U.S. GOVERNMENT ACCOUNTABILITY OFFICE

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July 28, 2023

The Honorable Bernard Sanders
Chair
The Honorable Bill Cassidy
Ranking Member
Committee on Health, Education, Labor, and Pensions

United States Senate
The Honorable Cathy McMorris Rodgers
Chair
The Honorable Frank Pallone, Jr.
Ranking Member
Committee on Energy and Commerce
House of Representatives

Over-the-Counter Drugs: Status of FDA's Implementation of Exclusivity Provisions in the CARES Act

Over-the-counter (OTC) drugs play an important role in the U.S. health care system by providing consumers quick access to health care products for a variety of uses without a prescription. These include, for example, painkillers to relieve minor aches and pains and sunscreen to help prevent sunburn and skin cancer. The Food and Drug Administration (FDA)—an agency within the Department of Health and Human Services (HHS)—is responsible for ensuring the safety and effectiveness of drugs, including OTC drugs. FDA regulates the safety and effectiveness of most OTC drugs through its monograph process, through which OTC drugs can be marketed without prior FDA evaluation and approval for each individual product.[1] FDA issues monographs to establish conditions—such as active ingredients, dosage forms, indications for use, and product labeling—under which an OTC drug in a given therapeutic category (e.g., sunscreen, antacid) is generally recognized as safe and effective for its intended use.

Both FDA officials and industry stakeholders, among others, have noted that the monograph process has limited FDA's ability to quickly update OTC monographs to allow additional products to be marketed for consumers, as we previously reported.[2] To expedite the monograph process and incentivize industry innovation in the development of new OTC drugs, in March

[1]We use the term OTC drugs in this report to refer only to OTC monograph drugs. These drugs are marketed in the United States without an approved new drug application (NDA) or abbreviated new drug application (ANDA), which is used for generic drugs. FDA may approve an individual drug for OTC marketing through the approval of an NDA or ANDA. An NDA must include data from clinical trials demonstrating the drug is safe and effective for its intended use, and an ANDA must include evidence demonstrating the generic drug is the same as a previously approved drug. See 21 U.S.C. § 355(b)(1)(A) and (j). Drugs approved under NDAs and ANDAs are eligible for their own periods of marketing exclusivity.

[2]See GAO, *Over-the-Counter Drugs: Information on FDA's Regulation of Most OTC Drugs,* GAO-20-572 (Washington, D.C.: Jul. 29, 2020).

2020, the CARES Act made several changes to the regulation of OTC drugs.[3] Among those changes, the CARES Act changed the monograph process to make it less burdensome on the agency to update and create new monographs. The CARES Act also allowed drug manufacturers, marketers, and others (hereafter "requestors") to request changes to a monograph and provided an 18-month period of marketing exclusivity if FDA makes certain requested changes.[4] This exclusivity—hereafter referred to as OTC monograph drug exclusivity—is intended to create an incentive for industry innovation for OTC drug products.

The CARES Act included a provision for GAO to examine and report on the implementation and impact of exclusivity for OTC drugs on industry innovation and consumer access and affordability 4 years after the enactment of the CARES Act, or by March 2024.[5] This report describes (1) the status of FDA's efforts to implement OTC monograph drug exclusivity provisions, and (2) research and stakeholder perspectives on how OTC monograph drug exclusivity may affect industry innovation for OTC drugs and consumer access to and affordability of these drugs.

To describe the status of FDA's efforts to implement OTC monograph drug exclusivity provisions, we reviewed FDA draft guidance, annual progress reports, and relevant legislation. We also interviewed FDA officials about their activities to implement the changes to the monograph process under the CARES Act.

To describe research and stakeholder perspectives on how OTC monograph drug exclusivity may affect industry innovation and consumers, we conducted a literature search to identify relevant studies published in peer-reviewed journals, government reports, and trade or research institute publications on the effect of exclusivity on industry innovation and consumers from January 2008 through April 2023.[6] We also interviewed FDA officials and representatives for industry stakeholders—selected on the basis of their participation in GAO's 2020 report on FDA's oversight of OTC drugs—about how exclusivity may affect consumers and industry innovation.[7]

We conducted this performance audit from January 2023 to July 2023 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our

[3]Pub. L. No. 116-136, tit. III, subtit. F, 134 Stat. 281, 435 (2020) (codified in significant part at 21 U.S.C. § 355h).

[4]Marketing exclusivity refers to a period of protection from competition during which only the requester may lawfully market a drug.

[5]Pub. L. No. 116-136, § 3851(b), 134 Stat. at 452-53.

[6]A research librarian constructed search strings to return results relevant to FDA over-the-counter drug oversight, FDA monograph reform, the FDA sunscreen monograph, OTC drug exclusivity, and innovation in OTC drugs and sunscreens. For the 91 articles we found relevant, we reviewed the full text of the article or abstract (if the full text article was unavailable) to identify whether the item provided evidence for claims relating to the effect of OTC exclusivity on consumer access or affordability and OTC drug innovation. Searches were conducted in Scopus; in the ProQuest databases Coronavirus Research Database, Criminology Collection, Education Database, ERIC, Global Newsstream, Health & Medical Collection, Policy File Index, ProQuest Dissertations & Theses Global, PTSDPubs, Publicly Available Content Database, Research Library, SciTech Premium Collection, and Sociology Collection; and in the ProQuest Dialog databases BIOSIS Toxicology, BIOSIS Previews, Embase, Embase Preprints, International Pharmaceutical Abstracts, MEDLINE, PAIS International, and SciSearch.

[7]We interviewed representatives from the Consumer Healthcare Products Association (CHPA) and the Personal Care Products Council (PCPC).These organizations are national trade associations representing OTC drug manufacturers and marketers and cosmetic and personal care product companies, respectively.

finding based on our audit objective. We believe that the evidence obtained provides a reasonable basis for our finding based on our audit objective.

Background

The CARES Act created section 505G of the Federal Food, Drug, and Cosmetic Act governing FDA's OTC monograph process. Among the reforms made by the CARES Act, section 505G replaced the rulemaking process for OTC monographs with an administrative order process to allow FDA to issue and revise monographs more quickly, including revisions to address safety issues. As we previously reported, FDA expects the time frames for issuing proposed and final administrative orders to be substantially shorter than those for issuing proposed and final rules.[8]

Section 505G also allowed requestors—such as drug manufacturers, marketers, processors, or developers—to request changes to OTC monographs by submitting an OTC monograph order request.[9] In addition, the CARES Act authorized FDA to assess new OTC monograph user fees to provide the agency with additional resources to regulate OTC drugs.[10] FDA began collecting OTC monograph user fees in June 2021.

The CARES Act provided exclusivity to requestors for certain types of OTC monograph changes made as a result of a monograph order request. OTC monograph drug exclusivity is available for (1) a change relating to an active ingredient (including any ester or salt of the active ingredient) not previously incorporated in a monograph drug or (2) a change in the conditions of use of a drug for which new human data studies conducted or sponsored by the requestor were essential to issuance of the final administrative order.[11] If FDA makes the requested changes to an OTC monograph, the requestor will receive 18 months of exclusivity to market their OTC drug incorporating the requested change.[12] For example, if an OTC drug manufacturer requests a monograph change for a new dosage form of an available OTC painkiller—e.g., a dissolvable film that can be taken without water—based on new human data studies and FDA makes the requested change, the manufacturer would receive an 18-month period of exclusivity. This means that for 18 months, the manufacturer would have exclusive rights to sell the OTC painkiller in the new dosage form.

OTC monograph drug exclusivity is not available under section 505G for safety-related changes, changes related to methods of testing safety or efficacy, or for certain other changes,

[8]See GAO-20-572.

[9]According to FDA officials, prior to the CARES Act, requested changes to OTC monographs were limited to products marketed prior to 1972 or changes for safety reasons.

[10]The CARES Act established two types of OTC monograph user fees: (1) annual facility fees and (2) fees for OTC monograph order requests. See 21 U.S.C. §§ 379j-71–379j-73. The CARES Act authorized FDA's OTC monograph user fee program from fiscal years 2021 through 2025. Fees are collected and available for obligation only to the extent and in the amount provided in advance in appropriations acts. For each of fiscal years 2021 through 2023, the amounts appropriated were the same as the amounts authorized under the CARES Act. In our July 2020 report, we found that both the rulemaking process and resource constraints limited FDA's ability to regulate OTC drugs. See GAO-20-572.

[11]See 21 U.S.C. § 355h(b)(5)(C)(ii). FDA officials told us that the phrase "active ingredient (including any ester or salt of the active ingredient)" refers to the active moiety, which is defined in FDA regulations as "the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance." 21 C.F.R § 314.3(b) (2022).

[12]Specifically, the requestor will be able to exclusively market a drug that incorporates the requested changes for a period of 18 months following the effective date of the final administrative order and beginning on the date the requestor may lawfully market the drug.

such as modifications to the directions for use and reordering of existing information on a product's drug facts label.

FDA Has Not Yet Received Monograph Order Requests Eligible for OTC Monograph Drug Exclusivity

As of May 2023, no companies have received OTC monograph drug exclusivity for any OTC drugs under section 505G. FDA officials told us that as of March 2023, the agency had not received any OTC monograph order requests. Officials also told us that they do not expect to receive any OTC monograph order requests until October 2023 at the earliest.

FDA is in the process of implementing OTC monograph reform, including the provisions in section 505G related to exclusivity. According to the agency's goals document, the agency anticipated that the first 3 years of implementing OTC monograph reform—fiscal years 2021 through 2023—would entail developing the infrastructure to carry out OTC monograph reform. This includes hiring and training staff, developing guidance for agency staff and industry, and constructing information technology (IT) platforms to, among other things, facilitate the review of OTC monograph order requests.[13] In addition, during this time, the agency expected that its capacity for reviewing OTC monograph order requests would be consumed by other monograph mandates and safety activities.[14]

For fiscal years 2021 and 2022, FDA reported that the agency had collected over $42 million in OTC monograph user fees, which it used in conjunction with the agency's regular appropriations to support all OTC monograph reform activities. This included hiring 32 new employees, implementing a public-facing OTC monograph IT dashboard, and designing an IT platform for FDA's OTC monograph review activities. FDA officials told us that the agency has started developing policies and guidance for both agency staff and industry related to changes made by the CARES Act. For example, in April 2023, FDA solicited public comments on the agency's draft guidance for the format and content of OTC monograph order requests.[15]

Additionally, officials told us that, as of March 2023, they have begun to develop the preliminary procedures needed to review OTC monograph order requests. Officials also told us that FDA is developing procedures related to how the agency will implement OTC monograph drug exclusivity.

Industry stakeholders from a national trade organization told us that a handful of their member companies are actively considering submitting an OTC monograph order request and are enthusiastic over the prospect of an 18-month period of exclusivity. However, industry stakeholders said the submissions may not occur until 2024. According to the potential timeframes described in the agency's May 2020 informational briefing on monograph reform,

[13]In anticipation of OTC monograph reform, FDA issued a goals document in June 2017 that was developed in collaboration with industry stakeholders to identify the OTC monograph user fee program performance and procedural goals. In 2021, FDA updated the OTC monograph user fee program performance goals and activities timeline to reflect fiscal years 2021 to 2025.

[14]FDA officials noted that the agency is not subject to timelines or OTC monograph user fee performance goals for reviewing OTC monograph order requests submitted before fiscal year 2024.

[15]88 Fed. Reg. 22,451 (Apr. 13, 2023).

FDA estimates an OTC monograph order request review would take 17 to 23 months before the agency could finalize a monograph change, including one related to exclusivity.[16]

Effect of OTC Monograph Drug Exclusivity on Innovation and Consumers Is Unknown

The potential effect of OTC monograph drug exclusivity on OTC drug innovation and consumers is unknown. Among the 91 journal articles we reviewed, none provided evidence for the effect that exclusivity could have on consumer access to OTC drugs, on the affordability of OTC drug products, and on OTC drug innovation. However, some noted that exclusivity would likely incentivize industry innovation in developing OTC drugs. For example, in a 2021 legal journal article on monograph reform, the authors noted that the combination of the faster administrative order process for monographs and an exclusivity period may facilitate the development of a wider variety of OTC drugs.[17] Similarly, another 2021 dermatology journal article noted that the OTC monograph drug exclusivity period for new active ingredients may incentivize industry innovation in developing new sunscreen products.[18]

FDA officials told us that they are unaware of a methodology that the agency could use to evaluate the effect of OTC monograph drug exclusivity. Consequently, FDA officials told us the agency does not plan to evaluate the effect that exclusivity has on industry innovation and consumer access to OTC drugs or the affordability of OTC drugs.

Industry stakeholders told us that exclusivity is a key incentive for the research investments that potential requestors would be making to support product innovation. One industry stakeholder representative said that a longer period of exclusivity (i.e., longer than the 18-month period under section 505G) would better spur innovation, considering the high costs and the period of time needed to conduct human clinical studies.[19]

Organizations representing consumers and industry stakeholders differed on how they expect OTC monograph drug exclusivity to affect consumer access and affordability.[20] For example, in a January 2018 letter to congressional leaders, an organization representing consumer interests publicly raised concerns that OTC drug companies may limit the availability of older but equally effective OTC drugs, pushing consumers to purchase newer, more expensive drugs that have received exclusivity.[21] In contrast, representatives from industry stakeholders told us they expect that innovations in OTC drug administration will increase consumer access to and utilization of OTC drugs. These stakeholders also told us they expect the effect of OTC

[16]Under the previous rulemaking process for monographs, monograph actions took several years to complete. FDA intends to reduce the time needed for action on monograph issues to a timeframe of less than 2 years in most circumstances, while still obtaining and considering public comment on proposed orders, and maintaining FDA's standards for safety and efficacy.

[17]Jason Gardiner and Aaron S. Kesselheim, "Over-the-Counter Monograph Safety, Innovation, and Reform Act," *The Journal of Law, Medicine & Ethics,* vol. 49 (2021): 321.

[18]Lisette Hilton, "Regenerative Skin Care," *Dermatology Times,* vol. 42 (2021): 36-37.

[19]Specifically, the industry stakeholder noted that a longer OTC monograph drug exclusivity period for requestors, such as a 36-48 month exclusivity period, would spur innovation and investment in new sunscreen active ingredients.

[20]In a January 2018 letter to the leadership of the House Committee on Energy and Commerce, one organization representing consumer interests questioned the need for exclusivity in the OTC drug market, noting that the then-existent exclusivity provisions in the prescription drug market have negatively affected consumers. See Public Citizen, "Letter to Congress Opposing the Proposal to Grant Two Years of Exclusivity for Certain Over-the-Counter Drugs," January 16, 2018, accessed May 2, 2023, https://www.citizen.org/article/letter-to-congress-opposing-the-proposal-to-grant-two-years-of-exclusivity-for-certain-over-the-counter-drugs/.

[21]The organization also questioned whether companies would effectively extend exclusivity by introducing a series of minor changes to obtain additional periods of exclusivity.

monograph drug exclusivity on OTC drug affordability for consumers to be minimal because of the availability of alternative OTC drugs, for example. Representatives from one industry stakeholder organization noted that, even where an OTC drug has received exclusivity, consumers will still have other options available, since therapeutic categories often have multiple alternative OTC products. For example, according to these industry stakeholder representatives, if a new sunscreen active ingredient is introduced to the monograph and receives exclusivity, other sunscreen products that use a different active ingredient will still be available to consumers, and thus consumers may not pick that new alternative. They also told us that after the 18-month OTC monograph drug exclusivity period, there will be competition from other manufacturers to produce generic products and ensure drug affordability for consumers.

Agency comments

We provided a draft of this report to FDA for review and comment. FDA provided technical comments, which we incorporated, as appropriate.

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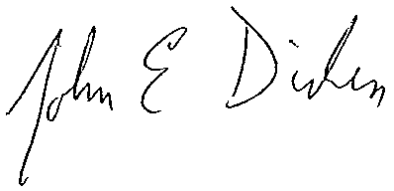
We are sending copies of this report to the appropriate congressional committees and the Secretary of Health and Human Services. In addition, the report will be available at no charge on the GAO website at https://www.gao.gov.

If you and your staff have any questions, please contact me at (202) 512-7114 or dickenj@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. Other key contributors to this correspondence included Kristi Peterson (Assistant Director), Jasleen Modi (Analyst-in-Charge), and Catherine Morrissey. Additional assistance was provided by Laurie Pachter and Kaitlin Farquharson.



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