October 8, 2007

Rec'd 10/24/07

Office of Generic Drugs
Food and Drug Administration
Attn: Cecelia M. Parise
7500 Standish Place
Rockville, MD 20855

Re: OGD #07-1254

To Whom It May Concern:

This letter is submitted in response to OGD's solicitation for comments posted September 26, 2007, regarding legal and regulatory issues pertaining to generic drug applications for Acarbose Tablets and any exclusivity pertaining thereto.

The purpose of this letter is to make the OGD aware that the solicitation for comments did not state a highly relevant fact, and the missing fact is critical to the exclusivity analysis. In particular, the solicitation for comments did not state the following information: U.S. Patent No. 4,904,769, the only Orange Book-listed patent, was disclaimed by the patentee. Omission or unawareness of that fact may have led to the erroneous assumption that some party is entitled to or eligible for a 180-day period of exclusivity.

The analysis provided below, which is based on the complete set of relevant facts, leads to the conclusion that no party is entitled to or eligible for a 180-day period of exclusivity. Furthermore, there is no need under the present facts for the OGD or the FDA to interpret the forfeiture provisions of 35 U.S.C. § 505(j)(5)(D) that are cited in the solicitation for comment. Any such interpretation would be premature and unnecessary.

U.S. PATENT NO. 4,904,769 HAS BEEN DISCLAIMED AND SHOULD BE DELISTED

U.S. Patent No. 4,904,769 issued on February 27, 1990 and is listed in the Orange Book for the drug product PRECOSE, the reference listed drug. Although U.S. Patent No. 4,904,769 may have been properly submitted by the NDA applicant and may have been properly listed in the Orange Book until recently, the listing of U.S. Patent No. 4,904,769 is no longer proper.

In December 2006, a disclaimer was filed with the United States Patent & Trademark Office ("USPTO") in regard to all claims of U.S. Patent No. 4,904,769 by Bayer Healthcare AG, the assignee of the patent. Subsequently, the NDA holder requested that the listed patent be removed from the Orange Book.

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35 U.S.C. § 253 provides statutory authority for the disclaimer of a complete claim of a patent by a patentee. 37 CFR § 1.321 specifies the mechanism relating to the statutory disclaimer provision. In particular, 37 CFR § 1.321(a) states (in part):

> A patentee owning the whole or any sectional interest in a patent may disclaim any complete claim or claims in a patent.... Such disclaimer is binding upon the grantee and its successors or assigns. A notice of the disclaimer is published in the Official Gazette and attached to the printed copies of the specification....

37 CFR § 1.321 further requires that a disclaimer must be signed by the patentee or an attorney or agent of record, that it identify the claims being disclaimed, that it state the patentee's ownership interest in the patent, and that the appropriate fee be paid.

According to the publicly available Patent Application Information Retrieval (PAIR) system, the disclaimer was approved by the USPTO on January 31, 2007. Approval of the disclaimer by the USPTO would appear to indicate that all requirements of 37 CFR § 1.321 were met, and that the disclaimer is binding.

Notice of the disclaimer was published in the Official Gazette on February 27, 2007. The Official Gazette notice reads as follows (see http://www.uspto.gov/web/offices/com/sol/og/2007/week09/patdisc.htm.):

> 4,904,769 - Erich Rauenbusch, Wuppertal, Fed. Rep. of Germany. HIGHLY PURE ACARBOSE. Patent dated Feb. 27, 1990. Disclaimer filed Dec. 20, 2006, by the assignee, Bayer Healthcare AG.
>
> Hereby enters this disclaimer to all claims of said patent.

Before any exclusivity issues can be considered, the threshold issue is whether the Orange Book-listed patent is properly listed under the present facts. 21 CFR § 314.53 requires that an applicant who submits a new drug application must include patent information specified in 21 U.S.C. § 355(b)(1). Specifically, 21 CFR § 314.53(b) states (in part):

> An applicant...shall submit the required information...for each patent that claims the drug or a method of using the drug that is the subject of the new drug application...***and with respect to which a claim of patent infringement could reasonably be asserted*** if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. (Emphasis added.)

Because U.S. Patent No. 4,904,769 has been disclaimed, no claim of patent infringement could reasonably be asserted against any person. Therefore, U.S. Patent No. 4,904,769 is improperly listed in the Orange Book for the drug product PRECOSE. The request submitted by the NDA holder on April 16, 2007 to remove the listed patent from the Orange Book was thus appropriate.

The proper status is that no patents should be listed in the Orange Book for the drug product PRECOSE, the reference listed drug. There is no remaining barrier to generic entry based on an enforceable patent.

NO ANDA TO PRECOSE SHOULD CONTAIN A PATENT CERTIFICATION

21 U.S.C. § 355(j)(2)(A)(vii) governs patent certifications that are required by ANDA filers. 21 U.S.C. § 355(j)(2)(A)(vii) reads in relevant part as follows:

> [An abbreviated application for a new drug shall contain] a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection ***and for which information is required to be filed under subsection (b) or (c) of this section***–
>
> (I) that such patent information has not been filed,
> (II) that such patent has expired,
> (III) of the date on which such patent will expire, or
> (IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted;
>
> ...(Emphasis added.)

Under the present facts, as described above, no patents should be listed for the drug product PRECOSE. That is, there is no patent for which information is required to be filed under subsection (b) or (c) of 21 U.S.C. § 355. Hence, no certification need be made under 21 U.S.C. § 355(j)(2)(A)(vii) by an ANDA applicant relative to the reference listed drug PRECOSE.

It has been FDA policy that an ANDA applicant's patent certification, if it becomes inaccurate due to a change in circumstances, is either automatically converted to an appropriate certification or the ANDA applicant is required to amend its factually inaccurate ANDA. This approach has been upheld by the D.C. Circuit – see *Ranbaxy Laboratories Ltd. v. U.S. Food & Drug Admin.*, 307 F. Supp. 2d 15 (D.D.C. 2004), *aff'd,* 96 Fed. Appx. 1 (D.C.Cir. 2004).

With respect to ANDA applicants for Acarbose Tablets, the FDA should either take the position that any patent certifications have automatically become moot, or that each ANDA applicant is required to amend its application to delete any patent certification.

NO EXCLUSIVITY FOR A GENERIC VERSION OF PRECOSE SHOULD BE AVAILABLE TO ANY APPLICANT

The 180-day exclusivity period available to some ANDA "first filers" is specified in 21 U.S.C. § 355(j)(5)(B)(iv). The threshold requirement for exclusivity is that the first-filer's application contain a certification described in 21 U.S.C. § 355(j)(2)(A)(vii)(IV), i.e., a "Paragraph IV Certification."

Since no ANDA applicant's application should contain a Paragraph IV Certification or a certification under any other sub-section of § 355(j)(2)(A)(vii), exclusivity cannot be triggered in favor of any first-filer.

Furthermore, in the event that OGD awards exclusivity under 21 U.S.C. § 355(j)(5)(B)(iv) to one or more first-filers under the present facts, OGD should note that such exclusivity is only vis-à-vis other ANDA applicants who also maintain a Paragraph IV Certification. Any ANDA applicant who files an application *without* a Paragraph IV Certification, or who amends its application to *remove* a Paragraph IV Certification, would not be subject to the first-filer's exclusivity period and could be approved regardless of the exclusivity period.

In other words, since there is no remaining patent barrier to generic entry, any other ANDA filer could amend its application to remove its Paragraph IV Certification. For such an applicant, OGD would have no grounds to postpone approval of the application based on enforceable patents or other exclusivity.

CONCLUSION

There is no need under the present facts for the OGD or the FDA to interpret the forfeiture provisions of 35 U.S.C. § 505(j)(5)(D) that are cited in the solicitation for comment. Any such interpretation would be premature and unnecessary.

U.S. Patent No. 4,904,769 has been disclaimed and should be removed from the Orange Book, as requested by the NDA holder. Consequently, no first-filer should be awarded a period of exclusivity based on a Paragraph IV Certification against that patent. To allow an exclusivity period under the present facts would frustrate one purpose of the Hatch-Waxman Act, which is to encourage availability of generic drugs upon the expiration of protected marketing periods for brand-name products.

For ANDAs referencing the reference listed drug PRECOSE, all applicants should be required to amend their applications to remove any patent certification, or the FDA should treat each application as containing no patent certification. There is no remaining barrier to generic entry based on an enforceable patent. That is, there is no barrier to regulatory approval, and no apparent barrier to market entry. Each ANDA applicant should be permitted to enter the market as soon as its application is otherwise approvable by OGD.

Sincerely,

Upsher-Smith Laboratories, Inc.

Sean Mahoney

Sean Mahoney
Intellectual Property Counsel