Congress of the United States

Washington, DC 20515

August 28, 2023

Dr. Robert M. Califf, M.D.
Commissioner of Food and Drugs
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Dr. Califf:

We are writing to you about the U.S. Food and Drug Administration's (FDA's) role and responsibilities in addressing the anti-competitive business practices that pharmaceutical companies use to keep drug prices high.[1] Big Pharma companies have abused their monopoly power to jack up prices for life-improving drugs, "straining the healthcare system"[2] and forcing patients to suffer the consequences, often going without necessary medications due to high costs and rising debts.[3]

As the agency that is "responsible for advancing the public health by helping to speed innovations that make medical products more effective, safer, and more affordable,"[4] the FDA approves and regulates medical products such as drugs, biologics, and devices.[5] The FDA also maintains the Orange Book, which contains a complete list of FDA-approved drug and related patent and exclusivity information, which sponsors of brand-name drugs can use to delay generic competition.[6] The agency should close loopholes in the patent system that pharmaceutical companies have exploited to rake in billions in profits.

As part of the existing drug approval process, the FDA requires brand-name drug companies to submit patent information that covers drug substances (active ingredient), drug product (formulation or composition), and method of use (indication).[7] After approval, the FDA

[1] American Economic Liberties Project and Initiative for Medicines, Access, and Knowledge (I-MAK), "The Costs of Pharma Cheating," May 2023, https://www.economicliberties.us/wp-content/uploads/2023/05/AELP_052023_PharmaCheats_Report_FINAL.pdf
[2] Initiative for Medicines, Access, and Knowledge (I-MAK), "Overpatented, Overpriced," September 2022, https://www.i-mak.org/wp-content/uploads/2023/01/Overpatented-Overpriced-2023-01-24.pdf
[3] Patients for Affordable Drugs, "Ten Reasons Why We Need Lower Drug Prices Now," July 2022, https://patientsforaffordabledrugs.org/wp-content/uploads/2022/07/P4AD-July-2022-Price-Hikes.pdf
[4] U.S. Food and Drug Administration, "What We Do," March 28, 2018, https://www.fda.gov/about-fda/what-we-do
[5] U.S. Food and Drug Administration, "What does FDA regulate?" January 18, 2022, https://www.fda.gov/about-fda/fda-basics/what-does-fda-regulate
[6] U.S. Food and Drug Administration, "Approved Drug Products with Therapeutic Equivalence Evaluations | Orange Book," June 9, 2023, https://www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book; U.S. Government Accountability Office, "Generic Drugs," March 2023, https://www.gao.gov/products/gao-23-105477
[7] U.S. Government Accountability Office, "Generic Drugs," March 2023, p. 6, https://www.gao.gov/products/gao-23-105477

publishes this patent information in the Orange Book.[8] Competing drug companies can then review the information to determine whether they will seek FDA approval for a generic drug they want to market, using information such as when the brand-name sponsored patent expires, key patents that cover a particular drug product, or whether their product shares the same characteristics.[9] The pharmaceutical patents in the Orange Book are considered some of the "most valuable patents in the world," but about 25 percent of active patents in the Orange Book have been invalidated in court.[10]

Pharmaceutical companies, especially brand-name companies, have routinely abused the Orange Book system by improperly listing patents to block the introduction of lower-cost generics.[11] If a brand-name drug company sues a generic competitor for infringing on an Orange Book-listed patent, it automatically triggers a 30-month bar on the FDA's ability to approve the competitor's generic drug, therefore blocking the competitor's generic drug from entering the market.[12] This creates an incentive for companies to intentionally list "sham" patents in the Orange Book as a way to hold off generic competition for at least 2.5 years, regardless of the outcome of any litigation.

The FDA has acknowledged these Orange Book-related problems to Congress[13] and to the public.[14] The agency, with the U.S. Patent and Trademark Office (USPTO), also has announced initiatives to help ensure the patent system "is not used to improperly delay getting more affordable generic drugs and biosimilars into the hands of Americans who need them," and has sought public comments on the matter.[15] We support these collaborative efforts, and we recommend that FDA consider the following actions to address Big Pharma's greedy business practices:

1. **Clarify guidelines for patents that can be listed in the Orange Book.** FDA regulations specify the types of patents for which manufacturers must submit information, including the drug substance (active ingredient), the drug product (formulation and composition), and method of use (indications).[16] Pharmaceutical companies regularly list patents that do

[8] *Id*.
[9] *Id.*, p. 7.
[10] Washington Law Review, "What Litigators Can Teach the Patent Office About Pharmaceutical Patents," S. Sean Tu and Mark A. Lemley, August 5, 2022, p. 1673, https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3903513
[11] U.S. Federal Trade Commission, "FTC Amicus Brief Challenges Abuse of FDA 'Orange Book' Listing Procedures to Block Drug Competition," press release, November 10, 2022, https://www.ftc.gov/news-events/news/press-releases/2022/11/ftc-amicus-brief-challenges-abuse-fda-orange-book-listing-procedures-block-drug-competition
[12] United States District Court for the District of Delaware, "Federal Trade Commission's Brief as *Amicus Curiae*," November 10, 2022, p. 1, https://www.ftc.gov/system/files/ftc_gov/pdf/P163500JazzPharmaAmicusBrief.pdf
[13] U.S. Food and Drug Administration, "The Listing of Patent Information in the Orange Book," January 5, 2022, https://www.fda.gov/media/155200/download
[14] Federal Register, "Listing of Patent Information in the Orange Book; Establishment of a Public Docket; Request for Comments," U.S. Food and Drug Administration, June 1, 2020, https://www.federalregister.gov/documents/2020/06/01/2020-11684/listing-of-patent-information-in-the-orange-book-establishment-of-a-public-docket-request-for
[15] *Id.*; U.S. Patent and Trademark Office, "USPTO – FDA Collaboration Initiatives," https://www.uspto.gov/initiatives/fda-collaboration

not fit these categories, such as devices with no active ingredients (such as inhalers[17]) and Risk Evaluation and Mitigation Strategies (REMS) that ensure safety through distribution requirements. Over the last few years, U.S. courts have found that listing device-only patents[18] or REMS[19] in the Orange Book is improper and not within the statutory limits on Orange Book patent listings.

The FDA has, in the past, neither verified whether submitted Orange Book patents meet the statutory listing criteria nor removed improperly listed patents.[20] The lack of additional guidance from FDA has led brand-name sponsors to take advantage of FDA's lax oversight to list more patents in the Orange Book.[21] FDA officials should explicitly declare which types of patents should be listed in the Orange Book and clearly communicate and enforce those guidelines.

2. **Work closely with the USPTO to develop a review and validation system for every patent that is listed in the Orange Book.** The FDA does not substantively review patents submitted for listing in the Orange Book for correctness, and this regulatory gap hands immense power to pharmaceutical companies.[22] Among the initiated USPTO-FDA collaborations, the agencies should review and validate patents together to eliminate invalid patents. Retroactively removing improperly listed patents in the Orange Book will help enable the earlier entry of generic competition and save resources later spent on costly patent litigation.

3. **Revise policies regarding 'suitability petitions.'** The *Drug Price Competition and Patent Term Restoration Act*, also known as the Hatch-Waxman Act, requires that

[16] U.S. Food and Drug Administration, "The Listing of Patent Information in the Orange Book," January 5, 2022, p. 4, https://www.fda.gov/media/155200/download

[17] Health Affairs, "From Health Affairs: Inhaler Patents Focus On Devices, Not Ingredients," May 17, 2022, https://www.healthaffairs.org/content/forefront/i-health-affairs-i-inhaler-patents-focus-devices-not-ingredients

[18] FISH, "First Circuit Finds Device Patent Improperly Listed in the Orange Book," Brian D. Coggio and Kayleigh E. McGlynn, June 26, 2020, https://www.fr.com/insights/thought-leadership/blogs/first-circuit-device-patent-improperly-listed-orange-book/; FDA Law Blog, "If FDA Won't Regulate, Maybe the courts Will: First Circuit Opines on Listing Device Patents in the Orange Book," Sara W. Koblitz, March 16, 2020, https://www.thefdalawblog.com/2020/03/if-fda-wont-regulate-maybe-the-courts-will-first-circuit-opines-on-listing-device-patents-in-the-orange-book/

[19] U.S. Federal Trade Commission, "FTC Amicus Brief Challenges Abuse of FDA 'Orange Book' Listing Procedures to Block Drug Competition," press release, November 10, 2022, https://www.ftc.gov/news-events/news/press-releases/2022/11/ftc-amicus-brief-challenges-abuse-fda-orange-book-listing-procedures-block-drug-competition; New York Times, "A Drug Company Exploited a Safety Requirement to Make Money," Rebecca Robbins, February 28, 2023, https://www.nytimes.com/2023/02/28/business/jazz-narcolepsy-avadel-patents.html

[20] United States District Court for the District of Delaware, "Federal Trade Commission's Brief as *Amicus Curiae*," November 10, 2022, p. 1-2, https://www.ftc.gov/system/files/ftc_gov/pdf/P163500JazzPharmaAmicusBrief.pdf

[21] U.S. Government Accountability Office, "Generic Drugs: Stakeholder Views on Improving FDA's Information on Patents," March 15, 2023, https://www.gao.gov/products/gao-23-105477?utm_campaign=usgao_email&utm_content=topic_health&utm_medium=email&utm_source=govdelivery

[22] United States District Court for the District of Delaware, "Federal Trade Commission's Brief as *Amicus Curiae*," November 10, 2022, p. 1-2, https://www.ftc.gov/system/files/ftc_gov/pdf/P163500JazzPharmaAmicusBrief.pdf

generic drugs have the same route of administration, dosage form, and strength as the branded drug.[23] If a generic has a different route of administration, dosage form, or strength, a manufacturer can submit a 'suitability petition' to the FDA for approval of the generic version.[24] The Act states that the FDA "shall approve such a petition" unless it finds that additional studies need to be conducted.[25]

But the FDA has placed two barriers in the path of suitability petitions: (1) FDA requires "therapeutic equivalence" which requires those three factors to perfectly match and (2) FDA rejects suitability petitions by generic companies if the petition proposes an administration, dosage, or strength that was previously approved for a branded drug.[26] This creates a regulatory pathway for brand-name manufacturers to engage in "product hopping," whereby a brand manufacturer will make cosmetic changes to a product with an entirely new set of patents, knowing that this creates barriers for generics under the suitability review.[27] Generic manufacturers that want to enter the market must prove that these new patents covering the cosmetic change are invalid, a challenging and costly endeavor, especially given the excessive patenting strategies such as patent thickets that have led to an excessive number of patents that must be invalidated.[28] These delays occur even though these secondary formulation patents are often invalidated when challenged in court.[29] FDA has adopted these barriers on its own outside of the Hatch-Waxman Act requirements, and revising its own policies to remove these barriers regarding "suitability petitions" could prevent pharmaceutical companies from engaging in product hopping and help generics enter the market.[30]

4. **Share chemistry, manufacturing, and control information provided by drug manufacturers in applications for Investigational New Drugs with the USPTO.** Brand-name pharmaceutical companies have attempted to accumulate an excessive number of patents or delay filing their patents in an effort to employ anti-competitive business practices such as building "patent thickets," "product-hopping," or

[23] 21 U.S.C. §§ 355(j)(2)(A).
[24] 21 U.S.C. §§ 355(j)(2)(C).
[25] *Id*.
[26] Health Affairs, "A Preferable Path For Thwarting Pharmaceutical Product Hopping," Arti K. Rai and Barak D. Richman, May 22, 2018, https://www.healthaffairs.org/content/forefront/preferable-path-thwarting-pharmaceutical-product-hopping
[27] *Id.*
[28] U.S. House Committee on Oversight and Reform, "Drug Pricing Investigation," Majority Staff, December 2021, p. 79, https://oversightdemocrats.house.gov/sites/democrats.oversight.house.gov/files/DRUG%20PRICING%20REPORT%20WITH%20APPENDIX%20v3.pdf
[29] Science, "Drug Patents at the Supreme Court," C. Scott Hemphill and Bhaven Sampat, March 22, 2013, https://www.science.org/doi/abs/10.1126/science.1235857; Congressional Research Service, "Drug Pricing and Pharmaceutical Patenting Practices," Hevin T. Richards, Hevin J. Hickey, Erin H. Ward, February 11, 2020, p. 17, https://www.everycrsreport.com/files/20200211_R46221_145095cd7a7d37a957722140d6e708a1d52de5a1.pdf
[30] Health Affairs, "A Preferable Path For Thwarting Pharmaceutical Product Hopping," Arti K. Rai and Barak D. Richman, May 22, 2018, https://www.healthaffairs.org/content/forefront/preferable-path-thwarting-pharmaceutical-product-hopping

"evergreening."[31] For example, a manufacturer seeking to patent a 'new' manufacturing process may have been using that process "for more than a year before patents on them were filed," which fails to meet the novelty requirements for filing new patents.[32]

The FDA has access to information that could help the USPTO determine whether brand-name companies are filing patents in a timely manner.[33] Specifically, drug sponsors must submit an Investigational New Drug (IND) application to the FDA before starting clinical trials.[34] The IND application includes chemistry, manufacturing, and control (CMC) information – important characteristics about the drug product that describe its composition or components used in the manufacturing process.[35] Of patent applications for the top ten marketed drugs in the U.S. in 2021, about two-thirds were filed to the USPTO *after* the FDA had already approved the drug, meaning the FDA already had the CMC information.[36] FDA's sharing of this information would help the USPTO determine whether applicants are intentionally delaying patent filings for manufacturing processes that are already in use, thereby extending their monopoly over a drug.[37]

FDA and USPTO should sign a memorandum of understanding to specify that the FDA will routinely provide to the USPTO drug-related CMC information and subsequent modifications, especially regarding biologics. This cooperation will help prevent manufacturers from intentionally staggering patents. Sharing the CMC information between the two agencies could also help USPTO scrutinize any manufacturing process patent filed by a manufacturer against *all* of the previously patented manufacturing processes created by that same manufacturer's marketed drugs.

Thank you for your attention and engagement on this important issue. We welcome further collaboration and discussion to address these anti-competitive pharmaceutical practices and make drugs more affordable. In addition to these recommendations, we request the FDA provide our office staff with a briefing, no later than September 30, 2023, on the implementation of these

[31] Congressional Research Service, "Drug Prices: The Role of Patents and Regulatory Exclusivities," February 10, 2021, p. 5, https://crsreports.congress.gov/product/pdf/R/R46679/2
[32] Nature Biotechnology, "The characteristics of patents impacting availability of biosimilars," Victor L. Van de Wiele, Reed F. Beall, Aaron S. Kesselheim, and Ameet Sarpatwari, January 18, 2022, https://www.nature.com/articles/s41587-021-01170-5
[33] Nature Biotechnology, "An administrative fix for manufacturing process patent thickets," Arti K. Rai and W. Nicholson Price II, January 11, 2021, https://www.nature.com/articles/s41587-020-00780-9
[34] U.S. Food and Drug Administration, "Investigational New Drug (IND) Application," July 20, 2022, https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application
[35] U.S. Food and Drug Administration, "IND Applications for Clinical Investigations: Chemistry, Manufacturing, and Control (CMC) Information," February 25, 2022, https://www.fda.gov/drugs/investigational-new-drug-ind-application/ind-applications-clinical-investigations-chemistry-manufacturing-and-control-cmc-information
[36] Initiative for Medicines, Access, and Knowledge, "Overpatented, Overpriced," September, 2022, p. 3, https://www.i-mak.org/wp-content/uploads/2023/01/Overpatented-Overpriced-2023-01-24.pdf
[37] Nature Biotechnology, "An administrative fix for manufacturing process patent thickets," Arti K. Rai and W. Nicholson Price II, January 11, 2021, https://www.nature.com/articles/s41587-020-00780-9; Nature Biotechnology, "The characteristics of patents impacting availability of biosimilars," Victor L. Van de Wiele, Reed F. Beall, Aaron S. Kesselheim, and Ameet Sarpatwari, January 18, 2022, https://www.nature.com/articles/s41587-021-01170-5

recommendations, and on any statutory or regulatory changes that may be necessary to end abuses of the patent system.

Sincerely,

Elizabeth Warren
United States Senator

Pramila Jayapal
Member of Congress