FINNEGAN | FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, LLP
WWW.FINNEGAN.COM

Anthony C. Tridico, Ph. D.
202.408.4000
anthony.tridico@finnegan.com

May 12, 2011

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

Request for Advisory Opinion Regarding Patents Listable in the Orange Book in connection with NDA No. 202-450

Dear Sir or Madam:

Pursuant 21 C.F.R. § 10.85, and on behalf of Forest Laboratories, Inc., ("Forest"), the undersigned submits this request for an advisory opinion of the Commissioner of Food and Drugs ("Request") with respect to the subject matter of certain drug delivery device patents submitted for listing in the Orange Book under Section 505 of the Federal Food, Drug, and Cosmetic Act ("FFDCA").

A. Issues Involved

The issue involved in this request is whether, in connection with a New Drug Application ("NDA"), a patent having the following characteristics should be submitted for listing in the Orange Book under Section 505 of the FFDCA (referred to herein as a "drug delivery device patent"):

a) the patent claims a drug delivery device: (i) whose use is integral to the administration of the active ingredient subject of the NDA, (ii) whose approval, therefore, is part of the approval of the active ingredient subject of the NDA, and (iii) that is recited in the "Indications and Usage" section of the Prescribing Information for the active ingredient subject of the NDA ("label"); and

b) the claims in the patent do not recite the active ingredient subject of the NDA.

AP

FDA-2011-A-0363

B. Statement of Facts and Law

The FFDCA requires, *inter alia*, that applicants filing an NDA submit for listing in the Orange Book the patent numbers and expiration dates of certain patents. Those patents are identified and characterized as:

> "[A]ny 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.

FFDCA § 505(b)(1) (2008); *see also* § 505(c)(2) (reciting similar requirement for patents issued after submission of the NDA); 21 C.F.R. § 314.53 (2010)(reciting equivalent and almost identical language).

The FDA has already recognized that for certain drug products, such as metered dose inhalers ("MDIs") and dry powder inhalers ("DPIs"), a drug product includes both the drug formulation *and* the drug delivery system:

> *The device with all of its parts*, including any protective packaging (e.g., overwrap), *and the formulation together constitute the drug product.* Unlike most other drug products, the dosing and performance and therefore the clinical efficacy of a DPI may be directly dependent on the design of the device

Draft Guidance for Industry: Metered Dose Inhaler (MDI) and Dry Powder Inhaler (DPI) Drug Products, lines 113-116 *(October* 1998) (emphasis added); *See also* lines 42-43 for a similar definition of an MDI drug product as including "the container, the valve, the actuator, the formulation, any associated accessories." The passage above suggests a reason for including an inhaler device as part of the drug product: the interdependence between the clinical efficacy of the drug and the performance of the inhaler device. Thus, a reasonable interpretation of 21 C.F.R. § 314.53 is a requirement to list a patent claiming such a drug delivery device integral to the administration of the active ingredient since the claims would encompass the inhaler component of the drug product as defined by the FDA.

Consistent with the statements above, the FDA has clarified that patents claiming a drug product in a "pre-filled drug delivery system," among other exemplary finished dosage forms, "*must* be submitted for listing." *Final Rule: Applications for FDA Approval to Market a New Drug: Patent Submission and Listing Requirements* 68 FR 36675 (June 18 2002) ("*Final Rule regarding Patent Submission and Listing Requirements*") (Comment 3 at 36680, emphasis added). This is in contrast to patents that only claim "packaging," which must not be submitted for listing. *Id.* The FDA explained that "[t]he

key factor is whether the patent being submitted claims the finished dosage form of the approved drug product." *Id.* Thus, if a patent claims a finished dosage form as part of a pre-filled drug delivery device, then that patent must be submitted for listing.

However, guidance regarding compliance with the listing requirement is not clear when the patent claims a drug delivery device integral to the administration of the active ingredient but does not recite the active ingredient. The undersigned is aware of NDA applicants who have requested an advisory opinion on issues similar, if not identical, to the one subject of this Request for Advisory Opinion. Letters dated January 10, 2005 (GSK, Docket No. 2005A-0015, Exhibit 1); August 10, 2006 (AstraZeneca, Docket No. 2006A-0318, Exhibit 2); and June 21, 2007 (AstraZeneca, Docket No. 2007A-0261, Exhibit 3). To the best of the undersigned's knowledge, the FDA has not responded publicly in a substantive manner to those requests.[1]

Forest believes that although neither the rules nor past guidance from the FDA address the issue in this Request explicitly: (1) a reasonable interpretation of the rules and (2) current FDA accepted practice regarding listing of drug delivery device patents require submission for listing in the Orange Book of drug delivery device patents as defined above.

a. The Rules Compel Submitting the Drug Delivery Device Patents for Listing in the Orange Book

The notice function included in the statute governing the listing of patents explains that the submitted patent is one "*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." FFDCA § 505(b)(1) (2008) (emphasis added). Thus, the statute imposes a duty on an NDA applicant to submit a patent for listing when the patent claims a drug product that can be asserted against a generic manufacturer in an infringement action.

In Forest's view, that duty exists when the patent claims a drug delivery device that is an integral part of the administration of the active ingredient to a patient, especially when the approval of the drug product NDA is conditioned on the concurrent approval of the drug delivery device. This duty should exists irrespective of whether the patent recites the active ingredient in the claims. This is because the patent would be, in either case, a patent with respect to which a claim of patent infringement could reasonably be asserted under the conditions recited in the statute.

[1] The undersigned is only aware of a template-like response in which the FDA has replied to each request indicating that the "FDA has been unable to reach a decision on your request due to the need to address other Agency priorities" and that the FDA "will respond to your request as soon as possible given the numerous demands on the Agency's resources." *See, e.g.*, Response to GSK dated July 7, 2005 in Docket No. 2005A-0015 (Exhibit 4). The undersigned is not aware of any response on the merits to any of these prior requests for an Advisory Opinion.

In such a case, a generic drug manufacturer seeking approval for the sale and marketing of a drug substance in an Abbreviated New Drug Application ("ANDA") would have to manufacture and sell the drug substance in the same type of drug delivery device approved in the original NDA. To the extent that this action raises the risk of being sued by the holder of the device patent, then (1) the generic drug manufacturer will benefit from the device patent being listed in the Orange Book, *and* (2) the patent holder is required to submit the patent for listing to comply with the notice function of the statute.

The importance of the notice requirement in the statute is also recognized by the FDA in the comments published with the final rule implementing the "Hatch-Waxman Amendments" relating to new drug applications and generic drug approvals. *Final Rule regarding Patent Submission and Listing Requirements* at Introduction. For example, the FDA mentions the balance the statute attempts to achieve between "the innovator companies' intellectual property rights and the desire to get generic drugs on the market in a timely fashion." This goal is carried out in part by "resolving challenges to patents in court before marketing begins." *Id.* An important part of the overall objective of the rules is, therefore, the identification of the innovator companies' patents, through the patent submission and listing requirements, that both the FDA and a generic drug manufacturer need to consider before a generic drug can be approved.

In that regard, the FDA listing in the Orange Book of the drug delivery device patents at issue in this Request would further the goal of both the statute and the regulations by providing a generic drug manufacturer with notice of patents whose infringement could prevent and/or delay the sale of a generic version of a drug product. In fact, because such drug delivery device patents do not claim the drug substance, those patents might not be uncovered in a search for the active ingredient. Thus, if "challenges to patents in court" are to be resolved "before marketing begins," as is the stated goal of the Hatch-Waxman Amendments, then the patent holder must make available to the generic drug manufacturer, by complying with the patent submission and listing requirement, the identities of those patents that claim the drug delivery device. For at least the foregoing reasons, Forest believes that the submission for listing in the Orange Book of drug delivery device patents at issue in this Request is not only proper, but required.

b. <u>The FDA Seems to Have Accepted the Practice of Listing in the Orange Book Pre-Filled Drug Delivery Device Patents That Do Not Recite the Drug Substance in the Claims</u>

As mentioned before, NDA applicants have requested an advisory opinion from the FDA on at least three separate occasions on issues similar, if not identical, to the one subject of this Request for Advisory Opinion.

In both of AstraZeneca's requests, AstraZeneca noted explicitly that AstraZeneca will continue to list drug delivery device patents not claiming the drug substance until it receives guidance from the FDA "that such listings are improper." In its request, GSK decided against listing that type of patents, but noted that, absent guidance from the FDA, such an approach could fail to meet the statutory requirements:

> Without further clear and explicit guidance from FDA, however, NDA-holders remain in a difficult position, *uncertain whether the kind of conservative, cautious approach that GlaxoSmithKline has adopted fully meets the statutory patent listing requirements as FDA would interpret them.*

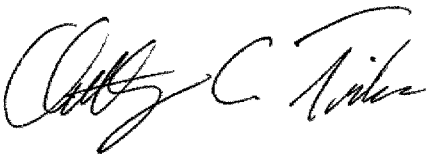
GSK Request for Advisory Opinion in Docket No. 2005A-0015 at p. 7 (emphasis added, Exhibit 1). Nonetheless, GSK reconsidered its original position and later decided to submit for listing drug delivery device patents "whose claims read on the drug product subject to FDA approval . . . *regardless of whether the approved drug substance is specifically mentioned in the claims of such patents.*" Letter from GSK to the FDA dated February 11, 2009 in Docket No. 2005A-0015 (emphasis added, Exhibit 5).

The following reasons strongly suggest that the FDA accepts the practice of submitting drug delivery device patents that do not recite the drug substance in the claims for listing in the Orange Book: (1) the FDA has not condemned the practice publicly, even after given the explicit opportunity to do so via the three requests for an advisory opinion cited above, and (2) the FDA accepts the submissions of such patents and later lists them in the Orange Book.

Accordingly, Forest respectfully requests guidance as to whether patents claiming drug delivery devices that are integral to the administration and approval of the NDA, but that do not recite the drug substance of the NDA, should be submitted for listing in the Orange Book. Because Forest believes that such patents should be listed, Forest will continue to list them unless it receives guidance from the FDA that such listings are improper.

The undersigned certifies that, to the best of his/her 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,



Anthony C. Tridico
Finnegan Henderson Farabow Garret & Dunner, LLP
901 New York Avenue, NW
Washington D.C. 20001
202-408-4000

Enclosures

Exhibits

Exhibit 1. Request for Advisory Opinion by GSK dated January 10, 2005, Docket No. 2005A-0015.

Exhibit 2. Request for Advisory Opinion by AstraZeneca dated August 10, 2006, Docket No. 2006A-0318.

Exhibit 3. Request for Advisory Opinion by AstraZeneca dated June 21, 2007, Docket No. 2007A-0261.

Exhibit 4. Response to GSK dated July 7, 2005 in Docket No. 2005A-0015.

Exhibit 5. Letter from GSK to the FDA dated February 11, 2009, in Docket No. 2005A-0015.

901 NEW YORK AVENUE, NW | WASHINGTON, DC 20001-4413
PHONE: 202.408.4000 | FAX: 202.408.4400