to somehow "clarify" its position along the lines suggested by FTC and Apotex, any such additional guidance should be provided through notice and comment rulemaking. GSK's submission of the patents in question was entirely consistent with FDA's regulation, 21 C.F.R. § 314.53. That provision, of course, is a substantive rule equally binding on FDA and private parties.[4] We would note, in particular, that the regulation contains no requirement for a declaration that a drug substance patent claims the specific drug product that is the subject of the NDA. For reasons already stated, such a requirement would be inconsistent with the case law. In any event, however, FDA would be bound to institute a new round of rulemaking if it wished to change the regulation to impose such a new limitation on patent listings for drug substance patents.[5]

Apart from being legally required, notice-and-comment rulemaking is particularly important in this case because the "interpretation" sought by the FTC raises a serious policy issue that goes to the heart of the Hatch-Waxman Act. The regulations, as interpreted by the FDA and the courts, currently provide symmetry between the forms of the active ingredient that qualify for ANDA approval and those that trigger the Orange Book listing requirement. This symmetry preserves the legislative compromise on which the Act was based. By eliminating this symmetry, the FTC's proposed change raises serious legal and policy questions that are best addressed through the open forum of notice-and-comment

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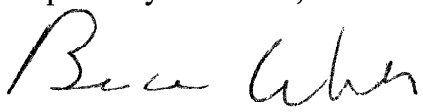
listing of drug substance patents even it concedes cover forms of the approved active ingredient.)

[4] D.C. Circuit law provides that a new "interpretation" of an existing rule must be implemented through "notice-and-comment" rulemaking. *Alaska Professional Hunters Ass'n v. FAA,* 177 F.3d 1030, 1033-35 (D.C. Cir. 1999); *see also Paralyzed Veterans of America v. D.C.Arena,* 117 F.3d 579, 586 (D.C. Cir. 1997); *Syncor Int'l Corp. v. Shalala,* 127 F.3d 90, 94-95 (D.C. Cir. 1997).

[5] *See Alaska,* 177 F.3d at 1033-35; *Paralyzed Veterans,* 117 F.3d at 586; *Syncor,* 127 F.3d at 94-95.

rulemaking. In the meantime, it would be impermissible for FDA to "clarify" its position on patent listings in a manner inconsistent with the existing regulation.[6]

Respectfully submitted,



Bruce N. Kuhlik
Counsel for GlaxoSmithKline Corporation

cc: Daniel E. Troy
Hugh L. Moore
Susan S. DeSanti

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[6] In fact, even if FDA believed that it was free under the existing regulation to change the requirements for listing of drug substance patents, it would be bound under its good guidance practice regulations to treat this as a level 1 guidance requiring issuance of a draft for public notice and comment prior to finalization. *See* 21 C.F.R. § 10.115(c)(1) and (g)(1).