November 26, 2012

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novo nordisk®

BY HAND DELIVERY

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

Dear Sir or Madam:

REQUEST FOR ADVISORY OPINION

Pursuant to 21 C.F.R. § 10.85, Novo Nordisk Inc. ("Novo Nordisk") submits this request for an advisory opinion of the Commissioner of Food and Drugs with respect to the requirements at Sections 505(b)(1) and 505(c)(2) of the Federal Food, Drug, and Cosmetic Act ("FDC Act") to submit to the Food and Drug Administration ("FDA") for listing in the Agency's *Approved Drug Products With Therapeutic Equivalence Evaluations* ("the Orange Book") information on certain types of patents. Specifically, Novo Nordisk seeks an advisory opinion from FDA with respect to the listing of information for certain patents that claim a pre-filled drug delivery device.

I. Issues Involved

Novo Nordisk markets several approved drug products – including NovoLog ® (insulin aspart [rDNA origin] injection) (NDA No. 020986), NovoLog® Mix 70/30 (70% insulin aspart protamine suspension and 30% insulin aspart [rDNA origin]) injection (NDA No.021172), Levemir® (insulin detemir [rDNA origin] injection (NDA No. 021536), Norditropin® (somatropin [rDNA origin] injection) (NDA No. 021148),and Victoza® (liraglutide [rDNA origin] injection) (NDA No. 022341) – that are available in pre-filled pen-injector presentations (FlexPen® or FlexPro®). NovoLog ® is also available in a pre-filled Penfill® cartridge for a Penfill® cartridge device. Although the pre-filled pen-injector systems (pre-filled pen injector, and pre-filled Penfill® cartridge), each of which is integral to its respective drug product, are covered by several issued patents, Novo Nordisk has not previously submitted information to FDA on those patents for listing in

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Novo Nordisk Inc.
100 College Road West
Princeton, New Jersey 08540
USA
Telephone:
+1 609-987-5800
Direct dial:
609-987-5282
E-mail:
jcsh@novonordisk.com
Internet:
www.novonordisk-us.com

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the Orange Book. Novo Nordisk's decision not to seek Orange Book listing has been due, in large part, to the lack of FDA guidance on the matter.

The issues involved in this request are:

(1) What constitutes an approved pre-filled drug delivery system for purposes of determining whether information on patents relating to that system should be submitted to FDA for listing in the Orange Book; and

(2) Whether information on patents relating to an approved pre-filled drug delivery system should be submitted to FDA for listing in the Orange Book if such patents: (a) disclose but do not claim the active ingredient or formulation of the approved drug product, or (b) neither disclose nor claim the active ingredient or formulation of the approved drug product.

II. Statement of Facts and Law

The FDC Act requires the sponsor of a New Drug Application ("NDA") to submit with its application information on:

> 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 reasonable be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.

FDC Act § 505(b)(1); see also FDC Act § 505(c)(2) (providing the same requirement for patents issued after submission or approval of an NDA).

In June 2003, FDA sought to clarify the types of patents that must and must not be submitted for listing in the Orange Book and amended 21 C.F.R. Part 314. In relevant part, 21 C.F.R. § 314.54(b)(1) states that information must be submitted to FDA:

> for each patent that claims the drug or a method of using the drug that is subject of the new drug application or amendment or supplement to it and with respect to which a claim of patent infringement could be reasonably asserted if a person not licensed by the owner of the patent engaged in

> manufacture, use, or sale of the drug product. For purposes of this part, such patents consist of drug substance (active ingredient) patents, drug product (formulation and composition) patents and method-of-use patents . . . . For patents that claim a drug product, the applicant shall submit information only on those patents that claim a drug product, as is defined in § 314.3, that is described in the pending or approved application . . . . [P]atents claiming packaging . . . are not covered by this section, and information on these patents must not be submitted.

In the preamble to the final rule, FDA noted several comments that distinguished between "packaging and devices such as metered dose inhalers and transdermal patches, which are drug delivery systems used and approved in combination with a drug." 68 Fed. Reg. 36,676, 36,680 (June 18, 2003). According to these comments, "patents claiming devices or containers that are 'integral' to a drug product or require prior FDA approval should be submitted and listed." Id.

FDA agreed that packaging and containers are distinct from the drug product and thus fall outside of the requirements for patent submission. See id. However, FDA further clarified "that if the patent claims the drug product as defined in § 314.3, the patent must be submitted for listing." Id. The term "drug product" is defined as "a finished dosage form, for example, tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients." 21 C.F.R. § 314.3(b).

FDA stated that a key factor in determining whether to list a patent, therefore, is whether the patent claims the finished dosage form of the approved drug product. See id. FDA noted that these finished dosage forms include "metered aerosols, capsules, metered sprays, gels, and pre-filled drug delivery systems" but do not include "bottles or containers and other packaging." Id.

FDA's distinction between pre-filled drug delivery systems and product packaging remains unclear, however, because the term "pre-filled drug delivery systems" is not defined. The Orange Book does not list "pre-filled drug delivery systems" as a dosage form in Appendix C (Uniform Terms); nor does FDA's Data Standards Manual Dosage Form Monograph (C-DRG-00201) provide any useful guidance.

On four separate occasions between 2005 and 2011, NDA sponsors have requested advisory opinions from FDA on virtually identical issues raised in this advisory

opinion request.[1] To date, FDA has not substantively answered the advisory opinion requests or otherwise publicly addressed the patent listing issues they raise. In the absence of FDA guidance, some companies have submitted patent information to FDA on drug delivery device patents, and the Agency, consistent with its ministerial role in Orange Book patent listing issues, has listed such information.

The decision to submit such patent information to FDA for listing in the Orange Book has not been without consequence. In at least one instance in the context of Hatch-Waxman patent infringement litigation, an applicant filed a counterclaim pursuant to FDC Act §505(c)(3)(D)(ii)(I) to seek the delisting of patent information from the Orange Book in connection with a device-related patent. See King Pharms., Inc. v. Intellijject, Inc., No. 1:11-cv-00065-UNA (D. Del. Jan. 19, 2011) (alleging that the patent at issue "does not claim either a composition or a formulation of epinephrine" and "does not disclose a composition or formulation of epinephrine" and should therefore be delisted). Although that litigation was eventually dismissed pursuant to a settlement agreement between the parties, it underscores the need for FDA to finally address the issues raised in this and previously submitted advisory opinion requests. An advisory opinion on the matter could reduce the likelihood of patent delisting litigation and is in the interest of judicial economy.

Moreover, to advance the goals of the Hatch-Waxman Amendments, FDA should provide more explicit guidance on the patent listing requirements as they apply to pre-filled drug delivery systems. Two key functions of the Hatch-Waxman Amendments, and the Orange Book, are to: (1) provide notice of patents that would be infringed were a company to manufacture a generic version of a drug or drug product; and (2) to provide an early opportunity for generic companies to challenge patents before products are marketed. These notice and opportunity functions are best accomplished with clear guidance from FDA as to whether patents should or should not be listed in the Orange Book. This is particularly true with respect to patents relating to drug delivery systems, such as pre-filled drug delivery systems, where such patents do not claim the drug substance. In that case, such patent are less likely to be discovered in patent due diligence directed to the drug substance.

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[1] See Request for Advisory Opinion by GlaxoSmithKline, Docket No. FDA-2011-A-0363 (Jan. 10, 2005); Request for Advisory Opinion by AstraZeneca, Docket No. FDA-2006-A-0063 (formerly 2006A-0318) (Aug. 10, 2006); Request for Advisory Opinion by AstraZeneca, Docket No. FDA-2007-A-0099 (formerly 2007A-0261) (June 21, 2007); Request for Advisory Opinion by Forest Laboratories, Inc., Docket No. FDA-2011-A-0363 (May 12, 2011).

III. Questions Advanced

Pursuant to the considerations above, Novo Nordisk requests an advisory opinion on:

1) What constitutes an approved pre-filled drug delivery system for purposes of determining whether information on patents relating to that system should be submitted to FDA for Orange Book listing; and

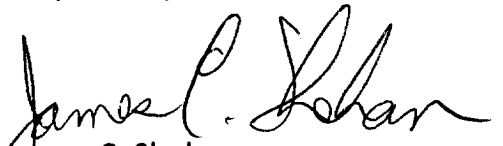
2) Whether information on patents relating to approved pre-filled drug delivery systems should be submitted to FDA for Orange Book listing if such patents neither disclose nor claim the active ingredient or formulation of the approved drug product.

Novo Nordisk currently believes information on patents relating to approved pre-filled drug delivery systems should be listed in the Orange Book regardless of whether or not the patents disclose or claim the active ingredient or formulation of the approved drug product. Thus, Novo Nordisk will submit to FDA information on relevant drug delivery device patents unless the company receives guidance from FDA that such listings are improper.

IV. Certification

The undersigned certifies that, to the best of his knowledge and belief, this request includes all data, information, and views relevant to the matter, whether favorable or unfavorable to the position of the undersigned, which is the subject of the request.

Respectfully submitted,



James C. Shehan
Corporate Vice President and General Counsel
Legal, Government, and Quality Affairs

Novo Nordisk Inc.