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FDA Regulation of Over-the-Counter (OTC) Drugs: Overview and Issues for Congress

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SUMMARY

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Agata Bodie
Analyst in Health Policy

FDA Regulation of Over-the-Counter (OTC) Drugs: Overview and Issues for Congress

The Food and Drug Administration (FDA), under the Federal Food, Drug, and Cosmetic Act (FFDCA), regulates the safety and effectiveness of nonprescription (over-the-counter, or OTC) drugs sold in the United States. To market an OTC drug, a company may follow one of two pathways. A company can either (1) submit a new drug application (NDA) to FDA for approval or (2) use the OTC drug monograph process, although not all drugs are eligible for this pathway.

OTC Drug Approval and Monograph Requirements

Both the NDA and monograph pathways involve a scientific decision by FDA; however, the two mechanisms are different. A primary difference is that approval of an NDA results in the approval to sell a specific *finished drug product*, whereas the OTC drug monograph process focuses on the safety and effectiveness of one or more *active ingredients* within a drug category. For the purposes of FDA marketing approval, the NDA process generally requires submitting data from clinical trials demonstrating the safety and effectiveness of a drug. In contrast, if an OTC drug product complies with a monograph, it does not need FDA approval of its NDA prior to marketing. A monograph establishes conditions, such as active ingredients and related conditions (e.g., dosage level, combination of active ingredients, labeled indications, warnings and adequate directions for use), under which an OTC drug in a given therapeutic category (e.g., sunscreen, antacid) is generally recognized as safe and effective (GRASE) for its intended use and thus may be marketed without an approved NDA. FDA assesses monograph compliance as part of its inspection process.

FDA established the OTC drug monograph process through rulemaking in 1972. Until enactment of the Coronavirus Aid, Relief, and Economic Security Act (CARES Act; P.L. 116-136), monographs were established and amended through a three-phase, public rulemaking process. The monograph process was intended to provide an efficient mechanism through which OTC drugs could be marketed without individual FDA evaluation and approval. However, the program had faced several challenges. For example, some monographs remained unfinalized for decades, resulting in OTC drugs being on the market without final safety and effectiveness determinations. Another challenge was industry's ability to propose innovations to marketed OTC drugs without submitting an NDA, along with limited FDA resources to support OTC monograph activities. To address these regulatory and resource challenges, legislation was introduced in the 115th and 116th Congresses proposing to reform the OTC monograph process.

Congressional Action

On March 27, 2020, the CARES Act was signed into law. Section 3851 of the CARES Act established a new FFDCA Section 505G, replacing the OTC drug monograph rulemaking process with the administrative order process—a less burdensome alternative. This new process allows FDA, on its own initiative or upon request, to issue an administrative order (rather than a rule) determining that a drug, or class or combination of drugs, is GRASE or not GRASE. Certain monograph changes (e.g., new active ingredient, new indication) that are industry-requested and subject to a final administrative order are eligible for 18 months of marketing exclusivity, meaning that a competitor may not market the same drug during that period of time. Among other things, FFDCA Section 505G

- requires that certain OTC drugs be marketed only pursuant to FDA approval via an NDA;
- provides an expedited process for the issuance of administrative orders in certain circumstances (i.e., a public health hazard determination, safety labeling changes);
- provides for circumstances under which minor changes in dosage form can be made without a new administrative order;
- requires FDA to publish on its website information related to final interim and administrative orders, to develop guidance, and to establish meeting procedures; and
- requires the Government Accountability Office (GAO) to conduct a study on the impact of the 18-month marketing exclusivity period for certain eligible OTC drugs.

In addition, the CARES Act made changes to regulation of sunscreen products and directed the Health and Human Services (HHS) Secretary to report to Congress on the agency's evaluation and revision of the cough and cold monograph with respect to children under age six. The law also established a legal framework for the HHS Secretary, beginning in FY2021, to assess

and collect fees—specifically, manufacturing facility fees and monograph order request fees—from certain OTC drug companies to support FDA's OTC monograph drug activities (e.g., review of order requests, inspections).

Additional Policy Considerations

The changes made by the CARES Act sought to address some of the previously identified limitations of the OTC drug monograph system. When evaluating future policy changes, Congress may consider additional issues that may not have been fully addressed by the enacted legislation. These issues include (1) continued marketing of drugs not yet subject to final GRASE determinations, (2) review of certain sunscreen ingredients, and (3) oversight of foreign OTC drug manufacturers.

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The Food and Drug Administration (FDA), under the Federal Food, Drug, and Cosmetic Act (FFDCA), regulates the safety and effectiveness of prescription and nonprescription (over-the-counter, or OTC) drugs sold in the United States. Prescription drugs require health practitioner supervision to be considered safe for use—due to drug toxicity, potential harmful effects, or method of use—and may be dispensed only pursuant to a prescription.[1] In contrast, OTC drugs may be used without a prescriber's authorization, provided they have an acceptable safety margin, low potential for misuse or abuse, and are adequately labeled so that consumers can self-diagnose the condition, self-select the medication, and self-manage the condition.[2]

Although prescription drugs are marketed pursuant to FDA approval via a new drug application (NDA) or an abbreviated new drug application (ANDA), most OTC drug products are marketed under a different mechanism, by complying with an OTC monograph. FDA describes OTC monographs as "standards for the marketing of nonprescription drug products not covered by new drug applications. These standards provide the marketing conditions for some OTC drug products including the active ingredients, labeling, and other general requirements."[3] In other words, OTC monographs set the conditions under which OTC drug products are generally recognized as safe and effective (GRASE) for their intended use. A monograph functions similar to a recipe, in that it covers active ingredients, dosages, formulations, and labeling claims. If an OTC drug product complies with the relevant monograph, it does not need FDA approval prior to marketing. FDA assesses monograph compliance as part of its inspection process.

Historically, monographs have been established and amended through rulemaking. The Coronavirus Aid, Relief, and Economic Security Act (CARES Act; P.L. 116-136), enacted on March 27, 2020, replaced the rulemaking process with the administrative order process—a less burdensome alternative.[4]

FDA established the monograph process in 1972 through rulemaking.[5] Although the monograph process was intended to provide an efficient mechanism through which OTC drugs could be marketed without individual FDA evaluation and approval, FDA described the rulemaking process as "inefficient and time consuming" with "limited speed and flexibility in responding to urgent safety issues."[6] Prior to the enactment of the CARES Act, FDA estimated that there were approximately 88 simultaneous rulemakings in 26 broad therapeutic categories, covering approximately 800 active ingredients for over 1,400 different therapeutic uses.[7] The agency stated that resource challenges were limiting its ability to carry out monograph activities, noting that it spent approximately 40 times as much budget authority on the process of reviewing Prescription Drug User Fee Act (PDUFA) products as it did on OTC monograph products.[8] To address these

[1] FFDCA §503(b)(1) [21 U.S.C. §355(b)(1)].

[2] FDA, "Regulatory Approaches for Prescription to OTC Switch," July 2, 2015, https://www.fda.gov/media/93193/download.

[3] FDA, "Small Business Assistance: Frequently Asked Questions on the Regulatory Process of Over-the-Counter (OTC) Drugs," https://www.fda.gov/drugs/cder-small-business-industry-assistance-sbia/small-business-assistance-frequently-asked-questions-regulatory-process-over-counter-otc-drugs#OTCmonographs.

[4] P.L. 116-136, Title III, Subtitle F.

[5] 37 *Federal Register* 85, January 5, 1972, 37 *Federal Register* 9464, May 11, 1972.

[6] Testimony from Janet Woodcock, MD, Director of the Center for Drug Evaluation and Research, in U.S. Congress, House Committee on Energy and Commerce, *Modernizing FDA's Regulation of Over-The-Counter Drugs*, hearings, 115th Cong., 1st sess., September 13, 2017, https://www.fda.gov/news-events/congressional-testimony/modernizing-fdas-regulation-over-counter-drugs.

[7] Ibid.

[8] Ibid.

regulatory and resource challenges, legislation was introduced in the 115th and 116th Congresses that proposed to modify the OTC monograph process. Such legislation also proposed to create a new user fee program to fund OTC monograph drug activities (e.g., review of order requests), whereby OTC drug manufacturers would pay user fees to FDA.

On March 27, 2020, the CARES Act was signed into law, replacing the OTC drug monograph rulemaking process with the administrative order process.[9] The CARES Act also created a user fee program to fund OTC monograph activities.

This report

- summarizes the history of OTC drug regulation in the United States;
- describes the pre-CARES Act framework under which FDA, until recently, has issued and modified OTC drug monographs;
- provides an overview of the challenges identified under the previous framework and changes made by the CARES Act to address those challenges;
- explains how OTC sunscreen products are regulated and actions taken by Congress and FDA to regulate sunscreen; and
- identifies existing issues for Congress.

Brief History of U.S. OTC Drug Regulation

The FFDCA was enacted in 1938 and has been subsequently amended on numerous occasions. As enacted in 1938, the FFDCA required that drug manufacturers submit, prior to marketing, an NDA demonstrating, among other things, that a new drug (i.e., a drug that was not generally recognized as safe under the conditions of its intended use) was safe.[10] In 1962, the Kefauver-Harris Drug Amendments to the FFDCA required drug manufacturers to provide *substantial evidence* of drug effectiveness, in addition to safety, prior to marketing a new drug (i.e., a drug that was not GRASE under the conditions of its intended use).[11] This standard became the basis for the drug approval process in place today.

Drugs introduced between 1938 and 1962 were considered safe but with unknown effectiveness. To address this issue, in 1966, FDA formed the Drug Efficacy Study Implementation (DESI), contracting with the National Academy of Sciences/National Research Council (NAS/NRC), to evaluate the effectiveness of those drugs that had been approved on the basis of safety alone.[12] Holders of NDAs approved between 1938 and 1962 were required to submit data and information supporting the effectiveness of drugs approved during that time to FDA for evaluation.[13] This

[9] P.L. 116-136, Title III, Subtitle F.

[10] P.L. 75-717. See also 37 *Federal Register* 85, January 5, 1972. Prior to the 1938 law, drugs were marketed in the United States without FDA review.

[11] P.L. 87-781. FFDCA §201(p) defines a *new drug* as "any drug ... the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof [i.e., GRASE] ... " or "any drug ... the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions."

[12] 31 *Federal Register*, 9426, July 6, 1966. FDA, "Drug Efficacy Study Implementation (DESI)," https://www.fda.gov/drugs/enforcement-activities-fda/drug-efficacy-study-implementation-desi.

[13] 31 *Federal Register*, 9426, July 6, 1966.

review was first conducted for prescription drugs, due to their greater potential for harm, and FDA determined that a similar review would be appropriate for OTC drugs.[14] However, such a review posed a challenge for OTC drugs, particularly due to the size of the market. At the time, FDA estimated that there were at least 100,000 (and potentially up to 500,000) OTC drug products on the market, made up of hundreds of different active ingredients.[15] Some OTC drugs had been approved under an NDA based on safety but not effectiveness, while others had never been approved at all.[16] This discrepancy and the volume of products on the market limited the feasibility of an FDA product-by-product review of these drugs.

To address this challenge, in 1972, FDA proposed the OTC Drug Review—a mechanism through which OTC drug products on the market prior to 1972 could be lawfully marketed pursuant to a GRASE determination, made by FDA through rulemaking, instead of individual evaluation and approval under an NDA.[17] The OTC Drug Review was intended to evaluate the safety and effectiveness of OTC drug products according to their respective therapeutic drug category (e.g., antacids).[18] This process became the primary pathway through which OTC drug products were marketed, with some modifications over time. For example, in 2002, FDA issued a rule establishing the time and extent application (TEA) process through which conditions marketed in the United States after 1972 or conditions without any U.S. marketing experience could be considered for inclusion in the OTC drug monograph system.[19] Prior to the TEA rule, many such conditions could not be added to a monograph; instead, they could be marketed only pursuant to an approved NDA.[20] In 2014, the Sunscreen Innovation Act (SIA; P.L. 113-195) created an administrative order process for determining whether certain new OTC sunscreen active ingredients or combinations of OTC sunscreen active ingredients were GRASE.[21] In March 2020, the CARES Act was signed into law, replacing the OTC drug monograph rulemaking process with an administrative order process. These changes are described in more detail below.

How FDA Regulates the Marketing of OTC Drugs

To market an OTC drug product in the United States, the manufacturer may follow one of two pathways. A manufacturer can either (1) submit an NDA for approval to FDA or (2) use the OTC drug monograph process.[22] Both the NDA and monograph pathways involve a scientific decision by FDA; however, the two mechanisms are different. A primary difference is that approval of an NDA results in the approval to sell a specific *finished drug product*, whereas the OTC drug monograph process focuses on the safety and effectiveness of one or more *active ingredients*

[14] 37 *Federal Register* 85, January 5, 1972.

[15] Ibid.

[16] Ibid.

[17] Ibid., 37 *Federal Register* 9464, May 11, 1972. See also https://www.accessdata.fda.gov/scripts/cder/training/OTC/topic3/topic3/da_01_03_0080.htm.

[18] 37 *Federal Register* 9464, May 11, 1972.

[19] 21 C.F.R. §330.14. This rule defined *condition*, for purposes of the TEA process, to mean "an active ingredient or botanical drug substance (or a combination of active ingredients or botanical drug substances), dosage form, dosage strength, or route of administration, marketed for a specific OTC use, except as excluded in paragraph (b)(2) of this section." 21 C.F.R. §330.14(a)(2).

[20] FDA, "Time and Extent Applications for Nonprescription Drug Products," Guidance for Industry, September 2011, p. 5, https://www.fda.gov/media/72219/download.

[21] 21 C.F.R. §330.15. 81 *Federal Register* 84465, November 23, 2016.

[22] FFDCA §505 [21 U.S.C. §355]. 21 C.F.R. Part 330.

within a drug category.[23] According to FDA, "[t]he OTC Monograph system provides lower regulatory burden for industry and helps to keep OTC drug costs low through the extensive array of potential products that final monographs can cover."[24]

OTC Drug Approval Under an NDA

As mentioned above, a new drug may not be introduced into interstate commerce without FDA approval.[25] To approve a drug, FDA requires data from clinical trials to provide evidence of a drug's safety and effectiveness, except under very limited circumstances. Once a manufacturer completes clinical trials, it submits the results of those investigations, along with other information, to FDA in an NDA.[26] In reviewing an NDA, FDA considers

- whether the drug is safe and effective for its intended use;
- whether the proposed labeling is appropriate; and
- whether the methods used to manufacture the drug and the controls used to maintain the drug's quality are adequate to preserve the drug's identity, strength, quality, and purity.[27]

For purposes of approval, an NDA must include *substantial evidence* of effectiveness, meaning evidence consisting of adequate and well-controlled investigations.[28] FDA has typically interpreted this provision as requiring two adequate and well-controlled trials, and the agency has some discretion to determine what evidence is necessary for NDA approval.[29]

Although manufacturers generally *must* obtain approval through an NDA (or an abbreviated NDA [ANDA], in the case of a generic drug) for all prescription drugs prior to marketing, a manufacturer *may* obtain such approval for OTC drugs. As part of an NDA for an OTC drug, FDA may require the sponsor to conduct label comprehension studies assessing the extent to which consumers understand the information in the proposed labeling.[30] FDA also may recommend that the sponsor conduct self-selection studies to assess whether consumers can appropriately self-select a drug based on the information in the labeling.[31]

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[23] FDA, "The ABCs of OTCs: Little-Known Facts About Over-the-Counter Drugs," presentation by Karen Murry Mahoney, MD, FACE, Deputy Director of the Division of Nonprescription Drug Products, Center for Drug Evaluation and Research, FDA, p. 29, https://www.fda.gov/media/97292/download.

[24] Testimony from Janet Woodcock, MD, Director of the Center for Drug Evaluation and Research, in U.S. Congress, House Committee on Energy and Commerce, *Modernizing FDA's Regulation of Over-The-Counter Drugs*, hearings, 115th Cong., 1st sess., September 13, 2017, https://www.fda.gov/news-events/congressional-testimony/modernizing-fdas-regulation-over-counter-drugs.

[25] FFDCA §505(a) [21 U.S.C. §355(a)].

[26] FFDCA §505(b) [21 U.S.C. §355(b)] and 21 C.F.R. §314.50.

[27] FFDCA §505(b), (d) [21 U.S.C. §355(b), (d)]. For additional information, see CRS Report R41983, *How FDA Approves Drugs and Regulates Their Safety and Effectiveness*.

[28] FFDCA §505(d) [21 U.S.C. §355(d)] and 21 C.F.R. §314.126.

[29] FDA, Draft Guidance for Industry, "Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products," December 2019, https://www.fda.gov/media/133660/download.

[30] FDA, Guidance for Industry, "Label Comprehension Studies for Nonprescription Drug Products," August 2010, https://www.fda.gov/media/75626/download.

[31] FDA, Guidance for Industry, "Self-Selection Studies for Nonprescription Drug Products," April 2013, https://www.fda.gov/media/81141/download.

If a manufacturer wants to transfer an approved drug from prescription to OTC status (called an Rx-to-OTC switch), the manufacturer must submit an NDA (or a supplement to an NDA)[32] to FDA with data to support the switch.[33] In addition, FDA may exempt a drug from the prescription use requirement by regulation if the prescription-only dispensing requirement is not necessary for the protection of public health.[34] FDA may issue such a regulation on its own initiative or in response to a petition from an interested party.[35]

OTC Drug Monograph Process

Unlike the NDA process, which requires the individual evaluation of each drug product, the OTC Drug Review resulted in the development of OTC monographs for specific drug categories.[36] The monographs set the conditions under which OTC drug products in specific drug categories may be marketed without individual product premarket approval, including the active ingredient(s) and related conditions (e.g., dosage level, combination of active ingredients, labeled indications, and warnings and adequate directions for use).[37] As explained in FDA monograph regulations, for purposes of a GRASE determination, general recognition of safety and effectiveness "shall ordinarily be based upon published studies which may be corroborated by unpublished studies and other data."[38]

Unlike the NDA process, the OTC drug monograph process does not require a manufacturer to submit clinical trial data demonstrating safety and effectiveness of an individual drug product, nor does it require an OTC drug product to be approved by FDA before marketing. This is because FDA had already evaluated the safety and effectiveness evidence as part of its monograph rulemaking. As long as the drug product complies with the conditions of the monograph, premarket approval is not necessary. For example, the "Nighttime Sleep-aid Drug Products for OTC Human Use" monograph defines the term *night-time sleep aid*, lists the active ingredients (within established dosage limits) that may be used in OTC night-time sleep aids, and requires that certain labeling accompany these drug products.[39] An OTC night-time sleep aid drug marketed in accord with those specifications does not need an approved NDA to be marketed.

The manufacturer of an OTC drug that does not meet the conditions of a monograph (e.g., if the drug differs in dosage form or contains a new indication other than that specified in the monograph) can apply for approval via the NDA process or by proposing a modification to an existing monograph pursuant to changes made by the CARES Act (see the "Monograph Modification and Innovation" section).

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[32] A supplement refers to a request submitted to FDA to approve a change to an approved application. FFDCA §735(2) [21 U.S.C. §379g(2)].

[33] 21 C.F.R. §310.200(b).

[34] FFDCA §503(b)(3) [21 U.S.C. §353(b)(3)].

[35] 21 C.F.R. §310.200(b).

[36] The 26 drug categories are listed in 21 C.F.R. §330.5: antacids, laxatives, antidiarrheal products, emetics, antiemetics, antiperspirants, sunburn prevention and treatment products, vitamin-mineral products, antimicrobial products, dandruff products, oral hygiene aids, hemorrhoidal products, hematinics, bronchodilator and antiasthmatic products, analgesics, sedatives and sleep aids, stimulants, antitussives, allergy treatment products, cold remedies, antirheumatic products, ophthalmic products, contraceptive products, miscellaneous dermatologic products, dentifrices and dental products (e.g., analgesics, antiseptics), and miscellaneous (all other OTC drugs not falling within one of the above therapeutic categories).

[37] 21 C.F.R. §330.10(a)(5).

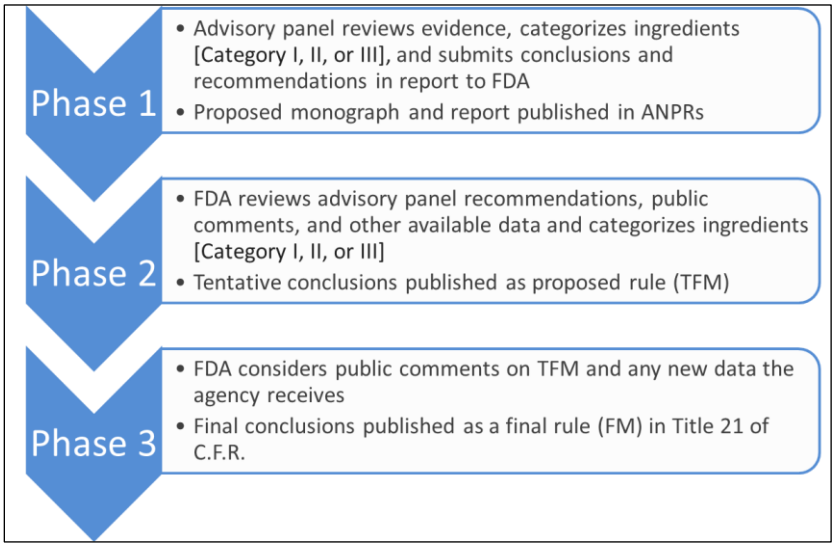
[38] 21 C.F.R. §330.10(a)(4).

[39] 21 C.F.R. Part 338.

Pre-CARES Act: Three-Phase Public Rulemaking Process

The OTC Drug Review was established as a three-phase public rulemaking process (see **Figure 1**). Prior to the enactment of the CARES Act, FDA published final monographs as regulations in the *Code of Federal Regulations* (C.F.R.).

Figure 1. Pre-CARES Act: OTC Drug Review



Source: Figure created by CRS based on 21 C.F.R. §330.10.

Notes: ANPR= Advanced Notice of Proposed Rulemaking; TFM= Tentative Final Monograph; FM= Final Monograph.

Phase I

In the first phase of the OTC Drug Review, which was completed, FDA convened advisory panels of qualified experts "to evaluate the safety and effectiveness of OTC drugs, to review OTC drug labeling, and to advise [the FDA Commissioner] on the promulgation of monographs establishing conditions under which OTC drugs are [GRASE] and not misbranded."[40] An advisory review panel was established for each category of OTC drugs, and every category was required to be considered by a panel.[41] For each category of drugs, the Commissioner published a notice in the *Federal Register* calling upon interested persons to submit specified data and information for review by an advisory panel.[42] After completing the review, each panel would submit to FDA a report containing its conclusions and recommendations regarding which active ingredients and related conditions within a drug category were GRASE (i.e., Category I). The panel could determine that certain conditions should be excluded from the monograph, resulting in a drug being not GRASE (i.e., Category II), or that data were insufficient to classify conditions as Category I or II and that further testing was required for those conditions (i.e., Category III).

[40] 21 C.F.R. §330.10(a)(1).

[41] Ibid.

[42] 21 C.F.R. §330.10(a)(2).

Following submission of the advisory panel's report, FDA then published in the *Federal Register*, with a public comment period, an advance notice of proposed rulemaking (ANPR) containing the following: (1) the advisory panel's report, (2) a proposed monograph(s) establishing the conditions under which a specific OTC drug(s) or category of OTC drugs would be considered GRASE (i.e., Category I), (3) a statement of the conditions excluded from the monograph based on the Commissioner's determination that they would result in a drug not being GRASE (i.e., Category II), and (4) a statement of the conditions excluded from the monograph because data were insufficient to classify conditions as Category I or II (i.e., Category III).[43]

OTC Monograph Categorization

Category I: GRASE. Category I includes conditions considered to be safe and effective on the basis of existing data and information.

Category II: Not GRASE. Category II includes conditions that are not GRASE.

Category III: Insufficient data. Category III includes conditions for which there is not enough information to place them in Category I or II.

Conditions: Include active ingredients, dosage strength, dosage form and route of administration, patient population, indications for use, required labeling (e.g., warnings).

Phase 2

In the second phase of the OTC Drug Review, FDA reviewed and evaluated the advisory panel's findings, public comments, and any new data submitted to the agency.[44] FDA regulations required FDA, after reviewing all comments and new data and information submitted with respect to the ANPR or proposed monograph, to publish in the *Federal Register* a tentative final monograph (TFM) proposing conditions under which a specific OTC drug(s) or category of OTC drugs were GRASE (Category I), accompanied by another public comment period.[45] The Commissioner was allowed to publish in the *Federal Register* a separate TFM containing a statement of those active ingredients and related conditions reviewed and proposed to be excluded from the monograph because they would result in a drug product not being GRASE (Category II).[46] FDA also could propose that data are insufficient to classify conditions as Category I or II (Category III).

Phase 3

The third phase of the OTC Drug Review was monograph finalization. In this phase, FDA considered the public comments provided in response to a TFM and any new data the agency received. FDA regulations provided for a period of public comment, specified processes for submission of new data and information by interested parties, and required FDA to schedule a hearing based on objections filed to a TFM, as specified. "After reviewing the objections, the entire administrative record including all new data and information and comments, and considering the arguments made at any oral hearing," FDA then would publish a final monograph (FM) as a final rule, delineating the active ingredients and related conditions under which OTC drug products in a specific therapeutic category are GRASE, to become effective as specified.[47] Only active ingredients classified as GRASE were included in an FM and thus the category

[43] 21 C.F.R. §330.10(a)(6).

[44] FDA, "Over-the-Counter (OTC) Drug Monograph Process," https://www.fda.gov/drugs/current-good-manufacturing-practices-cgmp-drugs-reports-guidances-and-additional-information/over-counter-otc-drug-monograph-process.

[45] 21 C.F.R. §330.10(a)(7)(i).

[46] 21 C.F.R. §330.10(a)(7)(ii).

[47] 21 C.F.R. §330.10(a)(9).

designations (i.e., I, II, or III) are not used in FMs. An exception to this is the "negative monograph" (codified at 21 C.F.R. §310.545), which lists conditions that are not GRASE.

In September 2017 testimony, then-Director of the Center for Drug Evaluation and Research (CDER) Janet Woodcock indicated that although some monographs were finalized using these three steps, in reality, the process had shifted. For example, her testimony included **Figure 2** below and noted that "this lengthy and circuitous path is not unusual."[48]

Figure 2. Selected Example: OTC Monograph Rulemaking for External Analgesic Drug Products

Burdensome, Multi-Step Rulemakings

Published	Federal Reg. Citation	Topic
12-4-79	**44FR69768**	**ANPR for External Analgesic Drug Products**
2-5-80	45FR7820	Correction
9-26-80	45FR63878	Reopening of administrative record
9-7-82	47FR39412	Reopening of administrative record
12-7-82	47FR54981	Correction
12-28-82	47FR57738	Extension of comment and reply periods
2-8-83	48FR5852	TFM (Tentative Final Monograph = Proposed Rule)
3-11-83	48FR10373	Correction
10-2-85	50FR40260	Amend TFM to add male genital desensitizer indication
7-30-86	51FR27360	Amend TFM to add seborrheic dermatitis and psoriasis indication
8-25-88	53FR32592	Amend TFM warnings and directions for external anal itching
4-3-89	54FR13490	Amend TFM to remove astringent drug products
10-3-89	54FR40818	Amend TFM to add poison ivy, poison oak, poison sumac, and insect bite indications
1-31-90	55FR3370	Amend TFM to address fever blister and cold sore indications
2-27-90	55FR6932	Amend TFM to make hydrocortisone 1% OTC
3-27-90	55FR11291	Correction
6-20-90	55FR25234	Amend TFM to address treatment and prevention of diaper rash
8-30-91	56FR43025	Hydrocortisone; Notice of Enforcement Policy
6-19-92	57FR27654	FR (Final Rule) Male genital desensitizer
12-18-92	57FR60426	FR (Final Rule) Diaper rash labeling
8-29-97	62FR45767	Amend TFM to add warning about diphenhydramine
11-19-97	**62FR61710**	**Reopening of administrative records to consider new data**

Source: Testimony from Janet Woodcock, MD, Director of the Center for Drug Evaluation and Research, in U.S. Congress, House Committee on Energy and Commerce, *Modernizing FDA's Regulation of Over-The-Counter Drugs*, hearings, 115th Cong., 1st session, September 13, 2017, https://energycommerce.house.gov/sites/democrats.energycommerce.house.gov/files/documents/Testimony-Woodcock-HE-Hrg-on-Modernizing-FDA%E2%80%99s-Regulation-of-Over-the-Counter-Drugs-09-13-17.pdf.

Monograph Modification

Once a monograph was finalized in regulation, it could be modified on the initiative of the FDA Commissioner, by an interested party via a citizen petition, or through submission of a time and extent application (TEA) by an interested party (typically a drug manufacturer). The filing of a citizen petition or TEA triggered a public rulemaking process to amend the appropriate OTC monograph. A TEA also could lead to the creation of a new OTC monograph. Alternatively, an

[48] Testimony from Janet Woodcock, MD, Director of the Center for Drug Evaluation and Research, in U.S. Congress, House Committee on Energy and Commerce, *Modernizing FDA's Regulation of Over-The-Counter Drugs*, hearings, 115th Cong., 1st sess., September 13, 2017, https://www.fda.gov/news-events/congressional-testimony/modernizing-fdas-regulation-over-counter-drugs.

NDA could be used to request approval of an OTC drug that deviates from the monograph. Historically, the citizen petition and TEA processes have taken more time than a final decision by FDA on an NDA.[49]

Citizen Petition

A citizen petition could be used to request that FDA amend or repeal conditions marketed in the United States *before* 1972 (i.e., conditions eligible for inclusion in the OTC Drug Review).[50] The petition had to be accompanied by data demonstrating the general recognition of safety and effectiveness of the amended condition. If FDA determined that such a request should be granted, the agency would issue a proposed rule, along with a period for public comment, and then a final rule amending the monograph or withdrawing the proposed rule.[51]

TEA

The TEA process, established by FDA through rulemaking in 2002, could be used to request, for the first time, that conditions marketed in the United States *after* 1972 or without any U.S. marketing experience be included in the OTC drug monograph system.[52] Prior to the issuance of these regulations, many conditions were ineligible for such inclusion and could be marketed only under an NDA. In November 2016, FDA amended its TEA regulations, as required by the Sunscreen Innovation Act (P.L. 113-195), to establish timelines for reviewing and acting on nonsunscreen TEAs.[53]

The TEA regulations established a two-step process for incorporating new conditions into an OTC drug monograph. The first step was eligibility—the interested party was required to submit a TEA to FDA demonstrating that the condition had been marketed for OTC purchase for a "material time" and to a "material extent" by submitting specified information to FDA.[54] If FDA determined that the condition was eligible for inclusion in the monograph, the second step was submission of safety and effectiveness data. FDA would publish a notice in the *Federal Register* asking interested parties to submit data and pertinent information to support the safety and effectiveness of the proposed condition.[55] FDA or an advisory panel then reviewed the data using the same safety and effectiveness standards as the OTC Drug Review. After reviewing the safety and effectiveness data, if FDA determined that the condition was GRASE for the intended use, the agency would publish a proposed rule to incorporate the new condition into an existing monograph, or create a new monograph if necessary.[56] FDA also could make an initial

[49] FDA, "Time and Extent Applications for Nonprescription Drug Products," Guidance for Industry, September 2011, p. 4, https://www.fda.gov/media/72219/download.

[50] FDA regulations describe the process by which FDA may amend or repeal an existing monograph in response to a citizen petition. 21 C.F.R. §330.10(a)(12). FDA, "Time and Extent Applications for Nonprescription Drug Products," Guidance for Industry, September 2011, p. 5.

[51] FDA, "Time and Extent Applications for Nonprescription Drug Products," Guidance for Industry, September 2011, p. 5.

[52] 21 C.F.R. §330.14. The TEA regulations defined a condition to mean an active ingredient or botanical drug substance (or combination of both), dosage form, dosage strength, or route of administration marketed for a particular OTC use [21 §330.14(a)(2)].

[53] 81 *Federal Register* 84465, November 23, 2016.

[54] 21 C.F.R. §330.14(c). "Material time" is defined as marketing for a minimum of five continuous years in the same country, and "material extent" is defined as marketing a sufficient quantity and is further described in FDA regulations.

[55] 21 C.F.R. §330.14(e) & (f).

[56] 21 C.F.R. §330.14(g)(3).

determination that the condition was not GRASE. After considering comments and information submitted with respect to the proposed rule, FDA would publish a final rule incorporating that condition into a final monograph (FM), or issue a re-proposal if necessary.[57] A condition submitted under a TEA for OTC monograph consideration could be marketed in accordance with an applicable FM only after the agency determined that the condition was GRASE and included it in the appropriate FM. If an OTC monograph had not been finalized and finalization was not imminent, FDA could publish a notice of enforcement policy allowing marketing to begin pending completion of the FM, as specified.[58]

NDA

An NDA may be used to request approval of an OTC drug that deviates from a monograph. An approved NDA would apply only to the product (and dosage, indications, manufacturing process, and labeling) covered explicitly by the NDA.

General OTC Drug Requirements

While most OTC drugs are not required to go through the premarket approval process, they are required to comply with various other statutory and regulatory requirements. For example, manufacturers of OTC drugs are required to register their facilities and list the OTC drugs manufactured there,[59] to comply with current good manufacturing practices (CGMPs), [60] to meet labeling requirements,[61] and to report serious adverse events to FDA.[62] In addition, OTC drugs may contain only those inactive ingredients that are safe in the amounts administered and that do not interfere with the effectiveness of the preparation.[63] FDA may inspect OTC drug manufacturing facilities and take enforcement action against violative OTC drugs through issuance of warning letters, import alerts, and voluntary recalls. FDA can, with DOJ assistance, pursue more stringent actions, such as product seizure or injunction.

The CARES Act and OTC Monograph Reform

The OTC Drug Review created by FDA in 1972 was one of the agency's largest and most complex regulatory programs.[64] While it was intended to provide an efficient mechanism through which OTC drugs could be marketed without individual FDA evaluation and approval, the program encountered several challenges. First, some monographs remained unfinalized for decades, resulting in OTC monograph drugs on the market that were not subject to a final determination regarding their safety and effectiveness. Second, FDA's ability to respond to safety concerns with OTC monograph drugs in a timely and efficient manner was limited under the

[57] 21 C.F.R. 330.14(g)(5).

[58] 21 C.F.R. 330.14(h).

[59] 21 C.F.R. §330.1(b).

[60] 21 C.F.R. §330.1(a).

[61] 21 C.F.R. §330.1(c).

[62] FFDCA §760 [21 U.S.C. §379aa].

[63] 21 C.F.R. §330.1(e).

[64] Testimony from Janet Woodcock, MD, Director of the Center for Drug Evaluation and Research, in U.S. Congress, House Committee on Energy and Commerce, *Modernizing FDA's Regulation of Over-The-Counter Drugs*, hearings, 115th Cong., 1st sess., September 13, 2017, https://www.fda.gov/news-events/congressional-testimony/modernizing-fdas-regulation-over-counter-drugs.

rulemaking process. Third, under the previous monograph framework, it was a challenge for industry to propose modifications to marketed OTC drugs without submitting an NDA, which limited innovation. Finally, by its own account, FDA had limited resources to support OTC monograph activities.[65] As described below, the CARES Act sought to address these regulatory and resource challenges by modifying the OTC monograph process and creating a new user fee program to fund OTC monograph drug activities. This new user fee program is referred to as the Over-the-Counter Monograph User Fee Act (OMUFA).[66]

Monograph Finalization

Although the OTC Drug Review began in 1972, some monographs have not been finalized. As a result, some OTC monograph drugs on the market have not received final GRASE determinations. According to a July 2020 Government Accountability Office (GAO) report, FDA officials indicated that as of December 2019, 7 of the 26 original OTC monograph categories had no FM in effect, and of the 17 that did have an FM in effect, 12 had proposed changes associated with them.[67]

The reforms made by the CARES Act aimed to facilitate monograph finalization, thus decreasing the OTC monograph drugs on the market not subject to a final determination regarding their safety and effectiveness. The act created a new process for issuing monographs through administrative orders rather than rulemaking. Specifically, FFDCA Section 505G, as added by the CARES Act, provides a process through which FDA, on its own initiative or upon request from a requestor(s), may issue an administrative order determining whether there are conditions under which a drug, or class or combination of drugs, is GRASE or not GRASE.[68] FDA publishes proposed and final administrative orders on its website.[69]

FFDCA Section 505G also specifies which OTC monograph drugs may continue to be marketed without an approved application prior to monograph finalization and which drugs may not be marketed. Specifically, FFDCA Section 505G

- deems as GRASE drugs that are classified in Category I in a TFM and that meet the applicable general requirements for OTC drugs;[70]
- allows for certain OTC monograph drugs not yet subject to a final GRASE determination to continue to be marketed, specifically if the drug is classified in Category III in a TFM or Category I under an ANPR and meets the applicable requirements for OTC drugs (these drugs are expected to eventually be subject to FDA-initiated administrative orders);[71]

[65] Ibid.

[66] P.L. 116-136, Title III, Subtitle F. FDA, "Over-The-Counter Monograph User Fee Program (OMUFA)," https://www.fda.gov/industry/fda-user-fee-programs/over-counter-monograph-user-fee-program-omufa. FDA, "Over-the-Counter Monograph User Fee Program Performance Goals and Procedures—Fiscal Years 2018-2022," https://www.fda.gov/media/106407/download.

[67] GAO, *Over-the-Counter Drugs: Information on FDA's Regulation of Most OTC Drugs*, GAO-20-572, July 2020 p. 9, https://www.gao.gov/assets/gao-20-572.pdf. The GAO report does not address the remaining two categories.

[68] FFDCA §505G(b)(1)(B) [21 U.S.C. §355h(b)(1)(B)].

[69] FDA, "OTC Monographs@FDA," https://www.accessdata.fda.gov/scripts/cder/omuf/index.cfm.

[70] FFDCA §505G(a)(1)(A) [21 U.S.C. §355h(a)(1)(A)].

[71] FFDCA §505G(a)(3) [21 U.S.C. §355h(a)(3)].

- provides that a drug classified in Category II in a TFM is a new drug and misbranded and cannot be marketed without an approved application beginning 180 days after enactment, unless FDA determines that it is in the interest of the public health to extend this period of time.[72]

FMs published in the C.F.R. and certain TFMs (i.e., those establishing conditions of use for a drug classified as Category I) have been deemed final orders.[73] Further, the provisions of 21 C.F.R. §310.545 (the "negative monograph"), as in effect on the day before enactment of the CARES Act, were deemed to be a final order.[74] The final order specifies that these active ingredients are not GRASE and cannot be legally marketed under FFDCA Section 505G.[75]

Issuance of Administrative Orders

In the case of FDA-initiated GRASE determinations, the agency must take the following steps in issuing an administrative order determining whether a drug or class or combination of drugs is GRASE (see **Figure 3**):

- notify (or make reasonable efforts to notify) sponsors who will be affected by the administrative order at least two days before issuing a proposed order;
- issue a proposed order with reasons for its issuance and provide for a public comment period of at least 45 days—if the proposed order concerns a determination that the drug is not GRASE, the notice must include the general categories of data necessary to establish that the drug is GRASE and provide a comment period of at least 180 days; and
- issue a final administrative order with a detailed statement of reasons, providing sponsors with the opportunity for formal dispute resolution, a hearing, and judicial review, as specified.[76]

With respect to industry-initiated requests, a requestor may submit an OTC Monograph Order Request (OMOR) asking FDA to issue an administrative order determining that a drug, or class or combination of drugs, is GRASE (see **Figure 3**).[77] An OMOR also could request that FDA issue an administrative order for a change to a monograph; for example, the addition of a new active ingredient or indication to a monograph that already has one or more ingredients that have been found to be GRASE.[78] Innovations or changes may be requested only for ingredients that have a final GRASE determination. If an ingredient does not (e.g., is classified in Category III in a TFM), the OMOR also must include a request for GRASE determination.[79]

[72] FFDCA §505G(a)(4) [21 U.S.C. §355h(a)(4)].

[73] FFDCA §505G(b)(8) [21 U.S.C. §355h(b)(8)]. 86 *Federal Register* 52474, September 21, 2021.

[74] FFDCA §505G(k)(2)(A) [21 U.S.C. §355h(k)(2)(A)]. 86 *Federal Register* 52474, September 21, 2021.

[75] FDA, " Non-Monograph Conditions NM900: Drug Products Containing Certain Active Ingredients Offered Over-the-Counter for Certain Uses," Order ID OTC000007, September 24, 2021, https://www.accessdata.fda.gov/scripts/cder/omuf/index.cfm?event=NewMonograph&ID=5AC274A6E59616F32A8E19D6DE726E9AA0C741220E8ABFFECF2E3FC5CA768476&OMUFID=OTC000007.

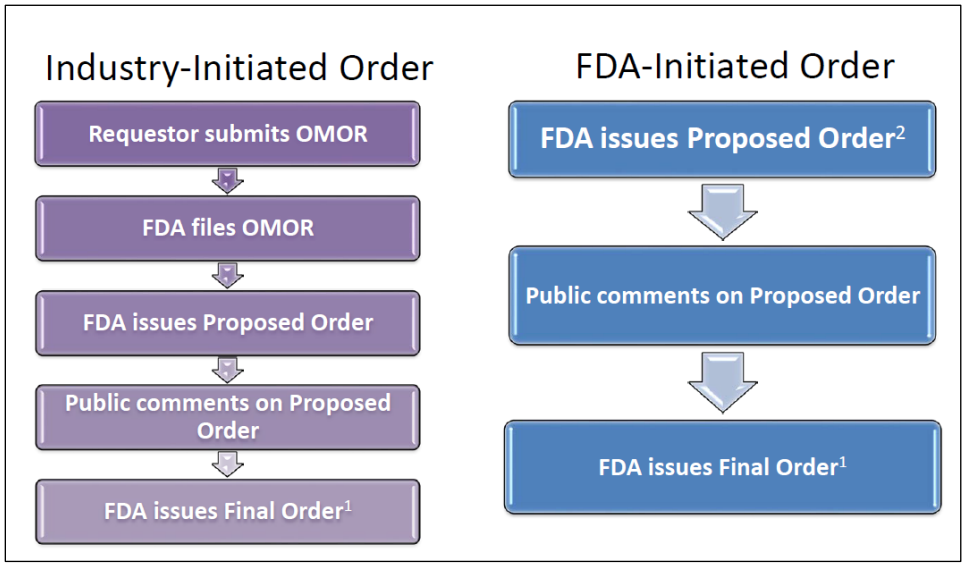
[76] FFDCA §505G(b)(2) [21 U.S.C. §355h(b)(2)].

[77] FFDCA §505G(b)(5) [21 U.S.C. §355h(b)(5)].

[78] FDA, "Over-the-Counter Monograph User Fee Program Performance Goals and Procedures—Fiscal Years 2018-2022," p. 10, https://www.fda.gov/media/106407/download.

[79] FFDCA §505G(b)(5)(B)(i)(II) [21 U.S.C. §355h(b)(5)(B)(i)(II)]. FDA, "Over-the-Counter Monograph User Fee Program Performance Goals and Procedures—Fiscal Years 2018-2022," p. 10.

Figure 3. Administrative Order Process



Source: FDA, "Monograph Reform is Here!" presentation by Theresa M. Michele, MD, Director Office of Nonprescription Drugs CDER, FDA, May 29, 2020.

Notes: [1] Final orders are subject to dispute resolution, administrative hearings, and judicial review. [2] FDA may initiate the administrative order process through expedited procedures (see the "Response to OTC Drug Safety Issues" section).

Based on discussions between FDA and industry, it is expected that most requests for GRASE finalization would be FDA-initiated, while OMORs for innovation or changes would be industry-initiated.[80] As an example, FDA would be expected to initiate the process to issue an administrative order finalizing the GRASE status of existing active ingredients, (e.g., those classified in Category III under a TFM). In contrast, industry would be more likely to submit an OMOR requesting, for example, the addition of a new active ingredient or indication to an existing monograph. In the OMUFA goals letter, FDA has agreed to specified timelines for OMOR review.[81]

Response to OTC Drug Safety Issues

FDA indicated that under the pre-CARES Act framework, the agency's ability to respond to safety issues related to OTC monograph drugs in a timely and efficient manner was limited due to certain regulatory requirements pertaining to the monograph process. For OTC drugs marketed under an NDA, FDA approves the labeling as part of the premarket review process and can require labeling changes once a drug is on the market if the agency becomes aware of new safety or effectiveness information.[82] For OTC drugs not subject to an NDA, however, FDA can require labeling changes through amendments to the monograph via rulemaking.[83] According to then-

[80] FDA, "Over-the-Counter Monograph User Fee Program Performance Goals and Procedures—Fiscal Years 2018-2022," p. 28.

[81] FDA, "Over-the-Counter Monograph User Fee Program Performance Goals and Procedures—Fiscal Years 2018-2022." FDA, "Updated Over-the-Counter Monograph User Fee Program Performance Goals Dates—Fiscal Years 2021-2025," https://www.fda.gov/industry/fda-user-fee-programs/over-counter-monograph-user-fee-program-omufa.

[82] FFDCA §505(o)(4) [21 U.S.C. §355(o)(4)].

[83] Testimony from Janet Woodcock, MD, Director of the Center for Drug Evaluation and Research, in U.S. Congress,

CDER-Director Janet Woodcock's September 2017 testimony, "a number of planned safety labeling changes for monograph ingredients have not yet taken place while similar changes have already been made to prescription drugs containing the same ingredient."[84]

One example of FDA's limited ability to address safety issues pertains to children's cough and cold medicines. Between 2004 and 2005, more than 1,500 children under two years of age were treated in U.S. emergency departments for adverse events associated with cough and cold medications.[85] In addition, concerns arose regarding the use of these medications in children under six years of age. In 2007, a citizen petition was submitted to FDA requesting that the agency amend the OTC drug monograph for Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products in 21 C.F.R. Part 341 to require that labeling for the covered OTC drugs state that they have not been found to be safe or effective in children under six years of age for the treatment of cough and cold and should not be used for such treatment in children that age.[86] In October 2007, FDA convened the Joint Meeting of the Nonprescription Drugs Advisory Committee and the Pediatric Advisory Committee to discuss the safety and effectiveness of OTC cough and cold products marketed for pediatric use.[87] The committees determined that the available published studies did not demonstrate that the cough and cold products in the monograph were effective in children and recommended additional studies.[88] FDA has not amended the monograph for Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products in 21 C.F.R. Part 341 to reflect this recommendation.

Absent rulemaking, FDA issued several consumer updates warning of the potential harms associated with the use of children's cough and cold medicines. FDA also issued guidance for consumers to help them select appropriate medicines for children. Manufacturers voluntarily removed OTC infant cough and cold products intended for children under two years of age and voluntarily updated product labeling to include the warning "do not use in children under 4 years of age."[89] However, such labeling changes were not required by FDA under the cough and cold monograph, and in order for FDA to require such labeling for these products, the agency would have had to amend the monograph through rulemaking.

To address these limitations, FFDCA Section 505G provides an expedited mechanism for issuing administrative orders to address certain safety issues. Specifically, in instances where a drug, class, or combination of drugs poses an imminent hazard to the public health, the HHS Secretary may issue an interim final administrative order with such determination, to take effect on a date

House Committee on Energy and Commerce, *Modernizing FDA's Regulation of Over-The-Counter Drugs*, hearings, 115th Cong., 1st sess., September 13, 2017, https://www.fda.gov/news-events/congressional-testimony/modernizing-fdas-regulation-over-counter-drugs.

[84] Ibid.

[85] FDA, "Use Caution When Giving Cough and Cold Products to Kids," https://www.fda.gov/drugs/special-features/use-caution-when-giving-cough-and-cold-products-kids.

[86] Citizen Petition to FDA from the Baltimore City Health Department et al., March 1, 2007, Docket ID FDA-2007-P-0050-0023.

[87] FDA, Center for Drug Evaluation and Research (CDER), "Joint meeting of the Nonprescription Drugs Advisory Committee and the Pediatric Advisory Committee," agenda, October 18 and 19, 2007, http://wayback.archive-it.org/7993/20170404050512/https://www.fda.gov/ohrms/dockets/ac/07/agenda/2007-4323a1-Final.pdf.

[88] Meeting minutes, Joint Meeting of the Nonprescription Drugs Advisory Committee and the Pediatric Advisory Committee October 18-19, 2007, http://wayback.archive-it.org/7993/20170404050526/https://www.fda.gov/ohrms/dockets/ac/07/minutes/2007-4323m1-Final.pdf.

[89] FDA, "Use Caution When Giving Cough and Cold Products to Kids," https://www.fda.gov/drugs/special-features/use-caution-when-giving-cough-and-cold-products-kids.

specified by the Secretary and before the public has had an opportunity to comment.[90] The Secretary must make reasonable efforts to notify affected sponsors at least two days prior to issuing the interim final administrative order and publish the order in the *Federal Register* with a statement of reasons and public comment period of at least 45 days, followed by a final order. This expedited procedure also applies to certain labeling changes for new warnings and other information to mitigate serious adverse events associated with the drug.[91] The Secretary must provide sponsors subject to the order with an opportunity for formal dispute resolution, a hearing, and judicial review, as specified.

The CARES Act further requires that, not later than one year after enactment and annually thereafter until FDA completes its evaluation, the HHS Secretary must submit a letter to the specified congressional committees describing FDA's progress in (1) evaluating the cough and cold monograph under 21 C.F.R. Part 341 with respect to children under age six and (2) revising the monograph, as appropriate, to address children under age six through the new administrative order process.[92]

Monograph Modification and Innovation

Under the previous monograph system, absent submission of an NDA, monographs could be modified in a timely manner through few mechanisms (see the "Monograph Modification" section). According to former CDER Director Janet Woodcock's September 2017 testimony, "restrictions in the monograph system may discourage manufacturers from innovating."[93]

FFDCA Section 505G allows companies to request changes to or propose new conditions of use for drugs that are GRASE through the administrative order process rather than rulemaking.[94] There are two types of OMORs that companies can submit: Tier 1 and Tier 2. A Tier 1 OMOR is defined as any OMOR not determined to be a Tier 2 OMOR and generally would be used to request more significant changes.[95] Tier 2 OMORs are limited to requests involving reordering existing information on a drug's label; addition of information to the "Other Information" section of the label; modification to directions for use consistent with a minor dosage form change; addition of an interchangeable term under 21 C.F.R. 330.1(i) (e.g., under these regulations, "administer" can be used interchangeably with "give"); a change to ingredient nomenclature to align with the nomenclature of a standards-setting organization; or standardization of the concentration or dose of a specific finalized ingredient within a particular FM.[96]

For example, a company may submit an OMOR requesting the addition of a new active ingredient to an existing monograph. An OMOR also could request the addition of a new indication or new route of administration that would apply to one or more active ingredients already found to be GRASE. Both would be considered Tier 1 OMORs. To incentivize

[90] FFDCA §505G(b)(4)(A) [21 U.S.C. §355h(b)(4)(A)]. FDA, "Monograph Reform is Here!" presentation by Theresa M. Michele, MD, Director Office of Nonprescription Drugs CDER, FDA, May 29, 2020, p. 20.

[91] FFDCA §505G(b)(4)(B) [21 U.S.C. §355h(b)(4)(B)].

[92] P.L. 116-136, §3855.

[93] Testimony from Janet Woodcock, MD, Director of the Center for Drug Evaluation and Research, in U.S. Congress, House Committee on Energy and Commerce, *Modernizing FDA's Regulation of Over-The-Counter Drugs*, hearings, 115th Cong., 1st sess., September 13, 2017, https://www.fda.gov/news-events/congressional-testimony/modernizing-fdas-regulation-over-counter-drugs.

[94] FFDCA §505G(b)(5)(B)(i) [21 U.S.C. §355h(b)(5)(B)(i)].

[95] FFDCA §744L(8) [21 U.S.C. §379j-71(8)].

[96] FFDCA §744L(9) [21 U.S.C. §379j-71(9)].

innovation, certain changes to marketed OTC monograph drugs (requested in an OMOR) are eligible for 18 months of marketing exclusivity upon issuance of a final administrative order from FDA determining that a drug marketed with such change is GRASE. Specifically, if FDA issues an administrative order that provides for a drug to contain a new active ingredient not previously incorporated into a monograph drug,[97] or provides for a change in the conditions of use of a drug for which new human data studies were essential to issuance of the order, the requestor may receive such exclusivity.[98]

If the requestor submits an OMOR to incorporate a new active ingredient into a marketed OTC drug, the OMOR must include information sufficient for a prima facie ("on its face") demonstration that the drug has a history of marketing and safe OTC use in the United States or another country under comparable conditions of use, as specified, or includes other information the Secretary determines is sufficient.[99] If the OMOR does not include such information, FDA must refuse to file the request. If FDA refuses to file the OMOR, the requestor may resubmit for filing only if (1) the drug is marketed OTC, under comparable conditions of use, for a period of time deemed appropriate by the Secretary (not to exceed five consecutive years), under an approved NDA or ANDA, and (2) during such period, 1 million retail packages of the drug, or an equivalent quantity as determined by the Secretary, were distributed for sale.[100]

FFDCA Section 505G also provides that minor changes in dosage form may be made without FDA issuing an administrative order if the requestor maintains information to show that the change will not affect safety or effectiveness of the drug and will not materially affect the extent of absorption or other exposure to the active ingredient.[101] This process will be available to industry once FDA issues a final order and guidance regarding the types of minor changes that can be made without submitting an OMOR.[102]

The CARES Act further required that any TEA application submitted to FDA be "extinguished" as of the date of enactment.[103]

Resource Challenges

In addition to the purported lack of flexibility within the pre-CARES Act monograph process, FDA also faced resource challenges that contributed to delayed monograph finalization. According to September 2017 testimony from former CDER Director Janet Woodcock, FDA

[97] For the purposes of exclusivity, FFDCA §505G(b)(5)(C)(ii) defines the term *drug* to refer to a drug that is subject to a FM or is classified in Category I in a TFM and that meets the applicable general requirements for OTC drugs; a drug not yet subject to a final GRASE determination that may continue to be marketed, specifically if the drug is classified in Category III in a TFM or Category I under an ANPR and meets the applicable requirements for OTC drugs; a drug subject to a final administrative order; an active ingredient subject to a final sunscreen order under the SIA; and a drug marketed without an approved application that is not subject to an administrative order to which FFDCA §505G(a)(1)-(5) does not apply.

[98] FFDCA §505G(b)(5)(C) [21 U.S.C. §355h(b)(5)(C)].

[99] FFDCA §505G(b)(6)(C) [21 U.S.C. §355h(b)(6)(C)].

[100] FFDCA §505G(b)(6)(D) [21 U.S.C. §355h(b)(6)(D)].

[101] FFDCA §505G(c) [21 U.S.C. §355h(c)].

[102] FDA, "Monograph Reform is Here!" presentation by Theresa M. Michele, MD, Director Office of Nonprescription Drugs CDER, FDA, May 29, 2020, p. 26.

[103] P.L. 116-136 §3854(d).

spent approximately 40 times as much budget authority on the process of reviewing Prescription Drug User Fee Act (PDUFA) drug products as it did on OTC monograph drugs.[104]

At the time, OTC monograph activities were funded solely by discretionary appropriations from the General Fund (i.e., budget authority). FDA's prescription drug[105] activities, however, were funded by a combination of budget authority and industry-paid user fees. (In 1992, PDUFA gave FDA the authority to collect fees from the pharmaceutical industry and to use the revenue to support "the process for the review of human drug applications."[106]) PDUFA connected prescription drug user fees to performance review goals negotiated between FDA and industry. That five-year authority has been renewed on five subsequent occasions, most recently as PDUFA VI in 2017.[107] Manufacturers of OTC drugs marketed under an NDA are subject to PDUFA fees, but manufacturers of OTC drugs marketed without an NDA and in compliance with a monograph are not.

To address these prior resource challenges, the CARES Act created a new OTC monograph user fee program (OMUFA). Specifically, in FFDCA Chapter VII the law added a new Part 10—"Fees Relating to Over-The-Counter Drugs"—and the following new FFDCA sections: Section 744L ("Definitions"), Section 744M ("Authority to Assess and Use OTC Monograph Fees"), and Section 744N ("Reauthorization; Reporting Requirements").[108] New FFDCA Section 744M establishes a legal framework for the HHS Secretary, through FDA, beginning with FY2021, to assess and collect facility fees and monograph order request fees (i.e., OMOR fees) to support FDA's OTC monograph drug activities (e.g., review of OMORs, inspections). With respect to facility fees, FDA is to assess a full facility fee to each person who owns an OTC monograph drug facility (MDF), and a reduced facility fee (i.e., two-thirds of the MDF fee) to each person who owns a facility identified as a contract manufacturing organization (CMO).[109] For FY2021, the OMUFA target facility fee revenue is $23,269,000, with MDF facilities paying $20,322 and CMO facilities paying $13,548.[110] In addition to the facility fees, under OMUFA, FDA also assesses a fee to each person who submits an OMOR. (OMOR fees are not included in the OMUFA target revenue calculation.) For FY2021, a Tier 1 OMOR is $500,000, and a Tier 2 OMOR is $100,000.[111] Certain safety-related OMORs are exempt from an OMOR fee.

Fees may be collected and spent only to the extent and in the amount provided in advance in appropriations acts, may remain available until expended, and may be transferred as specified for

[104] Testimony from Janet Woodcock, MD, Director of the Center for Drug Evaluation and Research, in U.S. Congress, House Committee on Energy and Commerce, *Modernizing FDA's Regulation of Over-The-Counter Drugs*, hearings, 115th Cong., 1st sess., September 13, 2017, https://www.fda.gov/news-events/congressional-testimony/modernizing-fdas-regulation-over-counter-drugs.

[105] For purposes of PDUFA, the term *prescription drug* includes both small-molecule, chemical drugs approved under Section 505 of the FFDCA and biologics (drugs derived from or made in living organisms) licensed under Section 351 of the Public Health Service Act (PHSA).

[106] P.L. 102-571.

[107] Title I of the FDA Reauthorization Act of 2017 (P.L. 115-52). For additional information, see CRS Report R44864, *Prescription Drug User Fee Act (PDUFA): 2017 Reauthorization as PDUFA VI*.

[108] P.L. 116-136, §3862.

[109] FFDCA §744M(a)(1) [21 U.S.C. §379j-72(a)(1)].

[110] FDA, "Fee Rates Under the Over-the-Counter Monograph Drug User Fee Program for Fiscal Year 2021," 86 *Federal Register* 16223, March 26, 2021.

[111] Ibid. FFDCA §744M(a)(2) [21 U.S.C. §379j-72(a)(2)]. These amounts are specified in statute. For FY2022 and each subsequent year, FDA must adjust these amounts by an inflation adjustment percentage, as specified.

monograph drug activities only.[112] Because this user fee program is authorized through FY2025, its reauthorization schedule diverges from the reauthorization of other medical product user fee programs (e.g., PDUFA).

FFDCA Section 744N requires the HHS Secretary, through FDA, to submit annual performance and fiscal reports on OMUFA fee collection and spending to the Senate HELP and House Energy and Commerce Committees. The performance and fiscal reports must be made publicly available on FDA's website. FFDCA Section 744N also specifies the process for reauthorization of the user fee program, requiring the HHS Secretary to consult with stakeholders on recommendations for future monograph activities and to transmit the recommendations to Congress no later than January 15, 2025.[113]

In exchange for FDA collection of OMUFA fees, FDA has agreed to meet certain performance goals (e.g., issuing guidance documents, reviewing OMORs in a specified period of time).[114]

OTC Sunscreen Products

Sunscreen products are regulated as OTC drugs. In 1978, FDA published an ANPR that included advisory panel recommendations on the safe and effective use of OTC sunscreens. The ANPR identified 21 sunscreen active ingredients and related conditions (e.g., a minimum SPF value of 2 and labeling requirements) that the advisory panel determined to be GRASE.[115] In 1993, FDA issued a TFM, proposing 20 active ingredients (all but one included in the 1978 ANPR) and related conditions to be GRASE;[116] the proposed rule was subsequently amended several times. In 1999, FDA issued a final rule establishing a sunscreen FM, which included 16 active ingredients and related conditions—including combinations of active ingredients, maximum concentrations, dosage forms, and labeling—that FDA determined to be GRASE.[117] The rule was published with an effective date of May 21, 2001, but was stayed indefinitely because FDA had not yet established ultraviolet A/broad spectrum testing and labeling requirements for OTC sunscreens.[118]

In the absence of an effective FM for OTC sunscreen products, in 2011, FDA issued guidance explaining the agency's enforcement policy with respect to certain OTC sunscreens marketed without an approved application.[119] Specifically, FDA explained that it would not take enforcement action against OTC sunscreen products marketed without an approved NDA if they contained only those 16 active ingredients or combinations of active ingredients and related

[112] FFDCA §744M(f) [21 U.S.C. §379j-72(f)].

[113] FFDCA §744N(d)(3) [21 U.S.C. §379j-73(d)(3)].

[114] FDA, "Over-the-Counter Monograph User Fee Program Performance Goals and Procedures—Fiscal Years 2018-2022," https://www.fda.gov/media/106407/download. Updated Over-the-Counter Monograph User Fee Program Performance Goals Dates—Fiscal Years 2021-2025, https://www.fda.gov/industry/fda-user-fee-programs/over-counter-monograph-user-fee-program-omufa.

[115] 43 *Federal Register* 38206, August 25, 1978.

[116] 58 *Federal Register* 28194, May 12, 1993.

[117] 64 *Federal Register* 27666, May 21, 1999.

[118] 21 C.F.R. Part 352 "Sunscreen Drug Products for Over-the-Counter Human Use [Stayed Indefinitely]." FDA, "Enforcement Policy—OTC Sunscreen Drug Products Marketed Without an Approved Application Guidance for Industry," May 2018, https://www.fda.gov/media/80403/download. (The draft guidance was issued on June 17, 2011).

[119] Ibid.

conditions that were listed in 21 C.F.R. Part 352 (the stayed sunscreen regulations) and complied with CGMP requirements and adverse event reporting, among other things.[120]

In 2002, FDA established the TEA process through which conditions marketed in the United States after 1972 or without any U.S. marketing experience could be considered for inclusion in the OTC drug monograph system.[121] This process provided a way for conditions marketed in foreign countries—for example, sunscreen active ingredients marketed in Europe—to be included in the U.S. OTC monograph system. However, at the time, the TEA regulations did not include deadlines for FDA review. Between 2002 and 2009, TEAs for eight new sunscreen active ingredients were submitted to FDA. These active ingredients were not included in the stayed sunscreen regulations and thus were not allowed to be marketed without an approved NDA. According to a 2017 GAO report, FDA took between 6 and 13 years to issue initial GRASE determinations for those eight TEAs.[122]

Industry and some Members of Congress perceived FDA to be delaying consumer access to new sunscreens, and legislation was introduced to bring transparency and predictability to the FDA review process.[123] In November 2014, the Sunscreen Innovation Act (SIA; P.L. 113-195) was enacted. The SIA modified the pathway for FDA review of new OTC sunscreen active ingredients, or combinations of OTC sunscreen active ingredients, and established timeframes for FDA review. Similar to the TEA process, the SIA procedure included an initial eligibility determination by FDA followed by submission of safety and effectiveness data. However, the SIA required FDA to make GRASE determinations in the form of administrative orders (i.e., proposed and then final orders), in contrast to the TEA rulemaking procedures.[124]

Changes made by the SIA were expected to facilitate the marketing of the eight pending sunscreen ingredients submitted to FDA between 2002 and 2009 under the TEA process. Among other things, the SIA required FDA, within 90 days of enactment, to issue proposed orders for pending sunscreen TEAs submitted prior to enactment of the SIA that did not receive feedback letters from the agency prior to enactment.[125] Feedback letters issued in response to TEAs submitted prior to enactment were deemed proposed sunscreen orders.[126] GAO reported that "for the eight sunscreen applications FDA received since 2002, FDA took between approximately 6 and 13 years to issue initial GRASE determinations starting from the date that the application was submitted. For six of the eight sunscreen applications, it took FDA more than 8 years to issue an initial GRASE determination."[127] For each of the eight pending sunscreen active ingredients, FDA's review resulted in initial determinations (i.e., proposed orders) that those ingredients were not GRASE due to insufficient data; the agency further requested additional safety and

[120] Ibid.

[121] 21 C.F.R. §330.14. FDA, "Additional Criteria and Procedures for Classifying Over-the-Counter Drugs as Generally Recognized as Safe and Effective and Not Misbranded," 67 *Federal Register* 3074, January 23, 2002.

[122] GAO, *SUNSCREEN: FDA Reviewed Applications for Additional Active Ingredients and Determined More Data Needed*, GAO-18-61, November 15, 2017, p. 19, https://www.gao.gov/products/GAO-18-61.

[123] H.Rept. 113-558, accompanying H.R. 4250 (113th Congress), "Sunscreen Innovation Act." See also S. 2141 (113th Congress), which was enacted as P.L. 113-195, "Sunscreen Innovation Act."

[124] FDA, Guidance for Industry, "Sunscreen Innovation Act: Section 586C(c) Advisory Committee Process," October 2016, https://www.fda.gov/media/94237/download.

[125] FFDCA §586C(b)(4) [21 U.S.C. §360fff-3(b)(4)).

[126] FFDCA §586C(b)(3) [21 U.S.C. §360fff-3(b)(3)).

[127] GAO, *SUNSCREEN: FDA Reviewed Applications for Additional Active Ingredients and Determined More Data Needed*, GAO-18-61, November 15, 2017, p. 19, https://www.gao.gov/products/GAO-18-61.

effectiveness data to support a GRASE determination.[128] Specifically, the agency requested submission of data from human clinical safety studies (including conduct of a Maximal Usage Trial [MUsT]), human effectiveness studies, and nonclinical animal studies, as well as submission of human safety data from adverse event reports and related postmarketing information.[129] Thus, despite enactment of the SIA in 2014, as of November 2021, no new sunscreen active ingredients—that is, ingredients beyond those listed in 21 C.F.R. Part 352 (the stayed regulations)—have been determined by FDA to be GRASE.[130]

The SIA had also directed FDA to amend and finalize its then-stayed sunscreen regulations at 21 C.F.R. Part 352 not later than five years after the date of enactment (i.e., by November 26, 2019).[131] In February 2019, FDA issued a proposed rule determining that of the 16 active ingredients listed in the stayed sunscreen monograph, 2 ingredients (zinc oxide and titanium dioxide) were GRASE for use in sunscreen; 2 ingredients (PABA and trolamine salicylate) were not GRASE for use in sunscreen due to safety issues; and the remaining 12 ingredients lacked sufficient safety data for a GRASE determination.[132] The proposed rule also would have (1) required that certain dosage forms of sunscreen (e.g., wipes and towelettes) be considered new drugs requiring an NDA due to a lack of data showing they were eligible for inclusion in the monograph; (2) clarified FDA's expectations for sunscreen testing and record keeping; and (3) proposed new sunscreen labeling requirements, among other things.[133]

Despite congressional efforts to facilitate marketing of new OTC sunscreens without an NDA (e.g., through enactment of the SIA in 2014), FDA has not issued any determinations finding new sunscreen ingredients to be GRASE, instead requesting that sponsors submit additional safety and effectiveness data. Given these challenges, in March 2020, the CARES Act included provisions to address the issuance of sunscreen administrative orders. Specifically, the law allowed a sponsor of an OTC sunscreen active ingredient subject to a proposed sunscreen order under the SIA to transition into the new administrative order process under FFDCA Section 505G (established by the CARES Act).[134] The sponsor must have notified FDA of its decision to transition to the new process within 180 days of enactment, as specified. Otherwise, the order would continue to be reviewed under the SIA.[135] Any final sunscreen orders issued under the SIA would be deemed final administrative orders under FFDCA Section 505G,[136] and certain final sunscreen orders issued under FFDCA Section 505G are eligible for 18 months of marketing exclusivity.[137] The

[128] GAO, *SUNSCREEN: FDA Reviewed Applications for Additional Active Ingredients and Determined More Data Needed*, GAO-18-61, November 15, 2017, pp. 16-17, https://www.gao.gov/products/GAO-18-61.

[129] GAO, *SUNSCREEN: FDA Reviewed Applications for Additional Active Ingredients and Determined More Data Needed*, GAO-18-61, November 15, 2017, pp. 18-19, https://www.gao.gov/products/GAO-18-61.

[130] FDA, "Regulatory Policy Information | Sunscreen Innovation Act," accessed November 16, 2021, https://www.fda.gov/drugs/guidance-compliance-regulatory-information/regulatory-policy-information-sunscreen-innovation-act.

[131] FFDCA §586E [21 U.S.C. §360fff-5], as added by the SIA, required FDA to amend and finalize regulations under 21 C.F.R. Part 352 concerning OTC sunscreen not later than five years after SIA enactment. The SIA was enacted on November 26, 2014.

[132] 84 *Federal Register* 6204, February 26, 2019.

[133] Ibid.

[134] P.L. 116-136, §3854(a).

[135] Ibid.

[136] FFDCA §586C(e)(3) [21 U.S.C. §360fff-3(e)(3)], as amended by P.L. 116-136 §3854(b).

[137] FFDCA §586C(f) [21 U.S.C. §360fff-3(f)], as added by P.L. 116-136 §3854(b)(3).

CARES Act sunsets at the end of FY2022, FFDCA Chapter V Subchapter I—Nonprescription Sunscreen and Other Active Ingredients (i.e., the provisions added by the SIA).[138]

The CARES Act also directed the HHS Secretary to amend and revise the final administrative order for OTC sunscreen, which, prior to CARES Act enactment, was represented by the stayed monograph at 21 C.F.R. Part 352. FDA announced the issuance of a deemed final order for sunscreens on September 24, 2021, which effectively maintains the pre-CARES Act conditions under which a sunscreen may be marketed.[139] The CARES Act further directed FDA to issue a proposed order revising this deemed final order for sunscreens not later than 18 months after enactment (i.e., by September 27, 2021), with no deadline for issuance of a final revised order.[140] On September 24, 2021, FDA announced its issuance of the proposed revised order, which if finalized, would replace the deemed final sunscreen order.[141] The proposed order specifies the conditions under which sunscreen products could be marketed and is substantively the same as the February 2019 proposed rule issued by FDA.[142]

Considerations for Congress

The changes made by the CARES Act aimed to address some of the previously identified limitations of the OTC drug monograph system. When evaluating future policy changes, Congress may consider three additional issues that may not have been fully addressed by the enacted legislation: (1) continued marketing of drugs not yet subject to final GRASE determinations, (2) review of certain sunscreen ingredients, and (3) foreign drug manufacturing.

First, as mentioned above, numerous OTC monograph drugs currently on the market are not yet subject to final GRASE determinations. Although the CARES Act attempted to remedy this issue by creating a less burdensome process for finalizing GRASE determinations, some OTC drug products may remain on the market before a final GRASE determination is made, just as under the Pre-CARES Act framework. In addition, consistent with the lower regulatory burden provided under the previous monograph rulemaking process, the modifications made by the CARES Act do not require a product-by-product review of OTC drug products.

Second, despite congressional efforts to facilitate marketing of new OTC sunscreens via the monograph process—for example, through enactment of the SIA in 2014—such efforts may not have had the intended effect. The CARES Act generally provided sunscreen companies with the option of either continuing through the SIA procedures (until a certain date) or switching to the administrative order process proposed in the OTC bills. However, it is not clear whether the new

[138] FFDCA §586H [21 U.S.C. §360fff-8], as added by P.L. 116-136 §3854(b)(4).

[139] FDA, "FDA Takes Steps Aimed at Improving Quality, Safety and Efficacy of Sunscreens," September 24, 2021, https://www.fda.gov/news-events/press-announcements/fda-takes-steps-aimed-improving-quality-safety-and-efficacy-sunscreens.

[140] P.L. 116-136 §3854(c)(1).

[141] FDA, "FDA Takes Steps Aimed at Improving Quality, Safety and Efficacy of Sunscreens," September 24, 2021, https://www.fda.gov/news-events/press-announcements/fda-takes-steps-aimed-improving-quality-safety-and-efficacy-sunscreens.

[142] 86 *Federal Register* 53322, September 27, 2021. In May 2021, FDA had announced its intent to prepare an environmental impact statement (EIS) prior to issuance of the proposed order, which included a public comment period to inform scoping of the EIS. As indicated by FDA, the purpose of the EIS is "to evaluate the potential environmental effects of revised conditions for marketing certain [OTC] sunscreen products" without an approved NDA. In particular, questions have been raised about two sunscreen active ingredients, oxybenzone and octinoxate, that may affect coral and/or coral reefs, and were considered GRASE under the stayed monograph at 21 C.F.R. Part 352. See 86 *Federal Register* 26224, May 13, 2021.

process would be advantageous to sunscreen companies given FDA's expectations regarding the submission of data from human clinical safety studies (including conduct of a Maximal Usage Trial [MUsT]), human effectiveness studies, and nonclinical animal studies, as well as the submission of human safety data from adverse event reports and related postmarketing information.[143] Some stakeholders have questioned the need for these additional studies because many of these sunscreen ingredients are available in other countries. In addition, some stakeholders have stated that these studies are as rigorous as, or more rigorous than, those required for NDA submission and would cost millions of dollars, while the profit margins for sunscreen products can be low.[144] On the other hand, companies now may be incentivized to conduct additional studies given the eligibility for marketing exclusivity.

Finally, recent reports have raised concerns about the quality of drugs manufactured abroad, including OTC drugs, and, in particular, a loophole regarding registration of facilities manufacturing OTC monograph drug ingredients.[145] CDER maintains a catalog of all establishments manufacturing drugs for the United States, whether they are doing so through an approved application (e.g., NDA) or by registering and listing with FDA to manufacture drugs for the U.S. market. The catalog includes manufacturers making active pharmaceutical ingredients (API) and finished drugs. However, the data available to CDER are limited. For example, CDER has little information about establishments that provide API for drug products that do not need an approved application from FDA to be marketed (e.g., OTC monograph drugs). According to testimony from CDER Director Janet Woodcock, "API suppliers for such products may not register their facility with FDA if they are sending material to a drug product manufacturer outside the United States to make the FDF [finished dosage form], which is then sold in the United States."[146] As an example, in the case of an establishment in China manufacturing an API that is exported to Germany to be made into a finished OTC monograph drug that is then exported to the United States, the establishment in China may not be registered with FDA, since it is not importing directly to the United States. Although FDA may obtain information about a foreign API manufacturer through the NDA process, the agency has limited information about upstream establishments involved in the manufacture of drug products not subject to an NDA or ANDA (e.g., OTC monograph drugs).[147]

[143] FDA, "Nonprescription Sunscreen Drug Products—Safety and Effectiveness Data," Guidance for Industry, November 2016, https://www.fda.gov/media/94513/download. GAO, *SUNSCREEN: FDA Reviewed Applications for Additional Active Ingredients and Determined More Data Needed*, GAO-18-61, November 15, 2017, p. 18, https://www.gao.gov/products/GAO-18-61.

[144] GAO, *SUNSCREEN: FDA Reviewed Applications for Additional Active Ingredients and Determined More Data Needed*, GAO-18-61, November 15, 2017, pp. 22-24, https://www.gao.gov/products/GAO-18-61.

[145] Statement of Janet Woodcock, MD, CDER Director, FDA, in U.S. Congress, Subcommittee on Health of the Committee on Energy and Commerce, *Safeguarding Pharmaceutical Supply Chains in a Global Economy*, hearings, 116th Cong., 1st sess., October 30, 2019, https://energycommerce.house.gov/sites/democrats.energycommerce.house.gov/files/documents/Testimony-Woodcock-API_103019.pdf.

[146] Ibid.

[147] Ibid. See also GAO, *DRUG SAFETY, Better Data Management and More Inspections Are Needed to Strengthen FDA's Foreign Drug Inspection Program*, GAO-08-970, September 2008, p. 18, https://www.gao.gov/assets/290/281366.pdf.

Appendix. Abbreviations Used in This Report

ANDA	Abbreviated New Drug Application
ANPR	Advance Notice of Proposed Rulemaking
CARES Act	Coronavirus Aid, Relief, and Economic Security Act
CDER	Center for Drug Evaluation and Research
C.F.R.	Code of Federal Regulations
CMO	Contracting Manufacturing Organization
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug, and Cosmetic Act
FM	Final Monograph
GAO	Government Accountability Office
GRASE	Generally Recognized as Safe and Effective
MDF	OTC Monograph Drug Facility
NDA	New Drug Application
OMOR	Over-the-Counter Monograph Order Request
OMUFA	Over-the-Counter Monograph User Fee Act
OTC	Over-the-Counter
PDUFA	Prescription Drug User Fee Act
SIA	Sunscreen Innovation Act
TEA	Time and Extent Application
TFM	Tentative Final Monograph

Author Information

Agata Bodie
Analyst in Health Policy

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