August 31, 2020

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: Docket No. FDA-2020-N-1127
Listing of Patent Information in the Orange Book, Establishment of a Public Docket, Request for Comments [FR Notice questions]

Dear Sir/Madam,

Novo Nordisk appreciates the opportunity to submit comments on the Request for Comments on "Listing of Patent Information in the Orange Book."

Novo Nordisk is a pioneer in biotechnology, a world leader in diabetes care and holds a leading position within obesity, hemostasis management, growth hormone therapy, and hormone therapy for women. Novo Nordisk manufactures and markets biopharmaceutical products and services, including combination products, that make a significant difference to our patients, the medical profession, and society.

Novo Nordisk is a member of the Pharmaceutical Research Manufacturers of America (PhRMA) and Biotechnology Innovation Organization (BIO) trade associations. As members of these organizations, we support their comments submitted to this docket and additionally have the following comments in response to FDA's questions.

Questions regarding "Listing of Patent Information in the Orange Book"

General Questions:

Q2: Given the general increasing complexity of products approved in an NDA (e.g., drug-device combination products, complex delivery systems, associated digital applications), are there any aspects of FDA's interpretation of the statutory requirement for NDA holders to submit information on a patent that claims the drug or a method of using such drug that are not sufficiently clear? If there is a lack of clarity, how could this be resolved?

Consistent with FDA's current practices, FDA should make clear that patents that claim a device or component of a device that are encompassed within (i.e. part of) a New Drug Application (NDA) approved drug-device combination product

should be listed. This includes patents with claims covering an entire delivery device or a component part of a delivery device that are encompassed within the NDA.

We believe FDA should make clear that if a patent claim covers a device constituent of an approved NDA drug-device combination product or a component thereof and that constituent or component thereof is part of the approved combination product, then the device constituent or a component thereof is considered integral to the NDA drug-device combination product and that patent, if it is under the control of the NDA sponsor, must be listed in the Orange Book. We believe the easiest way to clarify this scope of patent listing is for FDA to define "integral" to the NDA approved drug product as encompassing "patents claiming the device constituent of a drug-device combination product approved in an NDA or patents claiming a component thereof" as determined by the NDA sponsor's reasonable interpretation of the scope of the patent claim and knowledge of the approved drug product. Thus, if the device constituent or a component thereof that is within the approved drug product is patented, it is integral and must be listed if that patent is under the control of the NDA sponsor. We believe broadly interpreting "integral" to include such patents provides the necessary clarity on what patents should be listed, is consistent with the statutory language regarding Orange Book listings, is the most efficient and effective way of meeting the careful balance intended by the Drug Price Competition and Innovation Act, and provides an efficient mechanism for clear and proper patent listing even as technology advances and complexity increases.

Furthermore, with respect to a "patent under the control of the sponsor," this would only encompass patents that are wholly owned by the NDA sponsor, are fully assigned to the NDA sponsor, or where the patent owner and NDA sponsor have an agreement that the listing should be made. An NDA sponsor cannot be expected to list patents for which they don't have control or authority to make decisions on the listing, even if that patent covers the NDA approved product or a device constituent or component part thereof.

As an example, if the device is incorporated into the label of an NDA approved combination product, when the patent claims the device or a component part of the device, listing of that patent is appropriate because it is per se "integral" to the NDA approved product. The NDA sponsor is best positioned to determine if a patent claim covers the device constituent or component thereof of the NDA approved product.

During the patenting of devices, it is not always known what drugs will be incorporated into that device. Alternatively, a device may be developed with several drug products in mind. Furthermore, the way a novel and non-obvious device or component of a device is patented takes into account patent laws for protection of the device or a component thereof, not any regulatory or combination product standards outlined by the FDA. The goal of the Hatch-Waxman Act is to ensure that any patent where an Abbreviated New Drug Application (ANDA) or 505(b)(2) applicant's product could be said to infringe the claim of a patent, then that patent should be listed in the Orange Book. As such, the standard for inclusion of listing of a patent should rest on whether the patent claiming that device or component of a device is under the control of the NDA sponsor and part of or encompassed within the NDA approved drug-device combination product. We believe defining "integral" to encompass this scope is the easiest resolution to maintaining the current practice of patent listing and providing clarity on FDA's interpretation of the Statute.

Assessment of "integral" should be done by the application sponsor. FDA has traditionally taken a ministerial approach to patent listing, which we believe is appropriate. FDA should not determine or assess whether a patent claim covers a device constituent or component thereof that is integral to the approved product. It is neither necessary nor efficient for FDA to try to assess patent claim construction for a patent that claims a device that is "integral" to the approved product. Claim construction is a complicated process involving statutory standards, numerous court rulings on interpretation of those standards, United States Patent and Trademark Office (USPTO) Patent Trial and Appeal Board decisions and interpreting claims in light of the patent specification. It should be the role of the NDA approved product sponsor, with its patent counsel, to assess which patents cover device constituents or components thereof that are integral, and which are not. Thus to be Orange Book listed, we believe that the patent must actually claim the NDA approved drug-device combination product, the drug substance, the drug product , a component of the drug product, a composition of the drug product, a device constituent, or a component of the device constituent.

Listing patents claiming the device constituent of an NDA-approved drug-device combination product or a component thereof aligns with the Hatch-Waxman statute[1] and FDA regulations.[2] In summary, FDA should make clear that patents

[1] *See* FDCA §§ 505(b)(1), 505(c)(2).

[2] *See* 21 C.F.R. § 314.53(b)(1).

covering the device constituent or components thereof for an NDA approved drug-device combination product should be listed because they are per se integral to the NDA approved drug product. It likewise follows that patents claiming a method of using a device constituent or a component thereof in an NDA-approved combination product are also subject to Orange Book listing requirements when that method is part of the approved use of the NDA drug-device combination product.

Q3: How would NDA holders and prospective 505(b)(2) and ANDA applicants weigh any advantages that may result from listing of additional types or categories of patent in the Orange Book against the potential need to submit additional patent certifications that could result in a delay of approval of a 505(b)(2) application or ANDA?

Clarifying the need to list patents claiming a device constituent or components thereof for an NDA approved drug-device combination products as described above is important to achieve the patent transparency intended under the Hatch-Waxman Act.[3] Patent listing provides notice to follow-on product manufacturers for what patents cover the NDA approved products and the approved methods of using those products, whether drug products or drug-device combination products. As acknowledged by FDA, patent listing helps follow-on manufacturers know which patents cover the approved product and method of using the product. This permits the follow-on manufacturer to determine which patents may block early entry and determine their strategic approach, whether that be patent licensing, patent challenge, or waiting until patent expiration. The Hatch-Waxman Act is a carefully balanced Act that works to balance innovation with the desire for early competition. Patent listing has a critical role in informing on the patent environment, permitting early use and challenge of the patent, and allowing the involved parties to work out patent grievances through an efficient and transparent process for all parties involved. As such, listing of patents covering the NDA-approved product, including patented devices and component parts of devices, helps promote both the balance and transparency intended within the Hatch-Waxman Act. Absence of listing may result in "surprises" on all sides which works to delay certainty of outcome and is overall a potential disservice not only to the parties involved, but

[3] Formally called, The Drug Price Competition and Patent Term Restoration Act of 1984, and commonly known as the Hatch-Waxman Act, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended at 21 U.S.C. §355 and 35 U.S.C. §156, 271 and 282.

to patients in the long run.[4] One of the greatest successes of the Hatch-Waxman Act was the predictability built into the system for all parties irrespective of the circumstances and the timing around those circumstances. This positive success should be maintained. Anti-competitive laws and the two-part standard of reasonable and good faith claim interpretation[5], as discussed below, will further promote a balanced system and help prevent abuse of patent listings.

Furthermore, the best approach is to permit the listing of a patent that covers a device constituent or component thereof where that constituent or component thereof is believed by the sponsor to be "integral" (as defined above) to the approved drug product, and provide notification to follow-on sponsors of such listing as they are developing their drug, rather than providing that notification later in the development process. The absence of listing does not remove the possibility of an infringement litigation, but it may delay the awareness of the patent to a follow-on product manufacturer. A patent holder can bring an infringement suit even if a listing is not made. However, a balance the Hatch-Waxman Act promotes is early notice of possible patent infringement. Listing is critical to achieve this balance because it not only provides the follow-on product developer greater likelihood of awareness of the scope of patent infringement possibilities before determining product development strategies, but also permits that sponsor to challenge the listing as not being proper by utilizing existing procedures to have the patent delisted.[6] The Hatch-Waxman Act even provides a 180-day marketing exclusivity incentive for a patent challenger, which further emphasizes Congress' intent in having all patents that cover the approved drug product in-full or in-part to be listed. As such, patent listing promotes earlier and a greater understanding of patent scope to follow-on drug manufacturers, i.e. during drug development, rather than being surprised by a later patent infringement suit. Therefore, in turn, the "integral" standard as outlined above not only promotes proper Orange Book listing, but also promotes earlier notification of patent infringement possibilities and the ability to challenge such listed patents.

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[4] *See* Complaint, *Mut. Pharm. Co. v. Hoechst Marion Roussel, Inc.*, No. CIV. A. 96-1409, 1996 WL 34406666 (E.D. Pa. Feb. 23, 1996) ("Had the '129 patent been listed in the Orange Book, [the plaintiff] would not have expended over $500,000.00 to develop its generic . . . product . . . .").

[5] *See* MCI Commc'ns Corp. v. Am. Tel. & Tel. Co., 708 F.2d 1081, at 1138 (7th Cir. 1983).

[6] See 21 C.F.R. § 314.53(f)(1)(i) and 21 C.F.R. § 314.53(f)(1)(i)(A). Anyone may notify FDA in writing about a potential problem, and in response, FDA may require the NDA holder either to "confirm the correctness of the patent information," or "withdraw or amend the patent information." "Unless the NDA holder withdraws or amends its patent information in response to the patent listing dispute, [FDA] will not change the patent information in the Orange Book."

Q4: If you think FDA should clarify the type of patents that must be listed in the Orange Book, what factors should FDA consider in implementing this clarification? For example, should FDA consider specific factors in evaluating the timeliness of patent information submitted after such clarification?

Having FDA clarify that "integral" encompasses all patents that claim a device constituent or a component thereof that are encompassed within the NDA-approved drug product or combination product as a mandatory listing is the most important clarification that needs to be made.

We believe it is best to permit the application sponsor to determine which patents cover the approved drug product in-full or in-part with respect to those patents under the NDA sponsor's control. The burden should not be on FDA to determine what is "integral" given the increasing complexity of products involving drug-device combination products, digital components and other constituent device parts to the approved product. Furthermore, not only do drug products have increasing complexity, but claim construction is a complicated and legalistic process. The context of a claim is not always easily discernable without in-depth knowledge of the patent system and application of the laws and rules of claim construction. Thus, the NDA sponsor is in the best position to determine when a "claim of patent infringement could reasonably be asserted"[7] based on the approved drug product and the patent claims. Furthermore, the ability to challenge a listed patent is a sufficient process to address potential disputes, while maintaining the advantages of early notification through patent listing. It may be helpful, however, for FDA to provide some examples of an "integral" component (device constituent and component thereof) in potential future draft guidance.

Q5: Are there other issues related to the listing of patent information that we should consider?

Drug Product Patents:

Q1. Are there elements of FDA's regulatory definition of drug product or dosage form in § 314.3(b) that may be helpful to clarify to assist NDA

[7] *See* 21 U.S.C. § 355(b)(1), stating, "The applicant shall file with the application the patent number and the expiration date of 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 reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug."

holders in determining whether a patent claims the finished dosage form of an approved drug product?

A patent claiming a device or component part thereof in an NDA-approved combination product need not disclose or claim an active ingredient or formulation in order to be listable for the approved drug product. A device that is not part of a combination product would not be eligible for listing because it would not be "integral" (as defined in the comments to the "General Questions" above) to the NDA approved drug product.

FDA should make clear that a finished dosage form could be a drug sold in a pre-filled device or delivery system, and that a patent claiming these devices are required Orange Book listings if the device is part of or encompassed within the approved NDA drug-device combination product, and if that patent is under the NDA sponsor's control even if the patent does not claim the drug product . Since many delivery devices are marketed only under an NDA and are not separately cleared for marketing under FDA's device authority, patents covering these delivery devices of a product remain listable if the delivery devices are approved as part of the NDA drug-device combination product.

To require patents that claim a device constituent of a combination product approved under section 505 of the FD&C Act also claim and/or disclose the active ingredient or formulation of the approved drug product (or the drug product class) does not comport with basic patent law principles and how devices are usually patented. A better approach is to broadly apply the assessment of whether the device or component thereof is part-of and, thus, integral to the NDA approved drug product, as discussed above.

Q2. What factors should FDA consider in providing any clarifications related to whether device-related patents need to be submitted for listing as a patent that claims the drug? For example, what are the advantages and disadvantages of requiring patents that claim a device constituent part of a combination product approved under section 505 of the FD&C Act to also claim and/or disclose the active ingredient or formulation of the approved drug product (or the drug product class) to fall within the type of patent information that is required to be submitted to FDA for listing in the Orange Book? Also, how, if at all, should this analysis be affected by considerations about whether the device or specific component of device claimed in the patent is "integral" (see 68 FR 36676 at 36680) to the administration of the drug?

FDA should define what constitutes a drug delivery system and make clear that patents that claim pre-filled drug delivery devices should be listed if the approved product is a drug-device combination product that encompasses that device, even if the patent does not claim the active ingredient or a formulation of the drug product. For combination products, the pre-filled drug delivery system is "integral" to the drug product and patents covering this system, device or components should be listed to meet the notification, transparency, and certainty objectives of the Hatch-Waxman Act. Similarly, if a digital component of a drug-device combination product is part of the approved NDA, then patents that cover that digital component should be listed in the Orange Book because they meet the definition of "integral" as outlined above. If a digital application is approved as a 510K and is not part of the NDA approved drug-device combination product, then patents that cover that device would not be listed.

FDA requires a follow-on filer to focus on device characteristics in demonstrating sameness or therapeutic equivalence. This includes not only the context of use, but also the complexity of the device and the user environment. Human factors, biocompatibility, and usability studies, as well as comparative analyses on routes of administration, are all critical to the safe and effective use for drug-device combination products and necessary to demonstrate that the drug delivery device for the follow-on drug is equivalent to that of the NDA approved drug product. It is in the best interest of all parties involved to ensure that a patent claiming the drug delivery device is listed, so that a follow-on manufacturer is put on notice of that the claims of the patent are integral to the approved combination product and can then properly assess their desired actions to address the "integral" patent to the combination product (e.g. design around the patent, challenge the patent, and/or certify in accordance with the Hatch-Waxman certification with respect to the incorporated device or components thereof.)

Method-of-Use Patents

Q1: What information should FDA consider regarding when a patent that claims a method of using a device constituent part, or only a component of a device constituent part, might or might not meet the statutory standard for submission by the NDA holder for listing in the Orange Book as a method-of-use patent? Should FDA consider whether: (1) The patent claims and/or discloses the active ingredient or formulation of the approved drug product (or the drug product class)?; (2) the device constituent part is described in certain sections of the listed drug labeling?; or (3) use of the device is

described in labeling for the listed drug, but the device is not a constituent part of the drug product? Should FDA consider whether the drug product labeling states that the drug is only for use with the specific device? Should FDA also consider device labeling, for example whether the device labeling indicates the device is for use with the specific drug?

A patent claiming a method of using a device constituent or component thereof in an NDA-approved combination product is listable as long as the NDA approved product label supports that method of use. These patents should be listed regardless of whether the patent claims the active ingredient or formulation of the approved drug product (or the drug product class).

Q2. What information should FDA consider regarding whether there are circumstances in which a patent claiming the way an approved drug product is administered would meet the statutory standard for submission by the NDA holder for listing in the Orange Book as a drug product patent rather than a method-of-use patent?

We believe defining "integral" as described above helps clarify whether a patent should be listed or not, including for "the way an approved drug product is administered.". If a patent claim covers any part of an NDA approved drug product or the method of using that product that is "integral" to the approved product, then that patent should be listed. The way an approved drug product is administered is referenced in the "Prescribing Information" of a label. Thus, if a patent covers "the way an approved drug product is administered" and the Prescribing Information of the label references what is patented, then that claims are "integral" to the approved drug product. With respect to method of use, if the patent claims a method of use that is approved in the label of the product, that method of use should be listed if the method of use claim can be interpreted to cover a method of using the NDA approved drug product, a device constituent of that drug product, component thereof, or an active ingredient of that drug product. By permitting listings for patents that claim a drug product, constituent part of the drug product, or a component thereof, or a method of using that NDA approved drug product and defining "integral" to encompass such patents as determined by the NDA sponsor, FDA not only clarifies what patents can be listed, but also potentially improves the notification principle under the Hatch-Waxman Act by ensuring follow-on sponsors are aware of all patents that reasonably cover the NDA approved drug product or its method of use. This definition of "integral" also clarifies that patents covering products or devices that are not part of the NDA approved drug product are not to be listed.

Q3. What information should FDA consider regarding whether there are circumstances in which a method-of-use patent claiming the way an approved drug product is administered that is not described in FDA-approved product labeling would meet the statutory standard for listing in the Orange Book?

If a patent claims a method of use or the way an approved drug product is administered that is not described in the FDA-approved product labeling, then that patent should not be listed (unless it is listed because that patent also claims the approved drug product, active ingredient or a constituent part of the approved drug product, or a delivery device that is part of the approved drug product). Since mode of delivery is part of the "Prescribing Information" of the label, if the way an approved drug product is administered is not referenced in the FDA-approved product labeling, then it is not a part of the approved drug product and listing of the patent is not proper in this context. If it is referenced in the Prescribing Information, then listing is not only appropriate, but should be required.

Conclusion

Thanks again for the opportunity to provide feedback on these FR Notice Questions pertaining to Orange Book Listings. We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

Robert B Clark

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Robert B. Clark
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