United States Senate

COMMITTEE ON HEALTH, EDUCATION,
LABOR, AND PENSIONS

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VIA ELECTRONIC TRANSMISSION

The Honorable Robert Califf, M.D.
Commissioner of Food and Drugs
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20933

Commissioner Califf:

I write regarding the Food and Drug Administration's (FDA's) ongoing efforts to provide clarity to drug manufacturers regarding their obligations to list relevant patents in the Orange Book. For decades, FDA and industry have struggled with whether manufacturers must list patents for the device parts of drug-device combination products in the Orange Book. Despite repeated requests from Congress and brand and generic stakeholders for clarity, FDA has stayed silent on this question. In the absence of FDA leadership, the Federal Trade Commission (FTC) has taken repeated actions that implement the Food, Drug, and Cosmetic Act (FDCA) in a way that FDA has never done or sought. Letting FTC enforce terms of the FDCA is an extraordinary abdication of authority by FDA. Rather than defer to FTC accusations that drug manufacturers are breaking ambiguous rules, FDA should clarify the rules for brand and generic manufacturers alike.

In 1984, Congress created the Hatch-Waxman framework to allow American patients to benefit from the timely launch of generic versions of innovator drugs. The Orange Book is a core part of this framework.[1] Manufacturers of innovator, or reference listed, drugs must list patents that claim their drugs in the Orange Book, which gives generic manufacturers fair notice of the relevant patents that they must navigate in order to make copies of the innovator drugs.

The FDCA requires manufacturers of reference listed drugs to accurately list patents in the Orange Book that "claim" a drug or method of using a drug.[2] The question of which patents qualify as "claiming" a drug is complicated for drug-device combination products like auto-

[1] The official name for the Orange Book is *Approved Drug Products with Therapeutic Equivalence Evaluations*.
[2] 21 U.S.C. 355(b)(1) (requiring New Drug Application sponsors to file information about "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.").

injectors and inhalers. FDA generally defines a "drug" as including the entire finished product—including both the chemical molecule and the delivery device. As noted below, manufacturers have, for decades, asked FDA for clarity on their listing obligations for device-related patents.

Manufacturers must get this right—listing too many patents or too few patents may both violate the law. List too many patents, and manufacturers could be accused of blocking competitors. List too few, and manufacturers may be accused of deceiving competitors and hindering them from accessing valuable incentives like 180-day first-filer exclusivity. That is why clarity regarding patent listing obligations is critical. The timely listing of patents in the Orange Book facilitates patent litigation that ultimately allows for lower-cost generic drugs to reach American patients. Otherwise, generic manufacturers can face the uncertainty of patent enforcement outside of the Hatch-Waxman framework, including potential liability for patent infringement post-approval. Manufacturers of reference listed and generic drugs alike benefit from the predictability created by listing patents in the Orange Book.

Congress, in statute, charged FDA with administering the Orange Book. While courts, not FDA, referee whether specific patents should be listed in the Orange Book in the context of patent litigation, FDA nonetheless sets the rules for Orange Book listing. FDA promulgated the foundational regulations on patent listing at 21 C.F.R. 314.53, which address the listing of different types of patents for metabolites, intermediates, and polymorphs of reference listed drugs.[3] The FDCA furthermore directs FDA to grant and list exclusivity periods in the Orange Book, and requires the agency to update the Orange Book on a monthly basis to reflect changes. Congress made clear across this statute that FDA is responsible for ensuring the Orange Book remains a critical resource for patients, manufacturers, and health care professionals and to facilitate the resolution of patent disputes.

Despite Congress' clear charge to FDA to set the rules for listing patents in the Orange Book, FDA has been absent. The agency has refused to provide needed clarity on listing patents for drug-device combination products. Going back as far as 2005, manufacturers have sought clarity from FDA about such patent listings.[4] On June 1, 2020, FDA denied requests from multiple manufacturers for advisory opinions on this issue, stating instead that the agency would consider these issues through a Federal Register notice that it issued simultaneously.[5] Acknowledging the gap, FDA said in that notice that it was seeking comment specifically on "The listing of patents that claim a device constituent part of a combination [drug] product" and other related issues.[6]

[3] 21 C.F.R. 314.53(b)(1).
[4] *See, e.g.*, GlaxoSmithKline, Request for Advisory Opinion (Jan. 10, 2005), Docket No. FDA-2005-A-0476.
[5] Food and Drug Administration, Docket Nos. FDA-2005-A-0476, FDA-2006-A-0063, FDA-2007-A-0099, FDA-2011-A-0363, and FDA-2012-A-1169 (June 1, 2020), FDA-2005-A-0476-0006.
[6] Food and Drug Administration, *Listing of Patent Information in the Orange Book; Establishment of a Public Docket; Request for Comments*, 85 Fed. Reg. 33169, 33173 (June 1, 2020).

On January 5, 2021, the Orange Book Transparency Act of 2020 was signed into law, reflecting legislation that I led.[7] The Act clarified applicants' responsibilities to submit listing information to the Orange Book and codified certain related FDA regulations. Pursuant to the Act, both FDA and the Government Accountability Office (GAO) published reports that address the listing of device patents in the Orange Book. In its January 2022 report, FDA rehashed the points made in comments submitted on this issue, without taking any further position.[8] FDA noted that it would build upon this work by establishing a multidisciplinary working group to examine this issue further. For GAO's report, 12 of the 15 stakeholders GAO interviewed, including brand and generic companies, reported that FDA's patent listing guidance has been "insufficient for determining which device-related patents should be listed in the Orange Book."[9]

Despite nearly two decades of requests from manufacturers for more clarity, FDA has still not told industry how it should list patents for drug-device combinations. Meanwhile, FTC, with FDA's apparent encouragement, has filled the vacuum left by FDA.[10] FTC has encroached on FDA's jurisdiction by policing Orange Book listings under antitrust law.[11] For example, FTC has opined that in its view, "device patents that do not mention any drug in their claims do not meet the statutory criteria for Orange Book listing," and must be delisted.[12] This ostensible policy change was enacted without statutory or regulatory direction from Congress or FDA to the patent listing requirements. It is difficult to believe that FDA would similarly opine on provisions of the Federal Trade Commission Act. Some Democrats in Congress have likewise encouraged the FTC's detour into FDA's jurisdiction.

FTC's actions have sown confusion amongst manufacturers about how they should list patents for drug-device combinations, exacerbated by FDA's inaction. FDA is like a referee hiding the rulebook from athletes, then egging on a referee from another sport to enforce it. FDA's continued silence on this issue is untenable, and patients ultimately stand to benefit through clarity on these requirements. It is well within FDA's authority to identify the types of patents that manufacturers should, or should not, list in the Orange Book. Indeed, FDA has acknowledged this authority when it convened its working group "to evaluate whether additional clarity is needed" regarding the types of patent information that should be listed in the Orange

[7] Pub. L. 116-290. Senator Cassidy authored this provision in the Senate's version of the Lower Health Care Costs Act. Senator Bill Cassidy, *Cassidy Legislation to Reduce Health Care Costs Passes Committee* (June 26, 2019), https://www.cassidy.senate.gov/newsroom/press-releases/cassidy-legislation-to-reduce-health-care-costs-passes-committee/.

[8] U.S. Food and Drug Administration, *The Listing of Patent Information in the Orange Book* at 11-18 (Jan. 5, 2022), https://www.fda.gov/media/155200/download.

[9] Government Accountability Office, *Stakeholder Views on Improving FDA's Information on Patents* at 24 (March 2023) https://www.gao.gov/assets/gao-23-105477.pdf.

[10] Federal Trade Commission, *FTC Expands Patent Listing Challenges, Targeting More Than 300 Junk Listings for Diabetes, Weight Loss, Asthma and COPD Drugs* (April 30, 2024), https://www.ftc.gov/news-events/news/press-releases/2024/04/ftc-expands-patent-listing-challenges-targeting-more-300-junk-listings-diabetes-weight-loss-asthma (FTC press release touting FTC patent listing dispute filings that quotes Dr. Califf saying that "The FDA will continue to engage with the FTC" on these matters.).

[11] Cite to FTC's Statement Concerning Brand Drug Manufacturers' Improper Listing of Patents in the Orange Book

[12] Federal Trade Commission's Brief as Amicus Curaie at 2, *Teva v. Amneal* (D.D.NJ) (March 22, 2024), https://www.ftc.gov/system/files/ftc_gov/pdf/ftc_brief_as_amicus_curiae_teva_amneal.pdf.

Book, "consistent with the existing statutory requirements for patent listing."[13] Two-and-a-half years later, FDA is still yet to establish such clarity through prospective, broadly applicable rules, instead acceding to ad hoc FTC enforcement. Moreover, depending on the results of FDA's work in this space reflected in your answers to the questions below, it may make sense for Congress to step in to provide much-needed predictability.

I ask that you answer the following questions on a question-by-question basis by **October 25, 2024**:

1. In January 2022, FDA announced that it was creating a multidisciplinary working group on patent listing. 31 months later, what is the status of any work product from this group?

2. FDA has solicited comments through a public docket, published a 29-page report, and convened a multidisciplinary working group, all addressing the issue of the listing of patents for drug-device combination products. What is the cumulative result of FDA's work?

3. Where does FDA stand on the need to provide more clarity regarding the list of patents for drug-device combination patents? Why has FDA not clarified, through rulemaking, guidance, or otherwise, the scope of patents that must be listed in the Orange Book pursuant to Section 505(b)(1) of the FDCA?

4. On net, is it beneficial for patents related to the device constituent of drug-device combinations to be listed in the Orange Book? What are the pros of listing such patents, and what are the cons?

5. FTC has taken actions related to Orange Book patent listings under the purported justification that improperly listed patents delay competition from generic drugs.?

    a. Has a 30-month stay for a drug ever hinged solely on a patent for a device constituent of a drug-device combination product? If so, please provide details of such example(s).

    b. How often has FDA granted tentative approval to an Abbreviated New Drug Application or 505(b)(2) New Drug Application where the sole obstacle to full approval was a patent for a device constituent of a drug-device combination product? If so, please provide details of such example(s).

6. If FDA has stayed silent because of the negative unintended consequences that could come from restricting patent listings, why has the agency encouraged FTC to take enforcement action in this space?

[13] U.S. Food and Drug Administration, *The Listing of Patent Information in the Orange Book* at 24 (Jan. 5, 2022), https://www.fda.gov/media/155200/download.

7. In your view, should Congress step in to amend the FDCA to clarify the patent listing requirements?

Sincerely,

Bill Cassidy, M.D.

Bill Cassidy, M.D.
Ranking Member
U.S. Senate Committee on Health,
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