



Submission in Response to FDA Request for Comment
Docket No. FDA-2020-N-1127: "Listing of Patent Information in the Orange Book"

I. Introduction

On June 1, 2020, the Food and Drug Administration (FDA) specifically requested comments on several topics, including the submission and listing of patent information for patents that claim a device constituent part of a combination product (e.g., a drug delivery device). As part of its drug approval process, the FDA publishes its Approved Drug Products with Therapeutic Equivalence Evaluations, known in the industry as the "Orange Book." For listing in the Orange Book, the FDA requires a declaration that the patent claims the "drug substance," "drug product (composition/formulation)," or "one or more methods of using" the drug for which it is listed. See 21 C.F.R. § 314.53(c)(2)(i)(M)–(O). The plain text of the statute calls for the listing of patents "which claim[] the drug for which [an application is submitted] or which claim[] a method of using such drug." Id. § 355(b)(1). Based solely on the drug manufacturer's representation, the Orange Book lists patents for FDA-approved drugs. The FDA acts in a ministerial role and does not review Orange Book submissions for accuracy or relevance. Instead, applications are reviewed solely for completeness and facial ineligibility. Getting listed in the Orange Book arms the branded drug manufacturer with an automatic thirty-month suspension of the FDA's

approval of any potential generic competitor.¹ Because of this, the Orange Book eligibility requirements for patents are extremely important and are ripe for abuse by drug delivery device patents.

II. The Importance of Generic Drugs for American Consumers

Generally, competition in the free marketplace benefits consumers through lower prices, better quality, and increased innovation. In the prescription drug market, the benefits of competition cannot be overstated. The Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as “Hatch-Waxman,” created a unique framework that has benefitted consumers and drug makers alike. The law encourages innovation by giving branded manufacturers longer periods of market exclusivity for newly approved products, which increases financial returns on new drug research and development. At the same time, the law promotes price competition by creating a new regulatory pathway for the approval of generic drugs: abbreviated new drug applications (ANDAs). ANDAs speed up the approval process by allowing generic manufacturers, who have demonstrated bioequivalence to the reference product, to rely on the safety and efficacy evidence previously submitted by the branded manufacturer, thereby avoiding years of costly and duplicative clinical trials.

By many measures, the law has been an unqualified success. In 1984, generics were only 20% of prescriptions filled; today, they represent 90% of the market. More importantly, generic drugs save consumers and governments hundreds of billions of dollars a year.² However, due in part to

¹ The 30-month stay is triggered when a brand manufacturer/patent holder files an infringement action against an ANDA applicant within 45 days of receiving notice of an ANDA with a Paragraph IV certification.

² See Figure 1; See also “Other Important Statistics”

the improper practice of listing drug delivery device patents in the Orange book, the insulin market has resisted these positive developments.

III. The Severity of The Insulin Crisis

Insulin is a live-saving necessity for millions of Americans with diabetes and one for which there is no substitute. Serious questions about insulin access and affordability have grabbed national attention in recent years. The list prices of the four most common insulin formulations have nearly tripled³ in the past decade, even though nothing about their chemical formulas, safety, or efficacy has changed. The human cost of these skyrocketing prices is well-documented, and anecdotes of rationing are abundant. Indeed, 1 in 4 Americans with diabetes has reported cost-related skimping or skipping on an insulin dose.⁴ In the most tragic cases, rationing has led to ketoacidosis and death.

Despite having been discovered almost a century ago, there are few generic insulin products at least in part because insulin manufactures listed drug delivery device patents improperly in the Orange Book.⁵ As the FDA increasingly utilizes the Purple Book for biologics, the states ask that the same considerations be applied therein as well. Along with other legislative and regulatory measures, promoting competition in the insulin market will be crucial in halting and reversing this troubling trend in pricing. A recent judicial opinion echoes that sentiment and applies it to the Orange Book drug delivery device patent issues.

³ [Truven Health Analytics; Bloomberg](#)

⁴ Darby Herkert, Pavithra Vijayakuma, and Jing Luo, M.D., M.P.H., et al. [Cost-Related Insulin Underuse Among Patients with Diabetes](#). JAMA Intern Med 2019;179(1):112-114

⁵ Michael Fralick, M.D. and Aaron Kesselheim, M.D., J.D., M.P.H. [The U.S. Insulin Crisis- Rationing a Lifesaving Medication Discovered in the 1920s](#). N Engl J Med 2019, 381:1793-1795

IV. *In re Lantus Direct Purchaser Antitrust Litigation*

In February of this year, the First Circuit Court of Appeals held that pharmaceutical company Sanofi-Aventis improperly submitted a patent for a component of its insulin glargine disposable pen, the Lantus SoloSTAR, to the FDA for listing in the Orange Book.⁶ Sanofi filed a supplemental new drug application, or sNDA, on top of their existing patents for the insulin glargine drug Lantus itself and the SoloSTAR pen. Orange Book listings are limited to a patent that “claims the drug” or “claims a method of using such drug.” 21 U.S.C § 355(b)(1).

The First Circuit said, “We see nothing in the statute or regulations that welcomes such a further expansion of the already stretched statutory terms, whereby an integral part of an injector pen becomes the pen itself, and in turn is a drug.”⁷ The court further noted that the FDA has acknowledged that the Orange Book “was not designed to separately address combination product listings or to identify the specific type of drug delivery system.”⁸ And, the court declined to address whether it would have been proper under the statute for Sanofi to submit the pen component, referencing the specific drug, as a drug delivery device, leaving in place a regulatory ambiguity which the FDA should address through this public comment process.

V. Recommendation and Conclusion

As advocates for the citizens of Mississippi and the District of Columbia, Alaska, Colorado, Connecticut, Delaware, Hawaii, Idaho, Illinois, Iowa, Maine, Maryland, Michigan, Minnesota, Montana, Nevada, New Mexico, Oregon, Puerto Rico, Rhode Island, Virginia, Washington, and Wisconsin, the undersigned attorneys general are concerned with the safety, efficacy, and

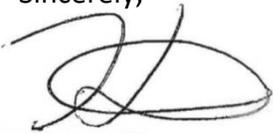
⁶ *In re Lantus Direct Purchaser Antitrust Litigation*, 950 F.3d 1 (1st Cir. 2020)

⁷ *In re Lantus*, 950 F.3d at 8.

⁸ *In re Lantus*, 950 F.3d at 9.

affordability of all drugs. Insulin is of particularly great concern, as Mississippi is home to over 370,000 people with diabetes.⁹ Allowing drug delivery devices or their components to be listed in the Orange Book causes ongoing exclusivity every time the device is modified and assists in the maintenance of oligopoly pricing. Consistent with the holding and reasoning of the First Circuit in *In re Lantus*, the undersigned attorneys general respectfully call upon the FDA to prohibit device and -component patents from being listed in the FDA's Orange Book. Only drug and method of use patents should be listed.

Sincerely,



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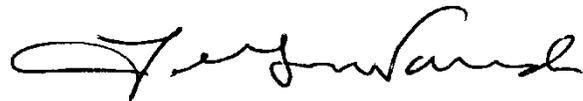
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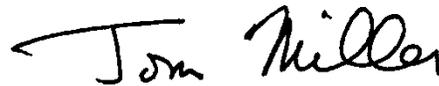
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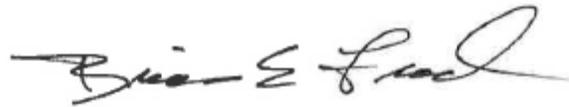


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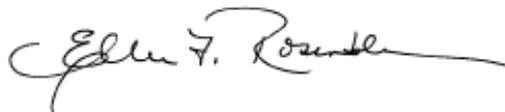
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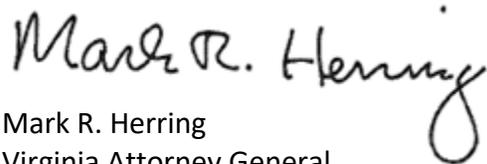
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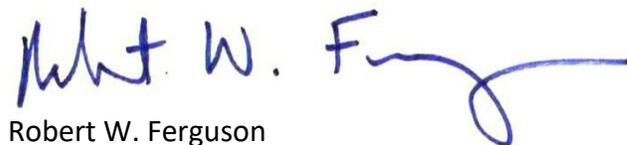
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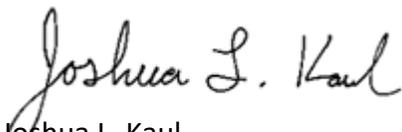
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