An Unofficial Legislative History of Over-the-Counter Monograph Reform

ELIZABETH GUO, RICHARD KINGHAM & DAVID SPANGLER

ABSTRACT

On March 27, 2020, President Trump signed into law the Coronavirus Aid, Relief, and Economic Security (CARES) Act in response to the COVID-19 pandemic in the United States. Title III, Subtitle F of the CARES Act enacted major reforms to FDA's regulatory system for over-the-counter (OTC) drugs.[1] This Article discusses the history of OTC monograph reform and explains the OTC monograph provisions in the CARES Act. Section I provides background and the history of nonprescription drug regulation in the United States until 1972, when FDA established a rulemaking process to classify OTC drugs as Generally Recognized as Safe and Effective (GRASE) and not misbranded ("OTC Drug Review" or the "Review"). Section II describes the challenges of the OTC Drug Review and provides historical context on the impetus for OTC monograph reform. Section III describes the growing interest in OTC monograph reform and initial discussions around what OTC monograph reform would look like. Section IV describes the legislative and stakeholder process between 2016, when Congress released the first discussion draft for OTC monograph reform, and 2020. Section V describes the provisions of OTC monograph reform, as enacted in the CARES Act. As Section VI explains, the history of the OTC Drug Review and the legislative history show how OTC monograph reform was a consensus, born out of the challenges of the Review and enacted after many years of discussions among stakeholders—including the Food and Drug Administration (FDA), Democrats and Republicans in the House and Senate, industry, physician associations, and consumer groups.

I. BACKGROUND

Modern federal regulation of nonprescription, or OTC, drugs began in 1938, with key developments in the 1970s. At first, federal regulation of nonprescription drugs proceeded under the same framework as prescription drugs. After enactment of the Drug Amendments of 1962, FDA established the OTC Drug Review and began regulating a subset of nonprescription drugs differently from prescription drugs and other nonprescription drugs approved under new drug applications (NDAs). Subsection A discusses federal regulation of prescription and nonprescription drugs,

[1] Coronavirus Aid, Relief, and Economic Security (CARES) Act, Pub. L. No. 116-136, Title III, Subtitle F, 134 Stat. 281 (2020). This Article uses the term "OTC monograph reform" to discuss legislation leading to enactment of Title III, Subtitle F of the CARES Act. Also, when discussing "industry" positions, the authors mean to refer to the general perspective of a manufacturer of an OTC drug regulated under the OTC monograph system. Therefore, "industry" positions should not be imputed to any particular company or group of companies, except where explicitly referenced.

and subsection B discusses the development of the OTC Drug Review, which established a separate framework for regulation of OTC monograph drugs.

A. The FDCA and FDA Regulation of Nonprescription Drugs

The Federal Food, Drug, and Cosmetic Act (FDCA), enacted in 1938, established the modern framework for drug regulation and remains the primary statute authorizing FDA's regulation of drugs. The FDCA was enacted in response to a tragedy. In 1937, at least seventy-three people died across the country after taking a sulfanilamide drug that contained diethylene glycol as a solvent, a fatal ingredient.[2]

The FDCA, as enacted in 1938, defined the terms "drug" and "new drug." The term drug meant, among other things, an article "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals" and an article, other than food "intended to affect the structure or function of the body of man or other animals."[3] This definition was intentionally broad and captured both prescription and nonprescription drugs. The statute also defined new drug to prevent a recurrence of the "Elixir Sulfanilamide" disaster. New drug meant a drug "which has not become generally recognized by qualified experts as safe for use under the conditions of use indicated in its labeling . . . or which has been found safe in investigations but which has not been actually used for a material extent or for a material time under the conditions of use indicated."[4] The general recognition concept remains relevant for the majority of nonprescription drugs today, as discussed in Section II.B.

The 1938 statute created separate regulatory requirements for new drugs and older drugs regulated under the FDCA. New drugs must be tested in accordance with regulations promulgated by the Secretary of Agriculture (the parent department for FDA at that time).[5] A sponsor must then submit safety data from clinical trials on the new drug in an NDA before the drug could be marketed.[6] Older drugs were not subject to the requirements for new drugs. Drugs that were generally recognized as safe (GRAS) and used "for a material extent or for a material time" were not new drugs and not subject to the NDA requirement.[7] Drugs that were "grandfathered" are also not subject to the requirement for premarket review. The definition of a new drug excluded "any drug previously subject to the Act as regard conditions of use for which it then had been represented."[8] Many of these products were drugs for nonprescription use.

---

[2] An investigation into the tragedy later showed that the manufacturer checked the product only for appearance, flavor, and fragrance. David Cavers, *The Food, Drug, and Cosmetic Act of 1938: Its Legislative History and Its Substantive Provisions*, 6 LAW & CONTEMP. PROBS. 2, 20 (1939). Tests on animals or an investigation of published literature would have revealed the lethal character of the solvent. *Id.*

[3] Federal Food, Drug, and Cosmetic Act of 1938, Pub. L. No. 75-757, § 201(g), 52 Stat. 1040, 1041 (1938).

[4] § 201(p), 52 Stat. at 1041–42. As we note in Section I.B, the Kefauver-Harris Amendments amended the definition of "new drug" to include "effective" in addition to "safe."

[5] Federal Food, Drug, and Cosmetic Act of 1938, Pub. L. No. 75-757, § 505(b), 52 Stat. 1040, 1052 (1938).

[6] *Id.*

[7] An earlier version of the bill would have established processes to enable the Secretary of Agriculture to find whether a drug was "not generally recognized as safe for use," but these provisions were not included in the enacted bill. Cavers, *supra* note 2, at 20.

[8] § 201(p), 52 Stat. at 1041–42.

In addition, the FDCA distinguished between prescription and nonprescription drugs for the first time. Section 503(b) of the FDCA exempted "drugs dispensed on a written prescription" from certain labeling requirements, so long as the prescription drug label contained the name and place of business of the dispenser, the serial number and date of the prescription, and the name of the prescriber.[9] It would not be until 1951, however, with the Durham-Humphrey Amendment, that section 503(b) of the FDCA would provide a statutory standard to differentiate prescription from nonprescription drugs. The Durham-Humphrey Amendment added a statutory provision that required a drug to be dispensed by prescription if, among other things, the drug, "because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, is not safe for use except under the supervision of a practitioner licensed by law to administer such drug."[10] FDA may, "by regulation," remove drugs from the prescription-dispensing requirement "when such requirements are not necessary for the protection of the public health."[11]

B. The Drug Amendments of 1962 and Establishment of the OTC Drug Review

1. The Drug Amendments of 1962 (the Kefauver-Harris Amendments or the 1962 Amendments)

In 1962, Congress passed the Kefauver-Harris Amendments, which substantially changed the FDCA. Among other things, the amendments added an effectiveness requirement to FDA's regulation of drugs.[12] The addition of the effectiveness requirement extended to OTC as well as prescription drugs. Drugs were grandfathered and exempt from the effectiveness requirement if the drug, on the day proceeding enactment 1) was commercially used or sold in the United States; 2) was not a new drug as defined in the 1938 Act; and 3) was not covered by an "effective application" for a new drug under the 1938 Act.[13]

The Kefauver-Harris Amendments subjected the "effectiveness" requirement to a "substantial evidence" standard.[14] A drug that is a new drug can only be marketed if substantial evidence exists that "the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling."[15] For a period of time, there was debate about whether the substantial evidence standard applied in determining whether a drug was generally recognized as effective. In 1973, the U.S. Supreme Court settled the debate in *Weinberger v. Hynson*, holding that "[t]he statutory scheme and overriding purpose of the 1962 amendments compel the conclusion that the hurdle of 'general recognition'

---

9 § 503(b), 52 Stat. at 1052.

10 Act of Oct. 26, 1951, Pub. L. No. 215-578, § 503(b), 65 Stat. 648, 648–49 (1951).

11 *Id.*

12 In 1960, the William S. Merrell Company submitted an NDA for Kevador (thalidomide) for use as a sleep medication. It had been used in Europe for several years, but FDA refused to clear the NDA. By 1961, the drug had been associated with serious birth defects.

13 Drug Amendments of 1962, Pub. L. No. 87-781, § 107(c)(4), 76 Stat. 781, 789 (1962).

14 § 102(c), 76 Stat. at 781.

15 *Id.*

of effectiveness requires at least 'substantial evidence' of effectiveness for approval of an NDA."[16]

In 1966, FDA established the Drug Efficacy Study Implementation (DESI) program to review the effectiveness of drugs cleared through the new drug procedures from 1938 to 1962.[17] Under the DESI program, panels of experts at the National Academy of Sciences–National Research Council (NAS-NRC) reviewed each drug and its claims.

FDA contended with numerous court challenges against its implementation of the DESI program. Many of these cases were resolved in the U.S. Supreme Court and affirmed FDA's approach. As discussed previously, in *Weinberger v. Hynson*, the Court held that Hynson's drug was not grandfathered and upheld FDA's "summary judgment" procedure under which it denied hearings to companies that failed to proffer at least some evidence meeting the standard of "adequate and well-controlled investigations."[18] In *Weinberger v. Bentex*, Bentex and other manufacturers argued that their pentylenetetrazol drugs were "generally safe and effective" and not new drugs. The Court held that FDA had primary jurisdiction to determine the new drug status of a product, thus that manufacturers could not raise the issue *de novo* in declaratory suits.[19] In *CIBA Corp. v. Weinberger*, the Court held that FDA has jurisdiction to determine whether a drug is a new drug in an administrative proceeding on proposed withdrawal of an effective new drug application, and in *USV Pharmaceutical Corp. v. Weinberger*, the Court upheld FDA's "me-too" policy with respect to identical, related, or similar drug products to those covered by an NDA so that these drugs are not exempt from the new drug efficacy requirements.[20]

2. The OTC Drug Review

After establishing the DESI program, FDA turned to OTC drugs. The DESI program addressed a small handful of OTC drugs that were subject to NDAs but not the thousands of OTC drugs without NDAs. Based on its experience with the DESI program and the multiple court challenges it faced, FDA proposed a new approach to determining the effectiveness and regulatory status of OTC drugs. On January 5, 1972, FDA issued a proposed rule to establish rulemaking procedures for classification of OTC drugs.[21] The procedures would determine whether OTC drugs were "unapproved new drugs and misbranded drugs" so that they need to either be "reformulated and/or relabeled to meet all requirements of the act or be removed from the market."[22]

In the preamble to the proposed rule, FDA indicated that the DESI program's case-by-case approach to determining the regulatory status of drugs would be unworkable if applied to the vast majority of OTC drugs. By 1972, the DESI program had reviewed 420 OTC drugs, which represented a very small portion of the estimated 100,000 to

---

[16] Weinberger v. Hynson, 412 U.S. 609, 629 (1973).

[17] Reports of Information for Drug Effectiveness, 31 Fed. Reg. 9426, 9426 (July 9, 1966).

[18] Hynson, 412 U.S. at 630.

[19] Weinberger v. Bentex Pharm., 412 U.S. 645, 653 (1973).

[20] CIBA Corp. v. Weinberger, 412 U.S. 640, 640 (1973); USV Pharmaceutical Corp. v. Weinberger, 412 U.S. 655, 656 (1973).

[21] Proposal Establishing Rule Making Procedures for Classification, 37 Fed. Reg. 85, 85 (January 5, 1972) (to be codified at 21 C.F.R. pt. 130).

[22] *Id.* at 86.

half million OTC drug products on the market at the time.[23] Few of the OTC drugs had been approved through the NDA notification process set forth under section 505 of the FDCA, and some OTC drugs would likely be excluded from the new drug requirements under the 1938 or 1962 grandfather clauses.[24]

In carrying out its responsibilities under the Drug Amendments of 1962, FDA determined that case-by-case challenges to individual OTC products would be too burdensome. Instead, FDA proposed to "deal with all OTC drugs through rulemaking by therapeutic classes on an industry-wide basis."[25] In doing so, FDA cited a number of factors:[26]

- FDA had limited resources.
- Litigation to remove violative OTC drugs would place an enormous burden on FDA and the courts.
- Litigation to determine the scope of the 1938 and 1962 grandfather clauses on a case-by-case basis would be too burdensome and time-consuming. It would be unfair to permit grandfathered drugs to remain on the market unchanged with false labeling while other items must be reformulated or relabeled.
- Inadequate consumer protection would be produced by product-by-product review, as it would allow a large number of violative drugs to remain on the market for long periods.
- Practically all of the OTC drugs marketed were compounded from an estimated 200 active ingredients (roughly 700 ingredients were ultimately reviewed). Although each OTC drug was a separate product, the same scientific and medical evidence would likely be relevant in reviewing all OTC drug products in a given therapeutic class.
- Any approach must be consistent with the FDCA. In administrative proceedings and litigation, FDA had required "published literature of adequate and appropriate medical documentation, consisting at least in part of controlled clinical investigations, as the test of whether a drug is no longer a new drug."[27] Uncontrolled studies and data may corroborate published and controlled findings. FDA would require a similar evidentiary approach here.

Therefore, FDA proposed to establish procedures to classify some OTC drugs as GRASE and "not misbranded under the prescribed, recommended, or suggested

---

[23] *See id.* at 85.

[24] *Id.*

[25] *Id.* at 86.

[26] *Id.*

[27] *Id.*

conditions of use."[28] Drugs that met the requirements would be GRASE and could be marketed so long as they met the other requirements for nonprescription drugs. For example, the company manufacturing the drug should be registered with FDA and list the OTC drug. The drug should also be manufactured in compliance with current good manufacturing practices (cGMPs). On the other hand, any OTC drug not meeting the requirements established according to the procedures would need an approved NDA prior to marketing. Shipment of a nonconforming OTC drug without an NDA in interstate commerce would be prohibited under section 301 of the FDCA.

II. THE OTC DRUG REVIEW AND CHALLENGES UNDER THE SYSTEM

A. The OTC Drug Review

The OTC Drug Review, as finalized on May 11, 1972, provided the procedures for how FDA would determine whether the conditions of use for certain OTC drugs are GRASE and not misbranded.[29] Conditions of use include, among other things, active ingredients, dosage form and strength, route of administration, and the specific OTC use or indication for use.[30] The OTC Drug Review would initiate notice-and-comment rulemaking and create "monographs" for categories of drugs that are GRASE and not misbranded. These monographs would set forth the acceptable ingredients, doses, formulations, indications, labeling, and other conditions of use under which an OTC drug is GRASE and not misbranded.[31] An OTC drug product can be marketed without an NDA if the drug is marketed under the conditions of use specified in an applicable "final monograph."[32]

1. The OTC Drug Review Process

The OTC Drug Review was originally envisioned as a four-step process.[33] First, FDA appointed advisory review panels of qualified experts to evaluate the safety and effectiveness of OTC drugs and to advise FDA on monographs establishing conditions under which OTC drugs were GRASE.[34] At the same time, FDA would carry out a literature search to obtain information for advisory review panels to evaluate.[35] The bibliography from the literature search would be available when FDA announced the proposed OTC category review and would be available to panel members and any interested party.[36] FDA would then publish a notice in the Federal Register with the bibliography and request information for data pertinent to a drug category but not found in the bibliography.[37]

---

[28] *Id.*

[29] Procedures for Classification of Over-the-Counter Drugs, 37 Fed. Reg. 9464, 9464 (May 11, 1972).

[30] 21 C.F.R. § 330.14(a) (2016).

[31] Procedures for Classification of Over-the-Counter Drugs, 37 Fed. Reg. at 9474–75.

[32] *Id.* at 9475.

[33] The process is currently codified at 21 C.F.R. Part 330.

[34] 21 C.F.R. § 330.10(a)(1).

[35] Procedures for Classification of Over-the-Counter Drugs, 37 Fed. Reg. at 9468.

[36] *Id.*

[37] 21 C.F.R. § 330.10(a)(2).

The advisory review panel would meet and deliberate on data with respect to a category of OTC drugs. The panel could consult with "any individual or group," and "[a]ny interested person may request an opportunity to present oral views to the panel."[38] Following deliberations and review of the evidence based on the standards set out in 21 C.F.R. § 330.10(a)(4), each panel would submit a report to FDA containing its conclusions and recommendations with respect to the safety and effectiveness of the category of OTC drugs.[39] The panel report would contain information about three categories of active ingredients: 1) category I ingredients and their conditions of use that were GRASE and not misbranded; 2) category II ingredients and conditions that were reviewed and excluded from the monograph because they were not GRASE or were misbranded; and 3) category III ingredients and their conditions of use that had insufficient information from which to determine whether a drug was GRASE.

After reviewing the panel's report, FDA would publish in the Federal Register a proposed monograph (later called an "advanced notice of proposed rulemaking" (ANPR)).[40] The Federal Register notice would propose a monograph with information about the three categories of drugs along with the full panel report.[41] FDA would then invite comment on the proposed monograph.

Next, FDA would publish a tentative final monograph (TFM) (i.e., a proposed rule) in the Federal Register after reviewing the public comments, establishing conditions under which a category of OTC drugs was GRASE and not misbranded (category I) and which were category II or category III.[42] The public again would have an opportunity to comment on the TFM. After reviewing objections filed in response to the TFM, FDA could, under its discretion, allow petitioners to have an oral hearing before the Commissioner to discuss objections among the parties.[43]

Finally, FDA would publish a final monograph establishing the conditions of use under which a category of drugs is GRASE and not misbranded and which drugs were not GRASE. The final rule would also specify the effective date of the monograph.[44] The monograph in the final rule constituted final agency action, and any party who disagreed with the final monograph could request an informal hearing, subject to FDA discretion, or file an appeal in the courts.[45]

2. The OTC Drug Review Standards

The OTC Drug Review specified the standards for safety, effectiveness, and labeling when reviewing drugs under the system. Safety meant a "low incidence of

---

[38] 21 C.F.R. § 330.10(a)(3).

[39] 21 C.F.R. § 330.10(a)(5).

[40] The terminology associated with each step evolved over the years. When OTC Drug Review first began, the ANPR concept did not exist in administrative law. When FDA issued the unaltered panel reports it called them "proposed monographs," and when it issued notice of proposed rulemakings ("NPRMs" or "proposed rules"), FDA called them "tentative final monographs." Later, FDA changed the terminology to align with newer concepts in administrative law. Section 505G of the FDCA uses both old and newer terminology when referring to the monograph system.

[41] 21 C.F.R. § 330.10(a)(6).

[42] 21 C.F.R. § 330.10(a)(7).

[43] 21 C.F.R. § 330.10(a)(8).

[44] 21 C.F.R. § 330.10(a)(9).

[45] Procedures for Classification of Over-the-Counter Drugs, 37 Fed. Reg. 9464, 9469 (May 11, 1972).

adverse reactions or significant side effects under adequate directions for use and warnings against unsafe use as well as low potential for harm which may result from abuse under conditions of widespread availability."[46] GRAS would "ordinarily be based upon published studies which may be corroborated by unpublished studies and other data."[47] Safety would also include "results of significant human experience during marketing.[48] In publishing these standards, FDA considered whether general recognition of safety should be based only on published studies and rejected that standard. The panel's evaluation "should be based on the best scientific evidence available. . . . Even where published studies are available for review and criticism, there is no reason to exclude unpublished work that may represent a more recent study."[49]

Effectiveness meant "a reasonable expectation that, in a significant proportion of the target population, the pharmacological effect of the drug, when used under adequate directions for use and warnings against unsafe use, will provide clinically significant relief of the type claimed."[50] Any investigations could be corroborated by "partially controlled or uncontrolled studies, documented clinical studies by qualified experts, and reports of significant human experience during marketing."[51] The "best possible data would consist of adequate and well controlled clinical studies of the drug" as described in FDA's regulations for NDAs, unless this is waived because "such studies are unnecessary or inappropriate."[52] FDA rejected "unscientific evidence as unsubstantiated opinion and marketing experience . . . [to] be regarded as sufficient to constitute adequate proof of effectiveness" but noted that these data may corroborate scientific evidence.[53] On the other hand, "[i]solated case reports, random experience, and reports lacking the details which permit scientific evaluation will not be considered."[54]

As with GRAS, generally recognized as effective (GRAE) "shall ordinarily be based upon published studies which may be corroborated by unpublished studies and other data."[55] FDA explained that in its view, published studies "have been subject to public scrutiny and peer review and thus present the best evidence. In addition, general recognition inherently implies general availability of the basis of the judgment."[56] The panel may, nevertheless, rely on unpublished data if "there is a sound scientific basis for such a decision which is sufficiently widespread to establish general recognition."[57] As with determining GRAS status, FDA should primarily rely on published studies to determine GRAE status.

---

46 21 C.F.R. § 330.10(a)(4)(i).

47 *Id.*

48 Procedures for Classification of Over-the-Counter Drugs, 37 Fed. Reg. at 9474.

49 *Id*. at 9469.

50 21 C.F.R. § 330.10(a)(4)(ii).

51 Procedures for Classification of Over-the-Counter Drugs, 37 Fed. Reg. at 9474.

52 *Id.*

53 *Id.*

54 *Id.*

55 21 C.F.R. § 330.10(a)(4)(ii).

56 Procedures for Classification of Over-the-Counter Drugs, 37 Fed. Reg. at 9469.

57 *Id.* at 9469.

B. Implementation of the OTC Drug Review

1. General Conditions for OTC Drugs

Shortly after FDA established the OTC Drug Review, FDA proposed and finalized regulations specifying the rules providing the general conditions applicable for all OTC drugs that are GRASE and not misbranded.[58] In proposing the first monograph for antacid OTC drug products, FDA discovered that several conditions applied to all OTC drugs and could be established in a single regulation rather than repeated in each monograph. This approach differed from drugs approved under NDAs, where FDA established the conditions of use and characteristics specific to each approved drug. These provisions were flexible enough to apply to all monograph products, but FDA recognized that specific monographs could modify these general conditions or create exceptions, where appropriate.[59]

2. Advisory Review Panels and Finalization of Monographs

FDA gave a lengthy charge to each OTC Drug Review Panel at its first meeting. These remarks instructed advisory committees on the scope of the OTC Drug Review. FDA charged them with reviewing active ingredients and claims in nonprescription drugs and asked panels to review any prescription drug ingredients that they felt could have safe and effective OTC claims. The Chief Counsel, Peter Barton Hutt, provided the following charge to the Antimicrobial II panel on July 26, 1974:

> What we want you to do is to take a totally fresh, independent, objective view of this entire field, come up with your best advice and give it to us. Now that includes, I might add, things that we have not even asked you to look at . . . . [I]f you want to put it in your report, please put it in your report. In short, don't feel constrained by some kind of legal boundaries that you believe may exist that I may have to tell you exist. We want your advice . . . . You should concern yourselves with the scientific and the medical issues that underlie this review, and I can't over-emphasize that.[60]

FDA initially anticipated establishing a panel for each of twenty-six therapeutic categories but eventually reduced the number to seventeen advisory panels. These panels engaged in a tremendous amount of work and "held 508 meetings over 1047 days and reviewed some 20,000 volumes of data on more than 700 active ingredients used in over 300,000 nonprescription drug products."[61] By the time the advisory panels published the last report in 1983, the panel had reviewed approximately 722 active ingredients or approximately 1,454 uses.[62] The panels recommended active

---

[58] General Conditions for OTC Drugs, 38 Fed. Reg. 31258, 31258–59 (Nov. 12, 1973).

[59] *Id.* at 31258.

[60] Remarks by Peter Barton Hutt, Esq., Assistant Gen. Counsel, Food and Drugs Div., Dep't of Health, Educ. and Welfare, to FDA's Panel for Review of Over-the-Counter Antimicrobial II (Topical Antibiotic) Products (July 26, 1974) (on file with the Committee on Government Operations).

[61] *See* U.S. FOOD & DRUG ADMIN., OTC ACTIVE INGREDIENTS (Apr. 7, 2010); *see also* PETER BARTON HUTT, RICHARD MERRILL & LEWIS GROSSMAN, FOOD AND DRUG LAW: CASES AND MATERIALS 979 (4th ed. 2014).

[62] BARTON, MERRILL & GROSSMAN, *supra* note 61, at 978.

ingredients fairly evenly among category I (30%), category II (34%), and category III (36%).[63]

The antacid monograph finalization process provides a good example of how the Review should work as intended. On February 22, 1972, FDA convened an advisory review panel on OTC antacid drugs. The panel held five working meetings through the course of the year and submitted a report with its recommendations to FDA on January 3, 1973.[64] After reviewing the report, FDA published the first proposed monograph under the Review. The monograph described FDA's proposals on which OTC antacid drugs were GRASE and not misbranded, taking the advisory review panel report into account.[65] The panel report recommended that thirteen categories of active ingredients be considered GRASE for antacid use (twenty-eight active ingredients total).[66] On the other hand, the panel could not find adequate and reliable scientific evidence to permit classification of nine active ingredients. These ingredients "have either no or negligible antacid action and there is inadequate evidence for their effectiveness. . . ."[67] The panel also determined that certain claims or indications were not truthful or accurate. For example, claims that the product may affect "nervous or emotional disturbance," "excessive smoking," "alcoholic beverages," cold symptoms, or "morning sickness of pregnancy" were inappropriate for use for an antacid drug.[68] FDA provided a sixty-day public comment period and a thirty-day reply period for comments received.[69]

After reviewing the public comments, FDA issued a TFM for antacid products on November 12, 1973.[70] The TFM largely retained the recommendations in the proposed monograph. The TFM also provided requirements for product labeling, including acceptable indications, required warnings, directions for use, and combinations with nonantacid active ingredients.[71] After reviewing the panel report and comments to the proposed monograph, FDA established a TFM for OTC antiflatulent products. In that TFM, FDA concluded that simethicone was not an antacid but was GRASE as an antiflatulent.[72] In the preamble to the TFMs for antacid and antiflatulent products, FDA discussed what should happen to drugs in category II and category III following finalization of the antacid and antiflatulent monographs.[73] FDA proposed a six month effective period to allow a manufacturer time to reformulate its product, remove it from market, or file an NDA.[74]

---

[63] *Id.*

[64] Proposed General Conditions for OTC Drugs Listed as Generally Recognized as Safe and Effective and as Not Misbranded, 38 Fed. Reg. 8714, 8715 (Apr. 4, 1973).

[65] *Id.* at 8714.

[66] Proposal Establishing a Monograph for OTC Antacid Products, 38 Fed. Reg. 8714, 8724 (Apr. 4, 1973) (to be codified at 21 C.F.R. pt. 130).

[67] *Id.* at 8722.

[68] *Id.* at 8721.

[69] *Id.* at 8724.

[70] 38 Fed. Reg. 31260, 31264 (Nov. 12, 1973) (to be codified at 21 C.F.R. pt. 130).

[71] *Id.* at 31269.

[72] *Id.* at 31266.

[73] *Id.* at 31266–67.

[74] *Id.* at 31269.

On June 4, 1974, FDA issued final monographs for GRASE antacid and antiflatulent products.[75] In all, a little over two years passed from the creation of the antacid advisory review panel to FDA's issuance of the final monograph.

C. Challenges Under the OTC Drug Review

The OTC Drug Review functioned effectively in the first few years but gradually fell into disarray due to multiple challenges. These challenges became the impetus for OTC monograph reform.

1. A Large Number of Drugs Fell Within the OTC Drug Review

From the beginning, FDA recognized the challenge in classifying hundreds of thousands of OTC products on the market. FDA had not anticipated, however, that the range of products would continue to broaden as the Review progressed. FDA's charge to advisory review panels and the promulgation of the "rush-to-market" rule significantly increased the number of products falling under the OTC Drug Review. These developments made it more difficult for FDA to examine and finalize products under the Review.

Before the OTC Drug Review, marketers of prescription drugs had limited options if they wanted to switch their products to OTC use. The Durham-Humphrey Amendments in 1951 added section 503(b)(3) to the FDCA, which allowed FDA to "remove drugs subject to section 505 from the requirements of [prescription drugs] when such requirements are not necessary for the protection of the public health."[76] Under this provision, FDA switched a number of drugs from prescription to OTC status using a "switch regulation," authorized under section 505(b)(3) of the FDCA.[77]

The OTC Drug Review added an additional pathway by which OTC drugs could be switched to nonprescription status. When the OTC Drug Review began, FDA intended to examine not just OTC drugs on the market at the time but also current prescription products to see if they should be considered for OTC use. In the preamble to the final rule establishing the OTC Drug Review, FDA stated that "the panel is charged with recommendations with respect to all drugs that should be on OTC status. Any interested person may, of course, submit data and views suggesting that a prescription drug should be moved to OTC status."[78] FDA reiterated this charge to advisory review panels. By evaluating both prescription and nonprescription drugs, FDA intended that the issuance of a final monograph would have the same effect as a switch regulation.[79]

FDA did not anticipate the significant amount of prescription drugs that would be suitable for OTC status. Robert Pinco, the Director of the Division of OTC Drug Evaluation at the time the Review began, stated, "those who organized the OTC review did not really expect that there would be many recommendations for movement of

---

[75] 39 Fed. Reg. 19862, 19862 (June 4, 1974).

[76] FDCA, Pub. L. No. 215, 65 Stat. 649 (1951) (allowing FDA to "by regulation remove drugs subject to . . . section 505 from the requirements of paragraph (1) of this subsection when such requirements are not necessary for the protection of the public health").

[77] FDCA § 503(b)(3); *see also* 21 C.F.R. § 310.201 (listing products switched from prescription to nonprescription use before OTC Drug Review).

[78] Procedures for Classification of Over-the-Counter Drugs, 37 Fed. Reg. 9464, 9470 (May 11, 1972).

[79] *See id.*

prescription drugs to OTC status; rather they expected the reverse to occur."[80] While the advisory review panels recommended relatively few prescription ingredients for OTC status ("perhaps 15 out of 1,000 ingredients being studied in the OTC review"), these ingredients "represent[ed] very broad economic interests in this highly competitive market."[81] Manufacturers of prescription drugs began marketing these drugs at risk for OTC use based on panel reports and proposed monographs and even after informal discussions by panels, anticipating that FDA would not take enforcement action against these products.[82]

By 1975, it became clear that the OTC Drug Review would continue for some time, and, during that time, advisory panels would continue to examine prescription drugs that should be switched to OTC use. Instead of waiting for the Review to be completed before allowing prescription drugs to be marketed as OTC drugs under a monograph, FDA issued a regulation governing prescription drugs covered under a proposed monograph or TFM. FDA hoped the policy would resolve the premature rush-to-market of prescription drugs accompanying the OTC Drug Review. The rule set forth FDA's policies regarding marketing OTC drug products containing an active ingredient that 1) was at a dosage level higher than that available in an OTC drug product on December 4, 1975; or 2) was limited to prescription use but regarded by an advisory review panel as suitable for OTC use. These products needed to be classified as category I in a proposed monograph or TFM and were subject to the risk that they would be taken off the market if FDA reached a different decision in the final monograph.[83] The rush-to-market rule clarified FDA's enforcement policy related to formerly prescription drugs but explicitly acknowledged that the OTC Drug Review pertained not just to OTC drugs but also to prescription drugs recommended for OTC use.

2. FDA Continued to Field Challenges to Allowing OTC Drugs Without GRASE Status to Remain on the Market

FDA recognized at the start of the OTC Drug Review that it was not possible to take action against all OTC drugs on the market that were not subject to a final monograph. Therefore, from the beginning of the Review, FDA relied on enforcement discretion to allow drugs subject to the OTC Drug Review to remain on the market pending a final decision.[84] Beginning in 1972, FDA publicly declared a "moratorium" on enforcement against OTC products, "except in cases of fraud or serious health hazard."[85]

---

[80] Robert Pinco, *The FDA's OTC Review - The Light at the End of the Tunnel*, 31 FOOD, DRUG, COSM. L. J. 141, 143 (1976).

[81] *Id.* at 144.

[82] *See id.* (describing "what the FDA [viewed] as a rush to market").

[83] 41 Fed. Reg. 32580, 32580 (Aug. 4, 1976).

[84] Even before FDA established OTC Drug Review, questions emerged about what would happen to OTC drugs on the market that FDA had not determined were GRASE. In *Veneman*, the court had held that FDA had acted contrary to the FDCA when it allowed drugs without evidence of efficacy to be marketed past the two-year grace period allowed by the 1962 amendments. Pub. Health Ass'n v. Veneman, 349 F. Supp. 1311 (D.D.C. 1972). In the order following the court's opinion entered on October 11, 1972, the court required FDA to take action on National Academy of Sciences/National Research Council (NAS/NRC) drug reports, but specifically excluded OTC drugs and authorized their transfer to OTC Drug Review. *Id.*

[85] Pinco, *supra* note 80, at 143.

FDA modified its enforcement policy several times over the next few years, but challenges remained. Consumer organizations challenged FDA's decision to allow OTC drugs on the market that FDA had not determined were GRASE. In *Cutler v. Kennedy*, for instance, consumers challenged the Review's regulations as unlawful to the extent they allow marketing of category III drugs while evidence was being developed as to the drug's safety or effectiveness.[86] The plaintiffs also claimed that FDA had a statutory duty to remove category III drugs on the market once it had concluded that the drugs were not supported by substantial evidence of safety or efficacy.[87] The court ultimately held that FDA's regulations allowing continued marketing of category III ingredients under a final monograph were not authorized by the FDCA.[88] The regulations were unlawful "to the extent they affirmatively sanction continued marketing of category III drugs."[89]

Following *Cutler v. Kennedy*, FDA rescinded its regulation affirmatively sanctioning marketing of category III drugs under a final monograph. In its place, FDA proposed a rule and announced its "general enforcement policy" for marketed products subject to the OTC Drug Review.[90] The general enforcement policy would enable FDA to "take regulatory action in an orderly fashion, commensurate with available resources, against those OTC drug products failing to meet the requirements of an applicable monograph."[91] FDA would prioritize enforcement against products that "most affect the public health and safety" to "provide equitable treatment among competing firms, and to utilize agency resources most efficiently."[92]

Shortly after FDA published the proposed rule, FDA issued Compliance Policy Guide (CPG) § 450.200. The CPG indicated that "[p]rior to the final publication of a proposed monograph, it would not be in the agency's interest to pursue regulatory action unless failure to do so poses a potential health hazard to the consumer."[93] Later, FDA would also issue CPG § 450.300 concerning the marketing of OTC products containing combinations of ingredients.[94] CPG §§ 450.200 and 450.300 would

---

[86] Cutler v. Kennedy, 475 F. Supp. 838, 838 (July 16, 1979).

[87] *Id.* at 853.

[88] *Id. at* 854.

[89] *Id.* at 855.

[90] 45 Fed. Reg. 31422, 31424 (May 13, 1980) (to be codified at 21 C.F.R. pt. 330).

[91] FDA noted that the enforcement policy was consistent with FDA's enforcement policies for prescription new drugs, outlined in FDA Compliance Policy Guide § 7132c.08 (Oct. 6, 1976). *Id.*

[92] *Id.* at 31424–25.

[93] U.S. FOOD & DRUG ADMIN., CPG SEC. 450.200 DRUGS - GENERAL PROVISIONS AND ADMINISTRATIVE PROCEDURES FOR RECOGNITION AS SAFE AND EFFECTIVE (Mar. 1995) (initially issued Oct. 1, 1980) [https://perma.cc/V6LF-4RAG].

[94] The guidance categorized OTC products into three buckets. CPG § 450.300. OTC drug combinations commercially marketed on or before May 11, 1972 should not be subject to enforcement on the basis of suspected labeling deficiencies unless "there is a reasonable basis to conclude that the deficiency constitutes a potential hazard to health." *Id.* OTC combination products not marketed on or before May 11, 1972 could be marketed if (1) each of the active ingredients in the combinations was marketed before May 11, 1972 and is subject to OTC review; (2) each of the ingredients is classified as category I in an ANPR; (3) the combination of ingredients has been classified as category I in an ANPR; and (4) the agency has not disagreed with the panel's recommendations. *Id.* A combination product not marketed on or before May 11, 1972 is considered a new drug and/or misbranded if (1) FDA has disagreed with a panel's recommendation that an ingredient or combination of ingredients should be category I; (2) a panel has determined that the combination should be categorized as category II or III; (3) a panel has recommended that one of the active

become the basis for manufacturers marketing OTC drugs under a non-finalized monograph for the next forty years.

On September 29, 1981, FDA issued its final rule, eliminating the marketing period for category III drugs following issuance of the final monograph but adding a twelve-month period following publication of the TFM for interested persons to present "new data and information to support a condition excluded from the monograph in the tentative order."[95] In the preamble to the final rule, FDA clarified the status of drugs with category III ingredients in response to *Cutler v. Kennedy*. FDA opined that the court in *Kennedy* did not address the legal status of OTC products containing a category III drug during the rulemaking process and that FDA did not "authorize" the marketing of OTC drugs during rulemaking.[96] Until FDA issued a final monograph, OTC monograph products were either GRASE or they were not.

In *Cutler v. Hayes*, consumers again challenged the legality of FDA's treatment of drugs under the Review and the progress of the OTC drug program. Consumers alleged that 1) FDA's Review regulations violate the FDCA; 2) "FDA's policy of nonenforcement of the efficacy requirement for marketing over-the-counter drugs in interstate commerce violates the agency's statutory duty"; and 3) "FDA's lack of progress in completing the review program and the unlikelihood that review will be completed in the near future infringes the provisions of the Administrative Procedure Act."[97] In support of the last point, plaintiffs pointed to FDA's failure to complete the OTC Drug Review more than ten years after it was initiated and over twenty years after the Durham-Humphrey Amendments.[98]

The District Court for the District of Columbia found for FDA on all three claims, and the plaintiffs appealed.[99] The D.C. Circuit found in favor of FDA on the first and second claim.[100] FDA's twelve-month data collection period was consistent with the FDCA, and FDA presented "reasonable justifications" for adopting the open record period.[101] Further, FDA's enforcement policy was not unlawful because "as an agency of limited resources, FDA reasonably may assign enforcement of a statutory requirement designed to prevent unnecessary consumer expense to a lower priority than that accorded one concerned with identifying and eliminating threats to human life."[102] "It would be a futile act," the court held, "as well as one financially disastrous for manufacturers of pharmaceuticals, were the agency to require removal of a potentially ineffective drug from interstate commerce only to find, on the basis of later unfolding information, that the drug should have been classified as generally recognized as effective."[103] The court did not determine whether FDA's progress on

---

ingredients in the combination should be classified as category II or III; or (4) no OTC advisory review panel has considered the combination. *Id.*

95 21 C.F.R. § 330.10(a)(7).

96 46 Fed. Reg. 47730, 47733 (Sept. 29, 1981).

97 Cutler v. Hayes, 818 F.2d 879, 879 (1987).

98 *Id.* at 885.

99 Cutler v. Hayes, 549 F. Supp. 1341, 1342 (D.D.C. 1982).

100 *Hayes*, 818 F.2d at 882.

101 *Id.* at 900.

102 *Id.* at 894.

103 *Id.* at 894.

the OTC Drug Review constituted an unreasonable delay but remanded the case back to the district court to scrutinize FDA's justifications for delay in completing the OTC Drug Review and balance the benefits against the consequences.[104]

FDA prevailed in judicial challenges to its authority and regulatory framework for drugs subject to the OTC Drug Review. Nevertheless, marketing of OTC drugs under enforcement discretion continued to present challenges. Many such drugs had not completed review and had not been determined GRASE. FDA continued to defend against allegations that the agency's failure to render a final opinion on OTC drugs deprived consumers of FDA's assurance of the drug's safety and efficacy. In *Cutler v. Hayes* and *Cutler v. Kennedy*, for example, plaintiffs claimed that allowing the marketing of drugs without GRASE status increased the risk that consumers "will purchase and consume unsafe or ineffective drugs."[105]

Reliance on enforcement discretion also placed drug manufacturers in a precarious legal position. As FDA reemphasized each time it announced its enforcement policy, FDA could decide to enforce against drugs under enforcement discretion at any time if it wished to do so. FDA had reiterated that "it will continue to take regulatory action at any time in the review against products that present a potential health hazard or a significant and substantial effectiveness question."[106] FDA could also modify its enforcement discretion policy "at a later date, with or without public notice."[107]

3. The OTC Drug Review Slowed to a Crawl

Initially, the OTC Drug Review proceeded slowly due to the sheer number of drugs under review and the legal challenges to FDA's authority. As time passed, FDA's progress on the OTC Drug Review slowed even more. Ten years after the OTC Drug Review began, the D.C. Circuit in *Cutler v. Hayes* found that "OTC drug review has progressed sluggishly at best since its inception in 1972."[108] Although FDA had indicated that TFMs would be completed by the end of 1983, "the vast majority of tentative final monographs and final monographs to be produced are yet to be completed and are not expected to be forthcoming for some time."[109] At the time, FDA had predicted that the OTC Drug Review could possibly be completed by 1990, while consumers presented evidence "suggesting that the OTC program will not be completed until close to year 2000."[110] Both FDA and consumers were too optimistic. By 2020, FDA still had not completed the OTC Drug Review, with many products marketed under TFMs or ANPRs and subject to FDA enforcement discretion.[111]

Two main factors resulted in the slowdown of the OTC Drug Review. First, the multi-stage rulemaking procedures that were deemed necessary in 1972 bogged down

---

[104] *Id.* at 898–99.

[105] Cutler v. Kennedy, 475 F. Supp. 838, 848 (July 16, 1979).

[106] 45 Fed. Reg. 31422, 31425 (May 13, 1980) (to be codified at 21 C.F.R. pt. 330).

[107] *Id.*

[108] *Hayes*, 818 F.2d at 885.

[109] *Id.*

[110] *Id.* at 885, n. 39.

[111] *See* U.S. FOOD & DRUG ADMIN., STATUS OF OTC RULEMAKINGS (Mar. 30, 2020), https://www.fda.gov/drugs/over-counter-otc-nonprescription-drugs/status-otc-rulemakings [https://perma.cc/8E6N-AV7Q] (providing the regulatory status of OTC monograph products, organized by therapeutic category).

the agency, particularly as Congress and the Executive Branch added more requirements for agencies issuing rules. Second, FDA lacked the resources needed to devote to OTC drug review. The decrease in funding accelerated after enactment of the Prescription Drug User Fee Act (PDUFA) in 1992. These factors were cited as reasons for OTC monograph reform years later.

FDA established the procedures for the OTC Drug Review out of necessity in the context of legal challenges to agency authority in the early 1970s. The Review began during a time when courts were questioning whether "interpretative rules" could have the same force and effect of a "substantive rule." In the early 1970s, courts were still debating whether regulations issued pursuant to section 701(a) of the FDCA were advisory only and subject to de novo challenge in court enforcement proceedings.[112] At the same time, a separate argument waged in the D.C. Circuit over "interpretative rules" and "substantive rules."[113] An "interpretative rule" serves an advisory function and only advises the public of an agency's view of what a law or regulation means. By contrast, a "substantive rule" binds the public and has the "full force of law."[114]

FDA wanted to ensure that regulations promulgated through the OTC Drug Review would have the binding force of law. At the time FDA established the Review, FDA wanted to build in procedural protections to mimic the procedural rights under section 701(e) and the rulemaking requirements under 5 U.S.C. § 553. Therefore, the OTC Drug Review gave manufacturers an opportunity to appear at panel hearings, a right to comment on panel recommendations, and the right to request an oral hearing before FDA issued the final monograph. It was FDA's view that if litigants challenged the final rules under the OTC Drug Review as "interpretative," it was unlikely that courts would accept those arguments in light of the Review's procedural safeguards. Although the debates about the FDCA's interpretive and "substantive" rules were eventually dispelled,[115] the OTC Drug Review procedures remained.

The procedures grew burdensome over time. After 1972, Congress enacted a number of statutes that added steps if an agency wanted to propose or finalize a rule. For example, the National Environmental Policy Act (NEPA), signed into law on January 1, 1970, requires federal agencies to consider the environmental effects of

---

[112] *See, e.g.*, Nat'l Nutritional Foods Ass'n v. Weinberg, 512 F.2d 688, 691 (2d Cir. 1975). Section 701(a) of the FDCA gave FDA authority to "promulgate regulations for the efficient enforcement of this Act . . . ." Section 701(e) of the FDCA provided specific procedures for how FDA would promulgate regulations to establish standards of identity of food products. Legislative history indicated that section 701(e) regulations "are not merely interpretative. They have the force of law and must be observed." However, there was no similar statement indicating that section 701(a) regulations were to have similar effect, leading to many litigants arguing that regulations promulgated under section 701(a) were "meant merely to grant authority to issue interpretive, non-binding advisory opinions with respect to matters of lesser importance." *Nat'l Nutritional Foods*, 512 F.2d at 695–96.

[113] *See, e.g.*, Batterton v. Marshall, 648 F.2d 694, 705 (D.C. Cir. 1980) (stating that an "interpretative rule serves an advisory function explaining the meaning given by the agency to a particular word or phrase in a statute or rule it administers"). *See also* Gibson Wine Co. v. Snyder, 194 F.2d 329 (D.C. Cir. 1952) (stating that "[a]n interpretative rule is one which does not have the full force and effect of a substantive rule but which is in the form of an explanation of particular terms in an Act").

[114] *Snyder*, 194 F.2d at 331.

[115] *See* Weinberger v. Hynson, 412 U.S. 609 (1973); Ciba Corp v. Weinberger, 412 U.S. 640 (1973); Weinberger v. Bentex Pharm., 412 U.S. 645 (1973). *See also Nat'l Nutritional Foods*, 512 F.2d at 697 (discussing the *Weinberger* decisions interpreting section "701(a) as giving FDA the power to promulgate substantive regulations having the binding force of law rather than mere 'interpretative' statements enforceable only on a case-by-case basis through plenary suits against those refusing to comply").

proposed major federal actions significant affecting the quality of the human environment.[116] The Paperwork Reduction Act, enacted in 1980, requires agencies to justify any collection of information from the public, including estimating the burden that the collection will impose on respondents.[117] The Regulatory Flexibility Act of 1980 requires federal agencies to assess the impact of their regulations on "small entities."[118] The Unfunded Mandates Reform Act of 1995 added requirements for agencies to analyze costs resulting from regulations containing federal mandates on state, local, and tribal governments and the private sector.[119] The Congressional Review Act, enacted in 1996, requires that "major" rules have a delayed effective date of at least sixty days and that agencies submit their rules to both houses of Congress and the Government Accountability Office (GAO) before the rules can take effect.[120]

In addition, in the 1980s and 1990s, presidents issued executive orders that would add more procedures in proposing or finalizing a regulation. In 1981, President Reagan issued Executive Order 12291, which, among other things, required agencies to submit to the Office of Management and Budget (OMB) a "Regulatory Impact Analysis" for all "major rules."[121] A "major" rule included any rule that would likely have at least a $100-million effect on the economy; impose a major increase in costs or prices; or have a significant adverse effect on competition, employment, investment, productivity, or innovation.[122] In 1993, President Clinton revoked Executive Order 12291 but issued Executive Order 12866. As with Executive Order 12991, Executive Order 12866 required an assessment of the costs and benefits of major rules and "reasonably feasible alternatives to the rule." Executive Order 12866 also required agencies to submit their pending major rules to OMB's Office of Information and Regulatory Affairs (OIRA) for review.[123] Arguably, most final monographs would affect a wide variety of OTC monograph drugs and could be considered a "major rule," requiring OIRA review.

The additional barriers to rulemaking coincided with a decrease in FDA funding for OTC monograph drugs. When the OTC Drug Review began, FDA was funded almost entirely through appropriations.[124] In the early years of the OTC Drug Review, FDA appropriations allowed FDA to convene panels and undergo the notice-and-comment rulemaking process. By the 2000s, FDA's funding for drug regulation depended more on user fees. Congress passed PDUFA in 1992 and started reauthorizing user fees for drugs approved under NDAs and for licensure of certain biological products under

---

116 42 U.S.C. §§ 4321–4347.

117 44 U.S.C. §§ 3501–3520.

118 5 U.S.C. §§ 601–612.

119 2 U.S.C. §§ 1532–1538.

120 5 U.S.C. §§ 801–808.

121 Exec. Order No. 12291, 46 Fed. Reg. 13193 (Feb. 17, 1981).

122 Exec. Order No. 12291, 3 C.F.R. § 128 (1981).

123 Exec. Order No. 12866, 58 Fed. Reg. 51735 (Oct. 4, 1993).

124 *See* CONG. RESEARCH SERV., R44576, THE FOOD AND DRUG ADMINISTRATION (FDA) BUDGET: FACT SHEET 3 (Apr. 2, 2020) (showing FDA spending from appropriations and user fees since 1992, when Congress passed the first user fee act) [hereinafter CRS, THE FDA BUDGET: FACT SHEET].

section 351 of the Public Health Service Act (PHSA).[125] The user fees set aside for the program could not be used to support programs that do not receive user fee funding.[126]

Although FDA's budget in nominal dollars had increased from the 1970s to the 2000s, much of that increase depended on user fees, particularly as user fees expanded to encompass generic drugs.[127] As a result, Congress appropriated less money to FDA for non-user-fee-funded uses when accounting for inflation, and FDA had fewer resources devoted to regulatory activities not funded by user fees, such as the OTC Drug Review. FDA's Center for Drug Evaluation and Research (CDER) Director Janet Woodcock testified in 2017 that congressional appropriations for prescription drugs in Fiscal Year (FY) 2016 was $320.9 million for prescription drugs compared to $7.9 million for OTC products.[128] PDUFA fees added an additional $836.9 million while OTC monograph drugs had no user fees.[129] In all, FDA spent $1.16 billion on PDUFA-funded drugs compared to $7.9 million for OTC monograph drugs despite more OTC monograph drug products on the market than branded prescription drugs.[130] Funding for OTC monograph drugs stagnated at approximately $7 to $8 million annually while funding for prescription drugs continued to increase.[131]

FDA's budget meant that FDA had limited resources to spend on regulating OTC monograph drugs. In 2016, FDA had a staff of fewer than thirty people who worked full-time to oversee the OTC monograph program.[132] Moreover, potentially available resources were often consumed by external mandates, including, for example, consent decrees and special statutes which required FDA to take action within a specified period of time. Director Janet Woodcock testified that in FY 2015–2017, "essentially all of FDA's monograph review capacity" was dominated by the statutory requirements of the Sunscreen Innovation Act (SIA), court-mandated requirements of the consent decree pertaining to antiseptic drug products, and urgent safety updates.[133]

The monograph process for antimicrobial hand sanitizers illustrates the long and winding process to finalization for some OTC monograph drugs. On January 7, 1972, FDA published a request for data and information on all antimicrobial active ingredients in drug products for repeated daily topical human use.[134] Shortly after, FDA appointed a panel to review data and information on the safety, effectiveness, and labeling of OTC products containing antimicrobial ingredients for topical human

---

[125] *Modernizing FDA's Regulation of Over-the-Counter Drugs: Hearing Before the Subcomm. on Health of the H. Comm. on Energy & Commerce*, 115th Cong. 10 (2017) [hereinafter *2017 House Hearing*] (statement of Janet Woodcock, CDER Director, FDA).

[126] *See, e.g.*, FDCA § 736(g) (specifying how FDA could use fees collected under the prescription drug user fee program).

[127] CRS, THE FDA BUDGET: FACT SHEET, *supra* note 124, at 4.

[128] *2017 House Hearing*, *supra* note 125, at 14 (statement of Janet Woodcock, CDER Director, FDA).

[129] *See* Stephen Barlas, *Congress Readying User Fee Program for OTC Products: Money Needed to Dig FDA Out of Its Review Ditch*, 43 PHARMACY & THERAPEUTICS 541, 541–43 (2018).

[130] *2017 House Hearing*, *supra* note 125 at 14 (statement of Janet Woodcock, CDER Director, FDA).

[131] *Id.*

[132] U.S. FOOD & DRUG ADMIN., PUBLIC MEETING: OVER-THE-COUNTER MONOGRAPH USER FEES 41, 43 (June 10, 2016) https://www.fda.gov/media/98882/download [https://perma.cc/XJ6Q-23HS] (Presentation by Donal Parks, FDA, on "User Fee Considerations in the Context of Over-the-Counter Monograph Drugs").

[133] *2017 House Hearing*, *supra* note 125, at 14 (statement of Janet Woodcock, CDER Director, FDA).

[134] 37 Fed. Reg. 235 (Jan. 7, 1972).

use, including for soaps, surgical scrubs, skin washes, skin cleansers, and first aid preparations. On June 29, 1972, the advisory review panel first convened and then met in fifteen working meetings between 1972 and 1974.[135] On July 24, 1974, the antimicrobial advisory review panel submitted a report to FDA. After reviewing the report, FDA published a proposed monograph for topical antimicrobial drug products on September 13, 1974.[136] The monograph proposed to categorize one active ingredient, iodine tincture, as GRASE and not misbranded for patient pre-operative skin preparation use and two types of active ingredients, quaternary ammonium and hexylresorcinol, as GRASE and not misbranded as a skin wound cleanser.[137] All other ingredients were proposed as category II or III. FDA issued a TFM for antimicrobial drug products on January 6, 1978. The January 1978 TFM maintained the active ingredients proposed as GRASE in the proposed monograph and added poloxamer 188 to be GRASE as a skin wound cleanser.[138] FDA did not propose any ingredients as GRASE for purposes of a skin wound protectant or surgical hand scrub.

FDA continued to modify the TFM for antimicrobial drug products for the next forty years. Following the January 1978 TFM, FDA received multiple petitions and requests to reopen the administrative record, and for the next fifteen years, reopened the administrative record for OTC topical antimicrobial drug products multiple times for consideration of new information and data.[139] As a result, in 1991, FDA published a separate TFM for first aid uses of topical antimicrobials "to expedite the completion of the first aid section of the antimicrobial monograph."[140] The TFM proposed classifying eighteen ingredients as GRASE and not misbranded for use as a first aid antiseptic.[141] On June 17, 1994, FDA issued a new TFM for "healthcare antiseptics," which included products used by consumers on a frequent basis and products intended for use by health professionals, such as patient preoperative skin preparations and surgical hand scrubs.[142] The TFM proposed classifying two active ingredients (alcohol 60–95% and povidone-iodine 5–10%) as GRASE for use as antiseptic handwash, five active ingredients (alcohol 60–95%, iodine tincture, iodine topical solution, isopropyl alcohol 70–91.3%, and povidone-iodine 5–10%) as GRASE for use as a patient preoperative skin preparation, and two active ingredients (alcohol 60–95% and povidone-iodine 5–10%) as GRASE for use as a surgical hand scrub.[143] Following this TFM, FDA took no further action on antiseptic active ingredients other than to reopen the administrative record in May 2003 to accept data and information on OTC healthcare antiseptic drug products.[144]

---

[135] 39 Fed. Reg. 33103, 33104 (Sept. 13, 1974) (to be codified at 21 C.F.R. pt. 333).

[136] *Id.* at 33103.

[137] *Id.* at 33141.

[138] 43 Fed. Reg. 1210, 1246 (Jan. 6, 1978) (to be codified at 21 C.F.R. pt. 333).

[139] *See, e.g.*, 44 Fed. Reg. 71428, 71428–29 (Dec. 11, 1979); 68 Fed. Reg. 32003, 32003–04 (May 29, 2003).

[140] 56 Fed. Reg. 33644, 33645 (July 22, 1991) (to be codified at 21 C.F.R. pt. 333, 369).

[141] *Id.* at 33673.

[142] 59 Fed. Reg. 31402 (June 17, 1994) (to be codified at 21 C.F.R. pt. 333, 369).

[143] *Id.* at 31435.

[144] 68 Fed. Reg. 32003, 32003 (May 29, 2003) (to be codified at 21 C.F.R. pt. 333).

Frustrated by FDA's lack of progress on antiseptic OTC drugs, consumer groups sued FDA to finalize the antiseptic TFMs. On July 27, 2010, the Natural Resources Defense Council (NRDC) filed a complaint against FDA, arguing that FDA's delay in finalizing the antiseptic monographs was unreasonable and contrary to the FDCA and sought an order requiring FDA to finalize the antiseptic monographs by a specific date.[145] NRDC was particularly concerned about the use of triclosan and triclocarban as active ingredients in OTC antimicrobial soap. NRDC believed that these active ingredients could contribute to the development of antibiotic-resistant bacteria.[146] At a July 19, 2013 status conference before the District Court for the Southern District of New York, FDA submitted a non-binding timetable for completing its regulation of triclosan in OTC drug products and finalized this timeline in a consent decree.[147]

Following the consent decree, FDA issued a flurry of documents related to the antiseptic monographs. On December 17, 2013, FDA amended the healthcare antiseptic TFM to establish consumer antiseptic washes separately from healthcare antiseptics.[148] On June 28, 2016, FDA published an amended tentative final monograph for consumer antiseptic rubs.[149] The TFM proposed removing alcohol and povidone-iodine as category I ingredients and reclassified them as category III for use as consumer antiseptic hand rubs.[150] On September 6, 2016, FDA published a final rule for consumer antiseptic washes.[151] With the exception of three deferred antiseptic wash ingredients (benzalkonium chloride, benzethonium chloride, and chloroxylenol), the rule finalized the non-monograph status of the remaining nineteen active ingredients identified in the 2013 consumer hand wash TFM, including triclosan and triclocarban.[152] On April 12, 2019, FDA also published a final rule on consumer antiseptic rubs, deferring rulemaking on three consumer antiseptic rub ingredients (benzalkonium chloride, alcohol, and isopropyl alcohol) and finalizing the monograph status of twenty-eight other active ingredients identified in the 2016 TFM.[153] FDA has yet to finalize the monograph for all OTC antiseptic drugs almost fifty years after the OTC Drug Review began.

4. The OTC Drug Review and FDA's Interpretation Offered a Limited Process for Changing Monographs

The FDCA's definition of new drug and FDA's interpretation of its authorities under the FDCA and the procedures for the OTC Drug Review offered limited opportunities for FDA or industry to modify proposed or finalized monographs. The result was a regulatory regime that limited the OTC Drug Review to drugs that had been marketed in the 1970s and provided few incentives for manufacturers to introduce new OTC monograph drugs into the market.

---

[145] *See* NRDC v. FDA, No. 10 Civ. 5690 (S.D.N.Y. Nov. 21, 2013) (consent decree).

[146] *See id.*

[147] *Id.*

[148] 78 Fed. Reg. 76444, 76444 (Dec. 17, 2013).

[149] 81 Fed. Reg. 42912, 42912 (June 28, 2016) (to be codified at 21 C.F.R. pt. 310).

[150] *Id.* at 42914.

[151] 81 Fed. Reg. 61106, 61106 (Sept. 6, 2016) (to be codified at 21 C.F.R. pt. 310).

[152] *Id.* at 61107.

[153] 84 Fed. Reg. 14847, 14848 (Apr. 12, 2019) (to be codified at 21 C.F.R. pt. 310).

a) Material Time of Material Extent

(1) The FDCA Does Not Define "Material Time" or "Material Extent"

The FDCA defines the term new drug to include drugs that have not been used "to a material extent or for a material time."[154] The definition of new drug includes "any 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."[155] In other words, a drug could be GRASE but would be a new drug if it had not been "used to a material extent or for a material time" under its conditions of use.

The "material time or extent" condition limits drugs eligible for consideration under the OTC Drug Review, and in 1973, the Supreme Court confirmed this limitation. In concluding that the 1962 Amendments were intended to apply to drugs already on the market, the Court pointed to the material time and extent language in the new drug definition. A drug "cannot transcend 'new drug' status until it has been used 'to a material extent or for a material time.'"[156] Therefore, the Act was designed so that certain drugs on the market that have been used for a material time and extent can "drop out of active regulation by ceasing to be a 'new drug.'"[157]

The FDCA does not define when drugs should be considered used for a "material extent" or a "material time," and the legislative history of the FDCA does not shed light on the matter. Many courts have considered the material time or extent provision but have not provided a standard for when a drug would have been marketed to a material extent or for a material time.[158] In *United States v. Premo Pharm. Lab.*, the court came close to offering a definition but declined to do so.[159] In assessing the company's assertion that these products were not new drugs, the district court considered the products' marketing history but did not definitely determine whether the products had been marketed to a material time and extent.

(2) FDA's Policy on Material Time or Material Extent in the Context of the OTC Drug Review

When FDA first established the OTC Drug Review, it did not explicitly address the issue of "time and extent" but considered "all active ingredients in OTC drugs on the market as of May 11, 1972, when the review began, regardless of specific marketing

---

[154] FDCA § 201(p); 21 U.S.C. § 321(p).

[155] *Id.*

[156] Weinberger v. Hynson, 412 U.S. 609 (1973).

[157] *Id.*; *see also* United States v. Generix Drug Corp., 460 U.S. 453 (1983) (holding that the term "new drug" applied to complete drug products rather than just active ingredients).

[158] *See* Farquhar v. FDA, 616 F. Supp. 190, 193 (D.D.C. 1985) (stating that the issue of whether a drug has been marketed for a material time or material extent "is not a question for the judiciary to properly consider in the first instance. The FDA has the established procedures and expertise as well as the statutory authority to make this difficult determination"); *see also* United States v. Atropine Sulfate, 843 F.2d 860, 860–61 (5th Cir. 1988), United States v. Undetermined Quantities of Various Articles of Drug, 675 F.2d 994, 1001 (8th Cir. 1982); United States v. Article of Drug Hormonin, 498 F. Supp. 424, 431–42 (D.N.J. 1980).

[159] United States v. Premo Pharm. Lab., 629 F.2d 785 (2d Cir. 1980).

history."[160] The 1972 regulations did not define the eligibility requirements for consideration in the OTC Drug Review or what would constitute marketing to a material extent or for a material time. Nevertheless, the May 11, 1972 date would form the basis for FDA's later determinations for deciding whether drugs were eligible to be considered under the OTC Drug Review.

Initially, FDA made case-by-case determinations about whether drugs were new drugs and could be eligible to be considered for the OTC Drug Review. Some of these questions arose as FDA reviewed advisory panel reports on OTC drugs. For example, in 1978, the advisory review panel on "OTC Contraceptives and Other Vaginal Drug Products" placed menfegol in category I as an OTC vaginal contraceptive based on foreign safety and efficacy data.[161] FDA disagreed with that conclusion and determined that menfegol was a new drug because it had "never before marketed as a drug in the United States."[162] FDA's case-by-case determinations became FDA policy.

For the first three decades of the OTC Drug Review, FDA took the position that a drug could not meet the material extent or material time requirement if a drug had been marketed as OTC in a foreign country but not the United States.[163] In 1988, FDA responded to a comment to the internal analgesic monograph requesting that the lysine salt of aspirin be included in the TFM for temporary relief from occasional minor aches, pains, and headaches. At that point, the lysine salt of aspirin had been marketed in a number of other countries for several years. FDA stated that it considered a lysine salt of aspirin as a new drug because FDA "interprets the terms 'material extent' and 'material time' to mean availability in the United States marketplace," and the agency was unaware "that lysine aspirin has ever been marketed as a drug in the United States."[164] FDA later changed its position when it implemented the time and extent application process, as we discuss in Section II.C.4.b.

FDA also took the position that a change in new strengths or dosage forms would result in an old drug becoming a new drug. In 1984, FDA denied a citizen petition requesting that FDA reopen the administrative record for OTC internal analgesic and menstrual drug products to consider a new dosage strength of ibuprofen. The 200 mg dose had only been approved for nonprescription use shortly before, and the agency stated that the 200 mg dosage strength was a new drug because it had not been used to a material extent and for a material time in the United States.[165] Later, however, FDA issued a modification to the internal analgesic TFM proposing to include ibuprofen at doses of 200–400 mg.[166] By then, ibuprofen had been extensively used for nonprescription use for many years.

An old drug could become a new drug based on a new condition of use that appears on labeling if the condition of use had never previously appeared on any marketed

---

[160] 61 Fed. Reg. 51625, 51626–67 (Oct. 3, 1996) (to be codified at 21 C.F.R. pt. 330). *See also* 37 Fed. Reg. 9464, 9464 (May 11, 1972) (noting that "there are only an estimated 200 active ingredients in the thousands of OTC drugs now marketed" and intending that OTC Drug Review would cover all drugs currently on the market).

[161] 45 Fed. Reg. 82014, 82014 (Dec. 12, 1980) (to be codified at 21 C.F.R. pt. 351).

[162] *Id.*

[163] 61 Fed. Reg. 51625, 51627 (to be codified at 7 C.F.R. pt. 17)

[164] 53 Fed. Reg. 46204, 46248 (Nov. 16, 1988) (to be codified at 7 C.F.R. pt. 310, 343, 369).

[165] 61 Fed. Reg. 51625, 51627 (June 10, 2020) (to be codified at 21 C.F.R. pt. 330).

[166] 67 Fed. Reg. 54139, 54152 (Aug. 21, 2002) (to be codified at 21 C.F.R. pt. 201, 343).

OTC drug product in the United States. In 1983, FDA refused to review data relating to use of fructose as an ingredient intended "to minimize or prevent inebriation" from alcoholic beverages. FDA said it was not aware of any drug product for the claim "to minimize or prevent inebriation" and therefore refused to consider that data for OTC drug review.[167] More recently, in 2007, FDA issued a warning letter to Procter & Gamble (P&G) alleging that its leave-on triclosan hand sanitizer was a new drug.[168] The hand sanitizer TFM directed triclosan users to rinse their hands with water after use, but P&G's directions for the Vicks Early Defense Foaming Hand Sanitizer said the product could be used anytime "when soap and water are not readily available."[169] While the active ingredient was eligible for use under the monograph, the directions for use made the product a new drug.

On the other hand, FDA did find that some products not marketed in 1972 met the material extent and material time requirement. In 1993, FDA received a petition requesting the agency to permit broad spectrum combination sunscreen products containing avobenzone to be marketed under the OTC sunscreen monograph. In 1996, FDA found that avobenzone, a sunscreen ingredient, was eligible for the OTC Drug Review because it had been "continuously marketed OTC in the United States under NDA's for approximately 8 years and subject to the NDA adverse events reporting requirements. Over 5 million units of avobenzone-containing products have been sold in the United States."[170]

b) Limited Procedures to Introduce Innovations Under the OTC Drug Review

A manufacturer hoping to introduce a new condition of use for a drug under the OTC Drug Review had limited options. FDA eventually provided two procedures for manufacturers to request approval for an NDA drug deviating from a final monograph, but these procedures were not widely used. As we discuss below, each procedure required submission of significant, new data that would require substantial financial investment. Yet, companies had few regulatory incentives to conduct the studies required to market the product. Because each procedure was not associated with exclusivity, it was possible that competitor products could enter the market soon after a GRASE determination, relying on the data from the original determination.

(1) NDA Deviation

The OTC Drug Review provided a procedure under which manufacturers could submit an NDA requesting approval for an OTC drug deviating from a final monograph.[171] The NDA application would conform with all other requirements for NDAs but would contain a statement that the product meets all the conditions of the applicable monograph, except for the deviation for which approval was requested.[172] The NDA would contain only information pertaining to the deviation. The deviation

---

[167] 48 Fed. Reg. 32872, 32873 (July 19, 1983).

[168] Ron Zapata, *FDA Claims Dirty Advertising Over P&G Sanitizer*, LAW360 (Sept. 19, 2007) (quoting a warning letter issued from Stephan Galson, FDA, to Alan Lafley, P&G).

[169] *Id.*

[170] 61 Fed. Reg. 48645, 48646 (Sept. 16, 1996) (to be codified at 21 C.F.R. pt. 352).

[171] 21 C.F.R. § 330.11.

[172] *Id.*

would be specific for the sponsor of the NDA and could not be used by other manufacturers.[173]

The NDA deviation procedure was rarely used. The Consumer Healthcare Product Association's (CHPA) comments to FDA's public hearing on OTC monograph reform provide reasons why the process failed to gain popularity.[174] First, the NDA deviation pathway required that products be in a final monograph before sponsors could use the procedure. As Robert Pinco stated, "that language arose back when everyone thought all of the monographs would be final two years after the Review began."[175] Because many OTC monographs were not finalized and many products marketed under TFMs, this limited the utility of the pathway.

Second, as implemented by FDA, the provision would have required submission of information beyond what was needed to support the proposed deviation. In 1998, a manufacturer submitted an NDA deviation from the monograph for OTC pediculicide drug products for a new dosage form. The manufacturer wanted to market its lice treatment product in a new dosage form, an aerosolized foam, but the monograph allowed only products in non-aerosol dosage forms.[176] In that case, FDA required not just information to support the proposed deviation but also *in vitro* effectiveness studies related to the safety and effectiveness of the active ingredient, as well as new chemistry, manufacturing, and control information.[177]

Third, the NDA deviation procedure was adopted prior to the enactment of the Hatch-Waxman Act in 1984. NDA deviation did not provide regulatory incentives for manufacturers to conduct clinical studies necessary for a change, unlike section 505(b)(2), which provided three years of regulatory exclusivity if the sponsor conducted "new clinical investigations (other than bioavailability studies)" that were essential to approval of the application.[178] Therefore, after the Hatch-Waxman Act passed and FDA began permitting manufacturers to use the 505(b)(2) route for drugs in category I under final monographs, the 505(b)(2) route became the mechanism of choice for manufacturers wanting to market drugs with conditions of use not permitted under existing monographs.

(2) Time and Extent Applications

In 1996, FDA proposed another path, the Time and Extent Application (TEA) process, for manufacturers to introduce new drugs within the OTC Drug Review.[179] The impetus for TEAs was driven by an industry effort to introduce new sunscreen active ingredients into the Review based on use in Europe. Many sunscreens had long been marketed in Europe as a cosmetic, but the costs of developing the data needed

---

[173] *See id.*

[174] Comments of the Consumer Healthcare Products Association in Response to the Notice of Hearing on the Over-the-Counter Drug Monograph System, at 8–9 (Docket No. FDA-2014-N-0202) (May 8, 2014).

[175] Robert Pinco & Michael Cogan, *Prescription to Over-the-Counter Switches: An Example of the Need for New Procedures in the Post-Monograph Era*, 39 FOOD DRUG COSMETIC L.J. 230, 237 (1984).

[176] 21 C.F.R.§ 358.160.

[177] *Bayer Rid Pediculicide Marketing Begins with Mousse Launch: Medical Review for Application 21-043*, TAN SHEET (June 26, 2000), https://www.accessdata.fda.gov/drugsatfda_docs/nda/2000/21-043_RID%20Mousse_medr.pdf [https://perma.cc/3GN5-DXHR].

[178] FDCA § 505(c)(3)(E)(iii).

[179] 61 Fed. Reg. 51627.

for an NDA approval prevented manufacturers from marketing these products in the United States. After issuing a proposed rule[180] and receiving comments, FDA finalized the process in 2002.[181]

The TEA process, as originally conceived, was intended to allow manufacturers to introduce new products through the OTC Drug Review by relying on only foreign data. The TEAs consisted of a two-step process. First, an applicant would submit a TEA to request that conditions be considered for inclusion in the OTC Drug Review, and FDA would determine whether the ingredient was eligible. A TEA could only be submitted for conditions if: 1) the condition was initially marketed in the United States after the OTC Drug Review began in 1972; or 2) the condition was marketed only outside the United States but would be regulated as OTC drugs in the United States.[182] To be eligible for inclusion, a condition must be marketed for OTC by consumers. If the condition was only marketed in a foreign country, the condition must have been marketed for "at least 5 continuous years in the same country in sufficient quantity."[183]

If FDA determined that the condition was eligible for inclusion in the OTC Drug Review, FDA would publish a notice of eligibility that requested the submission of data to demonstrate that the product was GRASE for the intended use and publish it for public comment.[184] The process would then proceed similarly to the regular process under the OTC Drug Review.[185]

The TEA process was only a bit more popular than the NDA deviation process. First, it was not clear whether the data requirements for TEAs would be any less significant than those required under NDAs. FDA's final guidance for TEAs indicated that proof of effectiveness should include "adequate and well-controlled" studies that are randomized and blinded, have a sufficient number of subjects, include an appropriate target population, and contain a control arm.[186] FDA would accept "only relevant studies."[187] An example of an irrelevant study "would be an in vitro effectiveness study when [FDA] would require clinical effectiveness studies to approve an NDA for the condition."[188] It was unclear what incentive a manufacturer would have to conduct clinical studies to receive approval through the TEA process when a manufacturer could conduct the same clinical studies but receive exclusivity for a drug approved under an NDA.

Further, applicants had no guarantee that their applications would be processed and reviewed in a timely manner. Any change to a monograph would still need to undergo the rulemaking process, which, as described above, was time-consuming and burdensome. The TEA applicant must survive multiple rounds of review before it could market products with the new ingredient, and FDA lacked resources for responding to and reviewing applications. The preamble to the final rule establishing

---

[180] 64 Fed. Reg. 71062, 71062 (Dec. 20, 1999).

[181] 67 Fed. Reg. 3060 (Jan. 23, 2002).

[182] 21 C.F.R. § 330.14.

[183] 21 C.F.R. § 330.14(b).

[184] 21 C.F.R. § 330.14(f).

[185] 21 C.F.R. § 330.14(g).

[186] U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: TIME AND EXTENT APPLICATIONS FOR NONPRESCRIPTION DRUG PRODUCTS 14 (Sept. 2011).

[187] *Id.*

[188] *Id.*

TEAs indicated that FDA would "strive to complete TEA evaluations within 90 to 180 days of receipt and will implement procedures to ensure that agency resources are used appropriately and result in timely action on safety and effectiveness submissions."[189] FDA estimated it would receive approximately fifty TEAs and approve thirty new OTC products each year under the TEA process.[190] These goals were wildly optimistic. By the time of passage of the CARES Act in March 2020, FDA had not permitted a single active ingredient for use under the TEA procedure, eleven years after FDA established the process.

III. DISCUSSIONS ON OTC MONOGRAPH REFORM

A. FDA's Public Workshop on OTC Monograph Reform

In November 2013, Director Woodcock met with the Board of CHPA and shared FDA's interest in holding a Part 15 public hearing on OTC monograph reform. On February 24, 2014, FDA published a notice in the Federal Register announcing a public hearing on "Over-The-Counter Drug Monograph System—Past, Present, and Future" to "seek input on possible ways to modernize the OTC Monograph Process to make the process more responsive to emerging safety information and scientific advances."[191] The notice acknowledged "significant challenges with the OTC Drug Review as it functions today" and described what FDA believed are the biggest challenges of the current system: 1) the large number of products marketed under the OTC Drug Review under a not-yet final monograph; 2) limitations on FDA's ability to require warnings or other labeling changes to address emerging safety or effectiveness issues; and 3) inability of the OTC Drug Review to accommodate innovative changes to products under the OTC Drug Review.[192]

FDA recognized that these challenges were not conducive to efficiently and effectively regulating products under the Review. The large number of products not covered by final monographs presented "unintended consequence[s]" for OTC drug regulation.[193] Because these products remain under enforcement discretion, the regulatory framework "creates negative incentives" for manufacturers to conduct studies or respond to safety concerns.[194] The OTC Drug Review also "presents challenges to FDA's ability to respond to emerging safety issues, keep pace with evolving science, and ensure the consistent safety and effectiveness of varying formulations."[195] FDA believed that the rulemaking process was not "agile enough" to quickly change a monograph to address new safety issues, such as adding a warning, narrowing an indication, or removing an active ingredient in the monograph.[196] It was also difficult to add new information into monographs, such as dosing and labeling instructions for pediatric indications. Further, FDA was concerned that "products in

---

[189] 67 Fed. Reg. 3065.

[190] *Id.* at 3072.

[191] 79 Fed. Reg. 10168, 10171 (Feb. 24, 2014).

[192] *Id.* at 10169.

[193] *Id.* at 10170.

[194] *Id.*

[195] *Id.*

[196] *Id.*

their final formulation are not specifically evaluated by the Agency to ensure product safety, effectiveness and consistency" and wanted more information about "specific varying formulations" of final finished drug products.[197] Finally, the OTC Drug Review was not facile in accommodating manufacturers wishing to develop new combinations of ingredients or new dosage forms. These products would require an NDA prior to marketing.[198]

FDA recognized that "many of the OTC Drug Review's present day challenges are systemic, and thus cannot be addressed solely by increasing resources."[199] Therefore, FDA proposed a number of solutions to overhaul the OTC Drug Review and asked stakeholders to comment on these issues. FDA wanted "streamlined processes" to finalize existing TFMs.[200] FDA was particularly interested in alternatives to notice-and-comment rulemaking for issuing monographs. FDA suggested issuing monographs by "administrative order," similar to the process enacted by the Food and Drug Administration Safety and Innovation Act (FDASIA) for device reclassifications. FDA also proposed that OTC manufacturers submit more information about their products before marketing, such as labeling, quality, and pharmacokinetic information. To address issues with innovation, FDA suggested expanding the NDA deviation process and was interested in why the NDA deviation process was not attractive for industry. In addition to its specific proposals, FDA asked for alternatives and other regulatory mechanisms that FDA should consider.[201]

FDA held the public hearing on March 25–26, 2014. During the public hearing, members from industry, academia, physician organizations, and other members of the public testified about potential changes to the OTC monograph system. William Soller, from the University of California San Francisco, questioned whether the Review could remain viable without user fees to support FDA.[202] Kathleen Neville, from the American Academy of Pediatrics (AAP), wanted the OTC Drug Review to "use modern standards for safety and efficacy," which would allow FDA "to easily and quickly require additional information or data necessary."[203] She also stated that the existing drug monographs were developed "with little or no data on the safety and efficacy of monograph drugs in children," and age-specific therapeutic data on monograph products are needed.[204]

Industry members supported the OTC monograph system and believed that the system should continue to underpin OTC drug regulation. As Scott Melville, President of CHPA emphasized, "we do not believe that the OTC monograph system is broken or that consumers should be concerned about the safety or efficacy of OTC medicines regulated under it."[205] At the same time, some industry witnesses urged FDA to

---

197 *Id.*

198 *Id.* at 10171.

199 *Id.*

200 *Id.*

201 *Id.* at 10172.

202 U.S. FOOD AND DRUG ADMIN., PUBLIC HEARING: OVER-THE-COUNTER DRUG MONOGRAPH SYSTEM – PAST, PRESENT, AND FUTURE 30–31 (Mar. 25, 2014) (statement of William Soller, University of California, San Francisco).

203 *Id.* at 210 (statement of Kathleen Neville, American Academy of Pediatrics).

204 *Id.* at 201.

205 *Id.* at 50 (statement of Scott Melville, CHPA).

improve its procedures for communicating with stakeholders concerning outstanding issues related to OTC drugs and the data that FDA needs to resolve those issues. Barbara Kochanowski, Senior Vice President of Regulatory and Scientific Affairs at CHPA, asked FDA to provide "a more transparent OTC monograph process where FDA and other participants explain the process and identify bottlenecks."[206] Industry also urged FDA to create more effective tools for including new changes to OTC monograph drugs, such as new active ingredients in the OTC review process.

Other industry members believed that the OTC Drug Review was not in need of fundamental change but FDA had not provided the resources necessary to complete the review in a timely manner or had not given the director of the OTC division the authority to require prompt decisions. Richard Kingham, a lawyer at Covington & Burling LLP, argued that FDA needed a "focused effort on the efficiency of the rulemaking process for OTC Drugs," including "good review practices, process management, and other arrangements" to ensure that decisions are made in a timely manner.[207] Peter Barton Hutt, from Covington & Burling LLP, argued that FDA had "all the money in the world" to fund the Review, but FDA had not provided the right people with authority to finish the process.[208] Gary Yingling of Morgan, Lewis and Bockius, argued that the issues with the OTC Drug Review stemmed from senior management not making the program a priority.[209]

B. In the Interim, Congress Passes the Sunscreen Innovation Act

As FDA began its initial conversations on OTC monograph reform, Congress was in the midst of another conversation on a subset of OTC monograph drugs. As far back as 1997, Sen. Jack Reed (D-RI) and other members of Congress had pressed FDA to complete their review of sunscreens and finalize the sunscreen monograph. By 2013, Sen. Jack Reed (D-RI) and other members of Congress began pressing FDA for tighter oversight for sunscreens.[210] Members of Congress wondered when FDA would publish the final rule on sunscreens and questioned why FDA had delayed review of eight sunscreen TEAs pending at the agency.[211] Meanwhile, frustrated by the lack of progress on sunscreen TEAs, sunscreen manufacturers formed the Public Access to Sunscreens (PASS) Coalition to advocate for a new regulatory pathway to market new sunscreen ingredients.[212]

On March 13, 2014, Reps. Ed Whitfield (R-KY) and John Dingell (D-MI) introduced the Sunscreen Innovation Act (SIA) (H.R. 4250) in the House. The Health Subcommittee of the House Energy & Commerce (E&C) held a hearing on the bill.

---

[206] *Id.* at 55 (statement of Barbara Kochanowski, CHPA).

[207] U.S. FOOD AND DRUG ADMIN., OVER-THE-COUNTER DRUG MONOGRAPH SYSTEM – PAST, PRESENT, AND FUTURE, FDA PUBLIC HEARING 37 (MAR. 26, 2014) (statement of Richard Kingham, Covington & Burling LLP).

[208] *Id.* at 84 (statement of Peter Barton Hutt, Covington & Burling LLP).

[209] *Id.* at 53 (statement of Gary Yingling, Morgan, Lewis and Bockius).

[210] Stephanie Beasley, *Lawmakers Seek FDA Action on Sunscreen Sprays, High SPF Products*, INSIDE HEALTH POLICY (June 3, 2013).

[211] *Id.*

[212] *See* PASS Coalition, Comment to Docket No. FDA-2014-N-0202: Over-The-Counter Monograph System – Past, Present, and Future; Public Hearing (May 12, 2014).

Although the discussion centered around sunscreens, OTC monograph reform inevitably entered the discussion. For example, Director Woodcock testified how FDA recognized "the entire OTC monograph process is outdated, and about 2 weeks ago, we had a public hearing to discuss ways we might be able to modernize the process."[213] Rep. Whitfield questioned Director Woodcock about why "the TEA process is not working very well" and asked "how difficult is it to get a more functional monograph process?"[214] Director Woodcock responded that FDA "would be delighted to work with you, although we would like to reform the whole process of the monographs. Because sunscreens are just a microcosm, as I said, of a process of [sic] has encountered tremendous problems."[215] Some industry pushed back. Scott Faber of the Environmental Working Group (EWG) believed, "with all due respect to Dr. Woodcock, that we should not have to wait for a reformation of the sense of the monograph process for FDA . . . to review and approved some of these very promising ingredients.[216]

On November 26, 2014, the SIA became law. The SIA provided a new review process for finalizing pending and new sunscreen ingredient applications and a new process for other, non-sunscreen ingredients with TEAs.[217] Even as SIA passed, Congress recognized that the larger OTC monograph system needed fixing. During discussions on SIA, Congress was already contemplating what OTC monograph reform might look like, such as replacing the notice-and-comment rulemaking process under OTC Review with an administrative order process. However, at the time, FDA clearly indicated that new legislation on OTC monograph reform would need to be accompanied by increased funding to allow FDA to implement the new system. Congress did not enact the SIA with user fees or significant, new appropriations for FDA, and in the coming years, the lack of resources and commitments from FDA would impede SIA's success. Congress recognized that further discussions between FDA and industry, including on user fees, were needed before Congress could enact legislation on OTC monograph reform.

C. Key Issues in Preliminary Discussions[218]

By the end of 2014, discussions between FDA, industry, and the Hill began in earnest. A number of key issues emerged, some of which were discussed during the public hearing and the passage of the SIA.

1. Regulatory Status of OTC Monograph Drugs

Industry and FDA both saw a need to efficiently finalize TFMs. FDA proposed a process where Congress could deem certain drugs in TFMs as GRASE. Industry agreed with the proposal but wanted to ensure that drugs with active ingredients in

---

213 *Improving Predictability and Transparency in DEA and FDA Regulation: Hearing Before the Subcomm. on Health of the H. Comm. on Energy & Com.,* 113th Cong. 71 (2014) (statement of Janet Woodcock).

214 *Id.* at 106 (statement of Rep. Edward Whitfield).

215 *Id.* at 107 (statement of Janet Woodcock).

216 *Id.* at 174 (statement of Scott Faber).

217 Sunscreen Innovation Act, Pub. L. No. 113-195, 128 Stat. 2035 (2014).

218 Much of the discussion in this section comes from the authors' firsthand knowledge of preliminary discussions between FDA, industry, and the Hill.

category III TFMs not deemed as GRASE could continue to be legally marketed until FDA issues a final determination. If FDA decided to finalize a monograph for category III active ingredients, industry wanted sufficient time to ensure that it could submit the information FDA needed to make its determination, particularly where FDA decided there were gaps in data.

Industry agreed with the deeming process but sought increased communication with FDA on non-finalized ingredients. Industry wanted a "dashboard" that would, among other things, provide advance notice of category III TFM and category I ANPR ingredients that FDA intended to consider in future administrative order proceedings. Industry and FDA agreed on a public-facing IT dashboard, which was set out in the "OTC Monograph User Fee Program Performance Goals and Procedures" (the "Goals Letter").[219] In addition, FDA and industry agreed that when FDA proposes an administrative order seeking submission of new data related to a category III TFM or a category I ANPR ingredient, FDA would include information on the types of data it expects to receive.

Industry and FDA also discussed the scope of OTC monograph drugs subject to OTC monograph reform. Homeopathic drugs had not been subject to the OTC Drug Review, and the homeopathic drug industry did not want to be regulated under OTC monograph reform.[220] FDA and industry agreed that homeopathic drugs would not be subject to the new OTC monograph reform provisions. At the time, FDA regulated homeopathic drugs under enforcement discretion, based on a 1988 Compliance Policy Guide titled "Conditions Under Which Homeopathic Drugs May be Marketed."[221] It was understood that homeopathic drugs would continue to be subject to enforcement discretion until FDA decides to take action.

Further, industry was concerned about drugs on the market with active ingredients that were not covered by a final monograph or a TFM or that were not category I in an ANPR. It was unclear which products were not covered by the contemplated categories, but industry wanted to ensure that FDA would not gain additional authority to enforce against these products as unapproved new drugs immediately after enactment. FDA wanted to ensure that OTC monograph reform would incorporate FDA's prior pronouncements on the eligibility of a drug for the OTC Drug Review. If FDA had issued a specific determination that a drug was not eligible for the OTC Drug Review, the product would be deemed to be a new drug after enactment of OTC monograph reform. If, for example, FDA had determined products not covered by the contemplated categories were new drugs before OTC monograph reform enactment, they would remain new drugs after enactment.

2. Administrative Orders

Industry and FDA agreed that notice-and-comment rulemaking did not provide an efficient approach to finalizing monographs. FDA wanted to ensure that any new

---

[219] U.S. FOOD & DRUG ADMIN., OVER-THE-COUNTER MONOGRAPH USER FEE PROGRAM PERFORMANCE GOALS AND PROCEDURES – FISCAL YEARS 2018–2022 7 [hereinafter GOALS LETTER].

[220] 37 Fed. Reg. 9466 (stating that because "of the uniqueness of homeopathic medicine, the Commissioner has decided to exclude homeopathic drugs from this OTC drug review and to review them as a separate category at a later time after the present OTC drug review is complete").

[221] CPG § 400.400. On October 25, 2019, FDA withdrew CPG § 400.400 and stated that it "intends to apply its general approach to prioritizing regulatory and enforcement action, which involves risk-based prioritization in light of all the facts of a given circumstance." 84 Fed. Reg. 57439, 57440 (Oct. 25, 2019).

process would not be subject to the extensive requirements and review associated with rulemaking. For example, FDA did not want the administrative order process to be subject to the Paperwork Reduction Act. FDA initially proposed to change monograph issuance to an administrative order process, similar to the process for device reclassification.

Industry agreed with an administrative order process in concept but did not want to adopt the process in place for device reclassification. Administrative orders produced through the device reclassification process did not contain explanations for the agency's decision or responses to public comments that were substantively comparable to the preambles accompanying TFMs or final monographs. Industry believed that a decision on whether there are adequate data to support the safety or effectiveness of an active ingredient and conditions of use was could be appropriately made through rulemaking or a similar proceeding. Where the agency does not receive comments or clearly explain the basis for an action, courts could set the agency's determination aside.

If OTC monograph reform were to incorporate an administrative order process, industry wanted to ensure that the process would be fair and transparent and provide adequate opportunities for interested parties to challenge FDA's decision, if necessary. Stakeholders should have an opportunity to comment on FDA's proposals, and FDA should need to take public comments into consideration before finalizing any administrative order. Industry members affected by FDA's finalization of TFMs should have the same opportunities to appeal an initial determination as participants in other user fee programs. Industry should have an opportunity to engage in formal dispute resolution and, if necessary, request a hearing if it disagreed with FDA's determination. Any disagreements should be adjudicated within the agency before a final determination went into effect.

Industry also wanted "FDA [to] improve its procedures for communicating with stakeholders" throughout the monograph finalization process.[222] Industry coalition groups argued there was not "sufficient transparency about the status of the remaining rulemakings . . . and what is preventing their finalization."[223] Specific improvements could include "one or more public meetings to discuss the status of the review process, along with establishment of an up-to-date website containing detailed information on the status of each monograph."[224]

Both FDA and industry agreed on clear milestones for completion of the monographs. The experience of sunscreen orders under the SIA underscored how a lack of timelines and agency commitments could make it difficult for FDA to make a determination on pending requests. Clear milestones would make it more efficient for industry to respond with data that it may already have on file or to discuss with FDA how best to meet its data needs. Industry and FDA looked to other user fee programs for how to structure a program that would hold FDA accountable while setting reasonable timelines.

---

[222] Consumer Healthcare Products Association, Comments in Response to the Notice of Hearing on the Over-the-Counter Drug Monograph System 6 (Docket No. FDA-2014-N-0202) (May 8, 2014) [hereinafter CHPA Hearing Comments].

[223] Personal Care Products Council, Comments in Response to the Notice of Hearing on the Over-the-Counter Drug Monograph System 3 (Docket No. FDA-2014-N-0202) (May 8, 2014).

[224] CHPA Hearing Comments, *supra* note 222, at 6.

3. Expedited Labeling Changes

Both industry and FDA agreed that FDA needed authority to quickly require changes to monographs to include new warnings on the basis of updated safety information. FDA wanted to remove some of the process limitations on FDA's ability to require new warnings or other labeling changes "to address emerging safety or effectiveness issues for products marketed under the OTC Drug Review in a timely and effective manner."[225]

Industry wanted to be able to quickly incorporate new safety information on drug labeling. In the past, certain manufacturers had wanted to add safety information on OTC monograph products due to new safety information, but industry had no sense of when and whether FDA would confirm that the new warnings were acceptable. The delay in incorporating warnings and other information in response to safety concerns increased manufacturers' product liability risks, but incorporating the new information before FDA agreement could risk FDA enforcement for unapproved labeling changes. At the time, industry had made voluntary several labeling changes to OTC products. For instance, a warning was added to benzocaine after an "FDA Drug Safety Communication," and makers of acetaminophen added a skin reaction warning based on a draft guidance.[226] Multiple label changes were voluntarily made to children's cough/cold products that were never added to applicable regulations. But industry and FDA agreed on the need for an expedited path to incorporating safety information on drug labeling. That said, industry wanted to limit expedited labeling changes to warnings and other similar labeling changes. Industry did not want FDA to have authority to use the expedited procedures to impose other modifications, such as changes to packaging, which would require extensive testing and formulation changes to implement.

4. Minor Dosage Form Changes

Industry wanted some sort of procedure for manufacturers to introduce new dosage forms without needing to submit an NDA or something similar to an NDA. Industry believed that FDA's position on the meaning of material time and material extent had frozen innovation on dosage forms to those that were in use in 1972. As we discussed previously, in 2007, FDA issued a warning letter to the marketer of a leave-on formulation of triclosan hand sanitizer, arguing that leave-on formulations of triclosan did not exist when the OTC Drug Review began.[227] FDA's position ultimately led to the withdrawal of the product from the market. In 2010, FDA issued a warning letter to the marketer of an OTC aspirin product in quick dissolving tablet form. The warning letter alleged, among other problems, that the "fast acting quick dissolve internal analgesic tablet" was a new dosage form and, therefore, was not generally recognized as safe and effective.[228]

---

[225] 79 Fed. Reg. 10168, 10170 (Feb. 24, 2014).

[226] *See* U.S. FOOD & DRUG ADMIN., DRAFT GUIDANCE: RECOMMENDED WARNING FOR OVER-THE-COUNTER ACETAMINOPHEN-CONTAINING DRUG PRODUCTS AND LABELING STATEMENTS REGARDING SERIOUS SKIN REACTIONS (2014); 79 Fed. Reg. 70879, 70879 (Nov. 28, 2014).

[227] Ron Zapata, *FDA Claims Dirty Advertising Over P&G Sanitizer*, LAW360 (Sept. 19, 2007) (quoting a warning letter issued from Stephan Galson, FDA, to Alan Lafley, P&G).

[228] Warning Letter from Reynaldo Rodriguez, U.S. Food & Drug Admin., to Fasprin Health/Nobel Laboratories (Oct. 21, 2010).

Industry wanted a new process, short of the full administrative order procedure, under which manufacturers could introduce new dosage forms without a drug-by-drug determination that each OTC drug was safe and effective. Industry also wanted to ensure that FDA would take into account the existing evidence available at the time as FDA determined which minor changes could be made without a new administrative order. FDA, on the other hand, did not want to be bound by external standard-setting organizations. As a compromise, FDA and industry supported language that would require FDA to "take into account relevant standards and standard practices for evaluating the quality of drugs," and FDA supported a reference in the Congressional Record that would refer to examples of specific standard-setting organizations.[229]

5. Exclusivity

Industry sought incentives for manufacturers to pursue OTC monograph innovations, and FDA agreed with the concept. During discussions, FDA had little input on the amount of exclusivity that was appropriate, as it considered the issue outside its substantive expertise. FDA and industry discussed what types of changes should qualify for exclusivity and what types of data would be sufficient for exclusivity. In doing so, FDA and industry looked to exclusivity provisions in other sections of the FDCA for reference. FDA and industry agreed that some data that would not have allowed a drug to receive exclusivity under an NDA could suffice for exclusivity under OTC monograph reform.

6. Time and Extent

FDA and industry discussed FDA's time and extent concept, including FDA's interpretation of what would constitute material time or material extent. FDA was not comfortable introducing prescription drugs as OTC drugs through the monograph process without some real-world experience of the drug's nonprescription use. Industry wanted more flexibility to introduce new drugs through the OTC monograph pathway without the data requirements needed for NDAs.

7. Sunscreens

Industry was dissatisfied with the TEA process, particularly as it applied to sunscreen ingredients. Manufacturers had submitted TEAs for several sunscreen ingredients, but by 2014 FDA had not completed review of any applications. Further, industry wanted sunscreens marketed in compliance with the stayed sunscreen final monograph to be allowed on the market while FDA completed its evaluation of sunscreen products. Industry had disagreed with some of the data requirements outlined in FDA's guidance on safety and effectiveness data[230] and wanted to ensure that current sunscreen products could continue to remain on the market.

One coalition of industry and other stakeholders, the PASS Coalition, wanted to ensure that any changes to the monograph program would not disadvantage companies with existing applications under the SIA. The PASS Coalition wanted some of the major benefits to manufacturers under the OTC monograph reform, such as exclusivity and confidential meetings, to accrue to manufacturers with pending submissions under

---

[229] This language was eventually incorporated in legislation that passed under the CARES Act. *See* FDCA § 505G(c)(3)(B).

[230] *See* U.S. FOOD & DRUG ADMIN., GUIDANCE, NONPRESCRIPTION SUNSCREEN DRUG PRODUCTS – SAFETY AND EFFECTIVENESS DATA (Nov. 2016).

the SIA. On the other hand, if sponsors of drugs with existing SIA orders wanted to switch to the administrative order pathway, members should not have to start from the beginning and submit a new, duplicative request to FDA.

8. User Fees and User Fee Goals

FDA clearly articulated a need for user fees to fund the OTC monograph program. Industry agreed with the need for user fees in theory but wanted to ensure that the user fees would be attached to FDA commitments, particularly commitments to timelines through the administrative order process. Discussions around user fees centered around the total amount, allocation of user fees, and prioritization for user fee spending.

In summer 2016 into early 2017, FDA and industry held a series of meetings to discuss aspects of what would become the Goals Letter. FDA and industry largely completed discussions within a two-week period in December 2016.[231] The key discussion areas related to timelines, OTC monograph reform activities, and FDA goals for implementing OTC monograph reform. Industry wanted shorter timelines for FDA review of changes to a monograph and commitments from FDA as early as possible after enactment of OTC monograph legislation. FDA wanted time to build the program, including hiring and training new employees, developing new IT infrastructure to handle OTC monograph reform program requirements, and developing guidance to implement the program. Industry and FDA also discussed the timelines associated with OTC monograph order requests (OMORs). FDA wanted sufficient time to review, develop, and address comments associated with each OMOR and proposed administrative order. Industry wanted shorter timelines for some types of OMORS. Some requests for changes (e.g., changing an ingredient name to align with United States Pharmacopeia (USP)) would be minor or technical and should not take the same amount of time as more substantive administrative orders (e.g., adding an active ingredient to a monograph). Goals letter timelines and commitments should reflect the variety of OMORs FDA could receive.

The second key area of discussion focused on the amount of user fees needed to fund the program. Most of industry agreed to calculate annual user fees based on the total amount of fees needed, divided by the number of OTC monograph facilities. Some contract manufacturers did not feel that they should pay the same amount as branded or private label manufacturers. FDA and industry also discussed whether there should be two tiers of user fees for requests to changes to administrative orders. As with timelines, industry believed that requests for minor or technical changes to a monograph should not cost the same amount as requests for more time-consuming changes. FDA wanted to ensure that it could meet user fee commitments. If certain timelines would be shorter, FDA wanted to specify exactly what types of changes would be subject to shorter timelines.

---

[231] U.S. FOOD & DRUG ADMIN., FDA AND INDUSTRY DISCUSSIONS, MINUTES OF MEETINGS BETWEEN FDA AND REGULATED INDUSTRY (June 5, 2017), https://www.fda.gov/industry/over-counter-monograph-user-fee-program-omufa/fda-and-industry-discussions [https://perma.cc/C57C-LJGQ].

D. Consensus Forms[232]

1. Draft Legislation

The first drafts of OTC monograph legislation emerged in 2015. Discussions between FDA, industry, and with members of Congress continued through 2016 to build consensus on the overall framework for OTC monograph reform. By mid-2016, the contours of OTC monograph reform legislation took shape to resemble the legislation eventually enacted under the CARES Act.

The draft legislation would change the regulatory status of drugs currently marketed under the OTC monograph system by "deeming" categories of products to have certain regulatory statuses. A drug that is in category I in a final monograph or TFM would be deemed GRASE and not misbranded. Drugs that are in category III under a TFM or category I in an ANPR would be permitted to remain on the market but would not be deemed GRASE. Drugs that are category II in TFMs must be removed from the market within 180 days of enactment.

The administrative order process would replace notice-and-comment rulemaking and would establish the conditions of use for OTC monograph drugs. There would be three procedures for administrative orders. FDA-initiated orders, those proposed by FDA under the ordinary procedure, would entail public notice, opportunity for comment, a dispute resolution procedure, an opportunity for an administrative hearing, and an opportunity for judicial review. Expedited orders are permitted when drugs are deemed to present "an imminent hazard to the public health" or when FDA makes changes to labeling that are "reasonably expected to mitigate a significant or unreasonable risk of a serious adverse event associated with use of the drug."[233] Industry-initiated proceedings will be based on submissions by sponsors seeking approval of new active ingredients, new dosage forms of existing acting ingredients, or other changes in currently marketed products. As with FDA-initiated orders, there would be an opportunity for public comment, dispute resolution, an administrative hearing, and judicial review.

Consensus legislation would also include provisions to allow manufacturers to make innovations for drugs marketed under the new OTC monograph system. While FDA and industry discussed that sponsors could receive a period of market exclusivity for industry-initiated orders in certain circumstances, the exact period was not discussed. FDA and industry also agreed on a procedure under which minor changes in dosage forms could be implemented without approval of administrative orders, provided that manufacturers carried out specified studies, which would be available to FDA on request, and notify the agency when changes are implemented.

There were also provisions related to increased communications between FDA and the public on the status of administrative orders and administrative order requests. OTC monograph reform would explicitly address the confidentiality of information submitted to FDA so that trade secret or confidential commercial information would remain exempt from public disclosure unless the requestor consents to disclosure. Sponsors could request meetings with FDA to support submissions or discuss other matters relevant to regulation of OTC monograph drugs. In response to industry

---

[232] Much of the discussion in this section comes from the authors' firsthand knowledge of preliminary discussions between FDA, industry, and the Hill.

[233] This language was eventually incorporated in legislation that passed under the CARES Act. *See* FDCA § 505G(b)(4).

concerns about non-finalized monographs, FDA agreed to establish, maintain, update, and make publicly available administrative orders issued, including a list of all FDA-initiated orders proposed and under development.

2. User Fees Goals Letter

By the end of 2016, consensus emerged on almost all of the major elements of a Goals Letter for the OTC Monograph User Fee Program, with wrap-up meetings in early 2017. The Goals Letter set out the timelines and goals associated with aspects of OTC monograph reform and the assumptions underpinning those goals.[234] FDA and industry did not discuss any changes to the Goals Letters after it was published in the spring of 2017.

The performance goals associated with OTC monograph reform assumed that FDA's first few years would be dedicated to hiring and building infrastructure needed to implement OTC monograph reform.[235] Most performance goals associated with industry-submitted requests for administrative orders and meeting requests would not begin until four years after the enactment of OTC monograph reform.[236] For example, FDA anticipated issuing the proposed administrative order and draft guidance pair for minor changes to solid oral dosage forms by the fifth year after enactment of OTC monograph reform.

The Goals Letter also set out timelines for industry-initiated requests for monograph actions. The Goals Letter laid out two types of industry-initiated administrative order requests. Tier One Innovations were any requests for changes that were not a "Tier Two Innovation." Tier Two Innovations are limited to requests for 1) reordering of existing information in the Drug Facts label; 2) standardization of the concentration or dose of a specific finalized ingredient within a particular finalized monograph; 3) an ingredient nomenclature change to align with nomenclature of a standards-setting organization; 4) addition of an interchangeable term; 5) modification to an existing Directions for Use; 6) addition of information in the "Other Information" section of Drug Facts labeling; and 7) other items that may be added at a later date.[237]

The timelines for requests that were Tier One Innovations were two months longer than requests for Tier Two Innovations. The timelines for specified safety changes to OTC monographs were even shorter. Specified safety changes are those intended to add or strengthen 1) a contraindication, warning, precaution, or adverse reaction; 2) a statement about risk associated with misuse or abuse; and 3) an instruction about dosage and administration that was intended to increase the safe use of the monograph drug product.[238]

The Goals Letter described classified meetings between industry and FDA and set timelines for when FDA would respond to each meeting request and when the meeting would occur. The structure for meetings and meeting requests was similar to those described in goals letters for other user fee programs.

---

[234] *See* GOALS LETTER, *supra* note 219, at 4.

[235] GOALS LETTER, *supra* note 219, at 4–8.

[236] GOALS LETTER, *supra* note 219, at 31.

[237] GOALS LETTER, *supra* note 219, at 10.

[238] GOALS LETTER, *supra* note 219, at 23.

IV. PROPOSED LEGISLATION AND OTHER DEVELOPMENTS

A. 115th Congress, First Session (2017)

During the 115th Congress, Republicans and Democrats in the House and Senate began formally debating OTC monograph reform. The overall contours of OTC monograph reform had bipartisan support, but Congress had not yet released legislative text at the beginning of 2017. That said, trade press reported that members in the House and Senate hoped to attach the bipartisan bill to must-pass prescription drug user fee legislation in the fall of 2017.[239] Supporters of OTC monograph reform had also hoped that the bill would be included in the pending FDA user fee reauthorization package.

1. Senate Discussion Draft

On May 10, 2017, Senators Johnny Isakson (R-GA) and Bob Casey (D-PA) published the first discussion draft of OTC monograph reform legislation during the Senate Health, Education, Labor, and Pension (HELP) Committee's user fee markup. Although the text was a discussion draft, stakeholders understood the bill represented the consensus between different parties on the OTC monograph reform.

In introducing the discussion draft, Sen. Isakson stated that reform should "bring about vital reforms to increase the responsiveness and innovation of OTC medicines and provide necessary resources to FDA. We are lagging as a nation in many over-the-counter drugs, which are operative and working overseas which are not approved in America because of an antiquated system for dealing with them."[240] Although Sen. Isakson did not attach the bill as an amendment to must-pass user fee legislation for prescription drugs, he hoped to attach the bill to the package at a later point.

The Senate Discussion Draft encapsulated the large majority of the structure and concepts for OTC monograph reform that was eventually enacted under the CARES Act. That said, the Senate Discussion Draft differed from the final version in notable ways. First, the draft did not include language addressing whether FDA could change requirements for packaging through the expedited administrative order process. Instead, the draft included only language clarifying that an interim final order issued under the safety labeling changes provision "with respect to the labeling of a drug may provide for new warnings and other information required for safe use of the drug."[241]

Second, the exclusivity section, titled "*product differentiation*," would have provided two years of exclusivity for a new OTC monograph drug.[242] The Senate Discussion Draft would have provided six months more exclusivity than in the CARES Act, but in practice, manufacturers likely would have lost a significant portion of the exclusivity period. Requiring that exclusivity begin on "the date on which the order is issued" provided manufacturers no flexibility to determine the date that exclusivity would begin.[243] Manufacturers would have lost exclusivity as they developed, tested,

---

[239] Beth Wang, *Isakson Hopes to Attach OTC Fees, Exclusivity to Final User Fee Package*, INSIDE HEALTH POL'Y (May 11, 2017).

[240] *Id.*

[241] SENATE DISCUSSION DRAFT, 115TH CONG. at 22 (May 10, 2017) (on file with FOOD & DRUG L.J.).

[242] *Id.* at 28.

[243] *Id.*

and manufactured their products after FDA issued the administrative order but before consumers could access the product. Manufacturers could not begin developing and manufacturing the new products before FDA issued a final administrative order unless they were willing to do so at risk. Further, the seasonality of many OTC monograph products (e.g., cough/cold products) would further erode exclusivity if FDA's timing in issuing a final administrative order did not match annual planning timelines for retail.

Third, the Senate Discussion Draft had limited provisions harmonizing OTC monograph reform with the SIA. The draft included a provision that would have required sunscreen monograph drugs to comply with the requirements in the stayed sunscreen monograph, except that effectiveness and labeling requirements would be those in 21 C.F.R. § 201.327. There were a few provisions that sought to harmonize OTC monograph reform with the SIA. The Senate Discussion Draft would have transformed "any proposed sunscreen orders issued . . . prior to the date of enactment of this Act" into "proposed administrative orders," and, presumably, these orders would have been finalized under section 505G's administrative order procedure.[244] The Senate Discussion Draft did not sunset the SIA, so the SIA would have been left intact as a parallel regulatory pathway.

A few other key provisions did not appear in the initial Senate Discussion Draft. Unlike the CARES Act, the Senate Discussion Draft did not exclude homeopathic drugs from the monograph reform system. Further, the Senate Discussion Draft would have regulated all nonprescription drugs not described in section 505G as "new drugs," even if these drugs had been marketed before enactment. The draft would have had fewer confidentiality protections for manufacturers. For example, FDA was required to publish a summary of "any meeting" held under section 505G and did not specify "raw data sets" as information FDA would keep confidential.[245]

2. House Discussion Draft

The House did not include OTC monograph reform in the user fee package that passed on July 12, 2017. Instead, the House began debating OTC monograph reform in earnest in the fall of 2017. On September 11, 2017, the House Energy and Commerce (E&C) Committee released a discussion draft of an OTC monograph reform bill ahead of a Health Subcommittee hearing on the topic.[246] Reps. Michael Burgess (R-TX), Gene Green (D-TX), Brett Guthrie (R-KY), Diana DeGette (D-CO), Bob Latta (R-OH), and Debbie Dingell (D-MI) sponsored the discussion draft.[247] Rep. Latta was the lead author of the draft but had closely worked with the other sponsors in drafting and negotiating the text.[248]

As with the Senate Discussion Draft, the House Discussion Draft was almost substantively identical to the provisions enacted under the CARES Act. There were a few notable differences between this draft and the Senate Discussion Draft, as well as the version of the bill enacted under the CARES Act. First, the House Discussion Draft introduced language explicitly describing what administrative order procedures could

---

[244] *Id.* at 69.

[245] *Id.* at 39.

[246] HOUSE DISCUSSION DRAFT, 115TH CONG. at 1 (Sept. 11, 2017) (on file with FOOD & DRUG L.J.).

[247] *See 2017 House Hearing*, *supra* note 125, at 4 (statement of Rep. Gene Green).

[248] *See id.* at 7 (statement of Rep. Greg Walden).

change OTC monograph requirements for packaging of a drug. The House Discussion Draft stated that "[a]n administrative order issued under paragraph (2), (4), or (5) may include requirements for the packaging of a drug to encourage use in accordance with labeling. Such requirements may include unit dose packaging, requirements for products intended for use by children, and other appropriate requirements to prevent abuse or misuse, including protection against unsupervised ingestion."[249] The language diverged from the Senate Discussion Draft, which had not included a packaging provision. Unlike the eventually enacted bill, the House Discussion Draft would have allowed FDA to use its expedited administrative order process to make packaging changes to a monograph if the change would "reasonably expect[] to mitigate a significant or unreasonable risk of a serious adverse event associated with use of the drug."[250] If, for example, FDA had decided that unit dose packaging was required to mitigate abuse or misuse of an OTC drug, it could have done so under its expedited administrative order authorities, finalizing an administrative order without public comment.

Second, the House Discussion Draft added more robust provisions concerning the interaction between OTC monograph reform and the SIA. The House Discussion Draft added a provision that would have sunset the SIA by September 30, 2023.[251] Until then, the sponsor of a proposed sunscreen order could elect to continue to proceed under the SIA pathway or under the new administrative order pathway.[252] If the latter, the proposed sunscreen order would be deemed to be an OMOR that had been accepted for filing.[253] Sponsors deciding to proceed under the SIA pathway would have opportunities to have confidential meetings with FDA.[254] The House Discussion Draft did not include an exclusivity provision for sponsors deciding to proceed under the SIA.

The House Discussion Draft also included a more favorable exclusivity provision for industry. Like the Senate Discussion Draft, an OTC monograph drug that was the subject of a successful OMOR could receive two years of exclusivity, but exclusivity would begin "on the date the requestor may lawfully market such drugs pursuant to the order."[255] The language would provide more flexibility for the sponsor of an OTC drug to determine the date exclusivity begins. Under the FDCA, a person may not lawfully market a drug unless drug listing information is submitted for the drug.[256] The new language would permit sponsors to determine the beginning date of the exclusive marketing period on the date the sponsor submits updated drug listing information for the new product.

Finally, the House Discussion Draft made changes to the user fee structure compared to the Senate Discussion Draft. The House Discussion Draft included

---

[249] HOUSE DISCUSSION DRAFT, 115TH CONG. at 36 (Sept. 11, 2017) (on file with FOOD & DRUG L.J.).

[250] *Id.* at 21.

[251] *Id.* at 54.

[252] *Id.* at 50–51.

[253] *Id.* at 51.

[254] *Id.* at 53–54.

[255] *Id.* at 28.

[256] FDCA § 510(j).

special user fee provisions for "contract manufacturing organization facilities."[257] Contract manufacturer organization facilities would pay two-thirds the ordinary OTC monograph facility fee. The change in fee structure resulted from conversations between industry groups, particularly the Pharma & Biopharma Outsourcing Association (PBOA), which objected to paying the same amount of OTC monograph facility fees as manufacturers distributing their own, branded products or directly producing private label products.

3. Hearing

On September 13, 2017, the Subcommittee on Health of the House E&C Committee held a hearing on "Modernizing FDA's Regulation of Over-the-Counter Drugs." Director Woodcock testified on behalf of FDA in support of OTC monograph reform. Other witnesses testifying at the hearing were Scott Melville, the president and CEO of the CHPA; Kirsten Moore, project director of Pew Charitable Trust Healthcare Products; Michael Werner, on behalf of the PASS Coalition; Bridgette Jones, for the AAP; and Gil Roth, president of the PBOA.

Members and witnesses were generally supportive of OTC monograph reform and the legislative language. Testimony and member questions at this hearing focused on the following issues: 1) the ability of the OTC monograph system to respond to safety concerns related to OTC drugs; 2) FDA's resources under the OTC Drug Review; 3) sunscreens and the SIA; 4) pediatric issues related to OTC products; and 5) incentives to innovation, including exclusivity.

Rep. Latta began by asking Director Woodcock about FDA's authority to regulate safe packaging of OTC drugs. Rep. Latta asked whether the discussion draft provided FDA with sufficient authority to prevent unintended consequences through packaging. Director Woodcock responded that the language provided FDA with such authority.[258] Rep. Green asked Director Woodcock how the current regulatory process posed harm to patient safety. To emphasize the challenges associated with responding to safety concerns through the OTC Drug Review, Director Woodcock described FDA's experience in responding to serious skin reactions associated with acetaminophen. She stated that the agency could not modify the applicable regulation quickly, so it instead issued a drug safety communication.[259] Although most manufacturers voluntarily included a warning statement and the allergy alert for severe skin reactions, some had not voluntarily done so.

Subcommittee members emphasized the resource challenges FDA faced. Rep. Green asked Director Woodcock to "elaborate on how reform without user fees is utterly unworkable," and Woodcock explained that, currently, the agency's resources for OTC monograph drugs were "completely taken up by implementing the Sunscreen Innovation Act."[260] Rep. Barton questioned why FDA had not discussed the challenges associated with OTC monograph drugs earlier and wanted to hold FDA to a timeline for when it could finish finalizing the monographs. Director Woodcock thought that a reasonable timeline to approve the monographs would be "two years," though she

---

[257] HOUSE DISCUSSION DRAFT, 115TH CONG. at 63–64 (Sept. 11, 2017) (on file with FOOD & DRUG L.J.).

[258] *2017 House Hearing*, *supra* note 125, at 69 (statement of Rep. Bob Latta).

[259] *Id.* at 70 (statement of Janet Woodcock, CDER Director, FDA).

[260] *Id.* at 71 (statement of Rep. Alexander Green).

noted that FDA wasn't "going to be able to do every single one at the same time in 2 years."[261]

Rep. Dingell and other members questioned how OTC monograph reform would affect sunscreens and interact with the SIA. Members asked about the "holdup" in approving sunscreen ingredients, and Rep. Dingell was concerned that Americans still had difficulty accessing sunscreen products that had been safely used for decades overseas.[262] Rep. Guthrie asked how OTC monograph reform would impact sunscreens, and Mr. Werner from the PASS Coalition replied that the "new over-the-counter process has to be flexible enough to accommodate sunscreens."[263] Mr. Werner believed that "the bill's draft legislation" provides another way to demonstrate safety and efficacy other than the NDA approval process, which was needed for sunscreens.[264]

Rep. Butterfield questioned Director Woodcock about the safety concerns related to pediatrics and OTC medicines. Director Woodcock explained that starting in the late 1990s, more people became aware that children were not tiny adults, but for OTC monograph drugs, "particularly, say, the cough and cold, and some of the other medicines," the agency was examining what was appropriate for children.[265] Director Woodcock explained how, for pediatric cough and cold medications, the monograph statements did not fully reflect the most updated information.[266] Director Woodcock also noted that it would work with the Consumer Product Safety Commission (CPSC) on packaging to make sure it was aware of anything FDA wanted to propose on packaging.[267]

The hearing also discussed exclusivity under OTC monograph reform. Rep. Green asked witnesses what Congress should consider to ensure a proper balance between innovation and public health. Ms. Moore from the Pew Charitable Trusts thought a two-year period represented "really well thought-through compromise on the part of a lot of parties" and struck the right balance between spurring innovation and improving the public health.[268] Mr. Melville from CHPA discussed the investment it would take to produce innovative products and how, if there were no exclusivity, there could be a private label of that product on the market the day after FDA allowed the innovative product on the market.[269]

B. 115th Congress, Second Session (2018)

At the beginning of 2018, lawmakers in the House and Senate hoped to pass OTC monograph reform along with must-pass legislation in reauthorization of the Animal

---

[261] *Id.* at 73 (statement of Janet Woodcock, CDER Director, FDA).

[262] *Id.* at 90 (statement of Rep. Debbie Dingell).

[263] *Id.* at 132 (statement of Michael Werner, PASS Coalition).

[264] *Id.* at 133 (statement of Michael Werner, PASS Coalition).

[265] *Id.* at 76 (statement of Janet Woodcock, CDER Director, FDA).

[266] *Id.* at 82 (statement of Janet Woodcock, CDER Director, FDA).

[267] *Id.* at 87 (statement of Janet Woodcock, CDER Director, FDA).

[268] *Id.* at 133–34 (statement of Kristen Moore, Pew Charitable Trusts).

[269] *Id.* at 134 (statement of Scott Melville, President and CEO, CHPA).

Drug User Fee Act. The House passed OTC monograph reform legislation in July 2018, but the bill failed to pass in the Senate.[270]

1. H.R. 5333

On January 12, 2018, Rep. Latta introduced H.R. 5333, the "Over-the-Counter Monograph Safety, Innovation, and Reform Act of 2018." Substantively, the bill was almost identical to the House Discussion Draft, except for a few changes. First, the packaging provision had been amended to state that "[a]n administrative order issued under paragraph (2), (4)(A), or (5) may include requirements for the packaging of a drug."[271] Excluding section (4)(B) from the packaging provision would have prohibited FDA from requiring packaging changes for OTC monograph drugs through the expedited safety labeling changes procedure. H.R. 5333 also included a section on pediatric cough/cold medicines, something that AAP had pushed for.[272] The new provision required FDA to submit a letter describing the agency's progress on the cough and cold monograph to the House E&C Committee and the Senate HELP Committee.

On January 17, 2018, the Subcommittee on Health of the House E&C Committee debated and marked up H.R. 5333. The subcommittee expressed bipartisan support for OTC monograph reform and passed H.R. 5333 by voice vote. However, the markup was not without debate, and exclusivity emerged as a contentious subject.

During the markup, Reps. Jan Schakowsky (D-IL) and Pallone argued that two-year exclusivity would be too long. Rep. Schakowsky introduced an amendment she later withdrew, which would have removed the exclusivity provision and argued that the subcommittee should "deny another monopoly to drug companies."[273] Rep. Pallone introduced an amendment, which was defeated, that would have shortened exclusivity to six months. Rep. Pallone did not believe exclusivity was necessary to incentivize innovation and criticized industry for "demanding exclusivity in exchange for paying the user fees." Rep. Pallone believed that two-year exclusivity would be "arbitrary and overlong," and "[i]t's not clear at all that you need exclusivity, certainly not for this long a period."[274] Not all Democratic members agreed. Rep. Anna Eshoo (D-CA) asked bill sponsors how they agreed on twenty-four months, while Rep. Diana DeGette (D-CO) acknowledged "it's difficult to see what the sweet spot on exclusivity is" but thought that six months was too short.[275]

Rep. Latta, the bill's lead sponsor, defended two-year exclusivity, arguing that the period "strikes that right balance for incentivizing new and innovative products to reach the market."[276] Industry defended the twenty-four-month period in a written statement, noting practical concerns associated with OTC distribution. CHPA stated

---

[270] *See* Bob Latta, Press Release: *U.S. House Passes Latta-authored Bill to Modernize and Reform Over-the-Counter Monograph System* (July 16, 2018).

[271] H.R. 5333, 115th Cong. § 101 (2018).

[272] Beth Wang, *Bipartisan OTC User Fee, Monograph Reform Bill Moves to Full E&C Committee*, INSIDE HEALTH POL'Y (Jan. 18, 2018) [hereinafter Wang, *Bipartisan OTC User Fee*].

[273] Malcolm Spicer, *OTC Monograph Reform Momentum Carries Potential Exclusivity Snag*, PINK SHEET (Jan. 17, 2018).

[274] *Id.*

[275] Wang, *Bipartisan OTC User Fee*, *supra* note 272.

[276] Spicer, *supra* note 273.

that a "new product takes several months for scale-up and labeling, and to get the new product on the shelf, companies must be included in retailers' annual planning cycles. If a manufacturer misses that planning cycle, they've missed a year."[277]

On March 19, 2018, Rep. Latta reintroduced H.R. 5333, reflecting a compromise between House Democrats and Republicans on exclusivity. The new bill was substantively the same as the version of the bill introduced in January, except that the exclusivity period was shortened to "a period of 18 months following the effective date of such final order."[278] Although the period of exclusivity was only six months shorter, the change would have shortened the period of exclusivity by more than six months in practice. As discussed in Section IV.A.1, having exclusivity begin on the date of the final administrative order provides no flexibility for industry to determine the date the exclusivity period begins. Exclusivity would likely begin before consumers would be able to access the new products and further decrease incentives for manufacturers to innovate on OTC monograph drugs through the OMOR process.

On May 9, 2018, the House E&C Committee marked up the new version of H.R. 5333. Exclusivity remained a topic of debate at the full committee markup. Rep. Pallone argued against including exclusivity in the legislation and argued that Congress should first pass OTC monograph reform and then assess whether exclusivity would be needed later down the road.[279] Acknowledging that lawmakers had tried to reach a compromise, Rep. Pallone offered an amendment to reduce the exclusivity period from eighteen months to twelve months.[280] The Democratic sponsors of the bill, Reps. DeGette, Green, and Dingell, believed that exclusivity was necessary and argued that exclusivity for OTC products was not the same as exclusivity for prescription products because, even with exclusivity, consumers could still access other, store-brand OTC products. Rep. DeGette stated that "[e]verybody agrees we need to have some exclusivity, but nobody agrees what the amount should be in this context. It's not the same type of exclusivity that we see with prescription drugs. . . . The Senate bill has 24 months as [did this] underlying bill and so we sort of compromised at 18 months, but we don't even know if that is the sweet spot to encourage innovation but also keep consumer costs low."[281] Rep. Burgess was more direct, stating that "reducing the period of exclusivity down to 12 months would jeopardize the legislation."[282]

Ultimately, the House Committee rejected the Pallone amendment by a party-line vote of 30-24.[283] H.R. 5333 passed by voice vote with an amendment from Rep. Latta, requiring the GAO to conduct a study after the bill's enactment to assess the impact of exclusivity, including the impact on consumer access. On July 16, 2018, Rep. Latta

---

[277] Wang, *Bipartisan OTC User Fee*, *supra* note 272.

[278] H.R.5333, 115th Cong. § 101 (2018).

[279] Beth Wang, *OTC Drug Reform Bill Heads to House Floor as Lawmakers Debate Exclusivity,* INSIDE HEALTH POL'Y (May 9, 2018) [hereinafter Wang, *OTC Drug Reform Bill*].

[280] *Id.*

[281] *Id.*

[282] Malcolm Spicer, *OTC Monograph Legislation Clears Another Hurdle Despite Exclusivity Concerns*, PINK SHEET (May 9, 2018).

[283] Wang, *OTC Drug Reform Bill*, supra note 279.

moved to pass the bill by unanimous consent, and the bill passed.[284] At the time of passage, the House issued a report with additional views to accompany H.R. 5333. Although generally supportive of OTC monograph reform, Rep. Pallone questioned the inclusion of an eighteen-month exclusivity award in H.R. 5333.[285] Rep. Pallone thought exclusivity was not warranted until "evidence is presented that the industry-initiated innovation pathway has not been sufficient in incentivizing innovation in the OTC drug market."[286]

2. S. 2315

OTC monograph reform suffered a different fate in the Senate. Initially, momentum for OTC monograph reform mirrored momentum in the House. On January 17, 2018, Sen. Isakson (R-GA) and Sen. Casey (D-PA) introduced S. 2315, the "Over-the-Counter Drug Safety, Innovation, and Reform Act." S. 2315 was substantively very similar to the Senate Discussion Draft and H.R. 5333, with a few key differences.

As in the Senate Discussion Draft, S. 2315 would have provided two-year exclusivity for innovative products marketed under a sponsor-initiated administrative order. Unlike the Senate Discussion Draft, exclusivity would begin "on the date the requestor (or any licensees, assignees, or successors in interest of such requestor with respect to the subject of such request and listed under paragraph (5)) may lawfully market such drugs pursuant to the order."[287] S. 2315 adopted the language in the House Discussion Draft which, as discussed previously, would have provided sponsors more flexibility to determine when exclusivity would begin.

S. 2315 added language on packaging that reflects the final language as enacted under the CARES Act. An administrative ordered issued "under paragraph (3), (5)(A), or (6) may include requirements for the packaging of a drug, such as to promote use in accordance with labeling, unit dose packaging, or requirements to prevent accidental overdose or ingestion, misuse, or abuse, including by pediatric populations."[288] Like H.R. 5333, S. 2315 would prohibit FDA from requiring changes to OTC monograph drug packaging through the safety labeling changes expedited process but would allow FDA to require these changes through the normal administrative order process or expedited orders to respond to drugs that pose an imminent harm to the public health.[289] S. 2315 would have explicitly allowed FDA to require packaging changes "to prevent accidental overdose or ingestion, misuse, or abuse"—language that does not appear in the version enacted under the CARES Act.[290]

S. 2315 also added more robust provisions harmonizing OTC monograph reform and the SIA. S. 2315 included a new provision that would give sponsors of sunscreen ingredients approved under the SIA two-year exclusivity—the same exclusivity sponsors would have received if FDA determined their products were GRASE under

---

[284] Beth Wang, *House Passes OTC Monograph Reform Bill with 18 Months Exclusivity*, INSIDE HEALTH POL'Y (July 16, 2018).

[285] *Id.*

[286] H.R. REP. NO. 115-827, at 95 (2018).

[287] S. 2315, 115th Cong. § 101 (2018).

[288] *Id.*

[289] *Id.*

[290] *Id.*

the administrative order pathway.[291] S. 2315 would have also required FDA to issue a revised final administrative order on sunscreen products, effective no later than November 26, 2019.[292] Sen. Jack Reed (D-RI), who authored the SIA, was frustrated by FDA's progress on the SIA and pushed for this provision.

On April 24, 2020, the Senate HELP Committee held a markup on S.2315. The bill had bipartisan support, and the committee approved the bill by a vote of 22-1.[293] Unlike the markup of the bill in the House, the Senate did not debate the time period for exclusivity. Sen. Richard Burr (R-NC) was the sole vote against the bill. Sen. Burr did not give a reason for the "No" vote at the time, but it was widely understood that Sen. Burr opposed new user fee legislation in principle.[294] Without unanimous support from the Senate, the bill stalled on the Senate floor.

3. H.R. 7328

On December 19, 2018, the House re-introduced OTC monograph reform, paired with the Pandemic and All-Hazard Preparedness and Advancing Innovation Act of 2018 (H.R. 7328). Most of the bill related to pandemic preparedness, such as reauthorization of the Biomedical Advanced Research and Development Authority (BARDA), but OTC monograph reform was incorporated as part of the bill. The bill was the result of negotiations between Republican and Democratic House leadership.

The OTC monograph provisions in the bill were almost identical to H.R. 5333, except for certain important modifications. First, exclusivity for OTC monograph drugs would be "for a period of 18 months following the effective date of such final order and beginning on the date the requestor may lawfully market such drugs pursuant to the order."[295] This differed from H.R. 5333, which referenced the eighteen-month period, but exclusivity would have begun on the "effective date of such final order."[296] Unlike H.R. 5333, the exclusive marketing period would not begin until the date that the requestor may lawfully market the relevant product (i.e., the date the sponsor submits updated drug listing information for the new product), instead of the date the order becomes effective.[297]

H.R. 7328 also made a few additional changes to the SIA. First, sunscreen requestors under the SIA may request confidential meetings, but the meetings would not be subject to any timelines. More significantly, H.R. 7328 included a new provision that would have required FDA to issue a proposed sunscreen administrative order by May 28, 2019, issue the final administrative order no later than November 26, 2019, and effectuate the administrative order no later than November 26, 2020.[298]

H.R. 7328 passed the House on December 20, 2018, but OTC monograph reform did not pass the Senate. At the time, press reported that Sen. Richard Burr (R-NC) blocked OTC monograph reform "because he was frustrated with FDA's proposal to

---

[291] *Id.* at § 103.

[292] *Id.*

[293] Beth Wang, *Senate Panel Clears Bill Reforming FDA's OTC Drug Review Process*, INSIDE HEALTH POL'Y (Apr. 26, 2018).

[294] *Id.*

[295] H.R.7328, 115th Cong. § 1001 (2018).

[296] H.R.5333, 115th Cong. § 101 (2018).

[297] *Id.*

[298] *Id.*

ban e-cigarette flavors."[299] Sen. Burr had placed a "hold" on the bill to exert pressure on FDA to change its approach to restrict sales of flavored products, and, in retaliation, Sen. Isakson placed a hold on reauthorization of the Pandemic and All-Hazard Preparedness Act (PAHPA), for which Sen. Burr was the lead author.[300]

C. 116th Congress, First Session (2019)

The impasse on OTC monograph legislation continued into 2019. In 2019, both the House and Senate introduced legislation on OTC monograph reform, but the legislation ultimately failed to pass as a free-standing bill.

On January 8, 2019, the House again included OTC monograph reform with PAHPA, which was one of the first bills to pass the Democrat-controlled House.[301] The House passed H.R. 269, the Pandemic and All-Hazard Preparedness and Advancing Innovation Act of 2019, by a vote of 401-17, marking the third time the House passed monograph reform. H.R. 269 included the same OTC monograph reform provisions as in H.R. 7328. Rep. Pallone again provided remarks on the passage of OTC monograph reform:

The bill streamlines the review process for future monograph changes, allows for expedited safety label changes, and establishes a user fee program to provide sustainable resources to implement these reforms. These are critical changes that I am proud to support. While this is not a perfect bill, and still contains unnecessary and unwarranted exclusivity for over-the-counter drugs and sunscreens, reform of our over-the-counter drug program is long overdue.[302]

The Senate failed to act on H.R. 269 for the same reasons that it did not act on H.R. 7328. Instead, on May 16, 2019, the Senate passed the pandemic preparedness bill without OTC monograph reform.

On October 30, 2019, Sens. Isakson and Casey reintroduced an OTC monograph reform bill as S. 2740, the Over-the-Counter Monograph Safety, Innovation, and Reform Act of 2019. S. 2740 changed the exclusivity provision to mirror the provision passed earlier in 2019 by the House. Exclusivity would be for "a period of 18 months following the effective date of such final order and beginning on the date the requestor may lawfully market such drugs pursuant to the order."[303] The Senate HELP Committee passed the bill on October 31, 2019, and the Senate passed the bill 91-2, with only Sens. Burr and Rick Scott (R-FL) opposing. Burr reiterated his opposition to user fee programs. "When the drug industry first agreed to user fees in 1993, the fee to file a new drug application was $100,000," Burr said, "Today, that fee is $2.1 million. To that end, FDA has struggled to uphold its end of the bargain—falling behind in its commitment to hire the number of employees the agency needs to actually

---

[299] Beth Wang, *Senate Passes Pandemic Preparedness Bill Minus OTC Reform Language*, INSIDE HEALTH POL'Y (May 17, 2019).

[300] Michael McCaughan, *"Lame Duck" Congress Has High Stakes for Pharma Companies*, PINK SHEET (Nov. 29, 2018).

[301] H.R. 269, 116th Cong. (2019).

[302] 116 CONG. REC. H263 (daily ed. Jan. 8, 2019).

[303] S. 2740, 116th Cong. § 101 (2019).

review the applications that cost millions of dollars to file."[304] The Senate passed S. 2740 on December 10, 2019.

This time, the House did not pass OTC monograph reform as a free-standing bill. Rep. Latta and others reintroduced H.R. 3443 as a free-standing bill on June 24, 2019, but the bill failed to go through a committee markup or vote.

D. 116th Congress, Second Session (2020)

Congress's COVID-19 stimulus bill finally provided a vehicle for OTC monograph legislation's passage. On March 24, 2020, OTC monograph reform was added to an updated draft of the Coronavirus Aid, Relief, and Economic Security (CARES) Act, H.R. 748, the Senate's COVID-19 stimulus bill. This version of the bill was identical to the version passed in the Senate at the end of 2019. Three days later, on March 27, 2020, President Trump signed OTC monograph reform into law as part of the CARES Act. As part of the Congressional Record following the House passage of the CARES Act, Rep. Latta, the lead sponsor of OTC monograph reform in the House, included a statement of intent on select provisions within OTC monograph reform.

First, Rep. Latta's statements distinguished the data requirements to determine a drug is GRASE from the requirements necessary to approve a drug under the NDA. Quoting language in 21 C.F.R. § 330.10(a)(4), Rep. Latta emphasized three types of evidence that should help form the basis of a GRASE determination. First, the regulations "clearly recognize the importance of what is now termed 'real world evidence,' including evidence from marketing" in determining GRASE status.[305] Second, clinical studies to support GRASE will in most instances be in published scientific literature, and "[s]uch publications seldom, if ever, contain the same level of detail as the clinical study reports and data tabulations submitted in support of new drug applications, but it has long been understood that they may form the basis for determinations of general recognition of safety and effectiveness under the OTC monograph system."[306] Further, sources other than published scientific literature "including, for example, unpublished data from studies carried out by federal government agencies or other competent bodies" should also be considered by FDA in determining whether a drug is GRASE.[307] "It is our intent," Rep. Latta stated, "that the FDA should continue to apply these standards in making determinations of general recognition of safety and effectiveness under the monograph reform legislation."[308]

Rep. Latta then provided a "Statement of Intent as to [the] Minor Changes Provision."[309] First, sponsors may submit OMORs to make minor changes in dosage form.[310] Second, in appropriate cases, sponsors can utilize the minor changes provision to make minor changes in dosage forms without prior approval from FDA.[311]

---

[304] Beth Wang, *Senate Passes OTC Monograph Reform Legislation*, INSIDE HEALTH POL'Y (Dec. 10, 2019).

[305] 166 CONG. REC. H1863-64 (daily ed. Mar. 27, 2020) (statement of Rep. Latta).

[306] *Id. at 1864.*

[307] *Id.*

[308] *Id.*

[309] *Id.*

[310] *Id.*

[311] *Id.*

However, neither an OMOR nor the minor changes provision should be required for changes otherwise permitted:

> Thus, changes in excipients or other inactive ingredients and similar aspects of formulation of monograph OTC drug products will be permitted without prior approval provided they are fully consistent with requirements of applicable monographs or administrative orders and with general requirements for OTC monograph drugs, including, among other things, requirements for the use of suitable inactive ingredients which are safe in the amounts administered and do not interfere with the effectiveness of the preparation or with suitable tests of assays.[312]

When such changes occur, sponsors will need to submit updated drug listing information, as was true under the OTC Drug Review.[313]

Rep. Latta also discussed what information FDA must consider in evaluating changes under the minor dosage changes provision. The bill "directs FDA to issue administrative orders and guidances describing the types of changes that can be made without prior approval and the data that manufacturers should have on file."[314] In issuing the administrative order and guidance, FDA should "take account of standard procedures and practices for evaluating the quality of drug products, including applicable provisions of the United States Pharmacopeia/National Formulary, as well as special needs of populations, including children."[315] Likewise, FDA should consider and take into account relevant public standards when determining what information manufacturers should have on file for minor dosage form changes.

Examples of the standards that FDA should take into account include the monographs and other provisions of United States Pharmacopeia/National Formulary and guidelines issued by the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). FDA is a major stakeholder in both organizations, and it is appropriate that any administrative orders it adopts should take account of relevant requirements issued by them.[316]

Finally, Rep. Latta's statement clarified the content of administrative orders. It is intended that administrative orders will be similar to the monographs FDA issued under OTC monograph review. "That is, they will contain provisions concerning active ingredients, dosages and dosage forms, and instructions for safe use of the products to which they apply and where appropriate, other conditions required to assure safety and effectiveness."[317] Therefore, as was true under the OTC Drug Review, "labels and labeling for nonprescription drugs may contain additional information, including brand names, promotional statements, and other information, provided that any such information is truthful and non-misleading."[318]

---

[312] *Id.*

[313] *See id.*

[314] *Id.*

[315] *Id.*

[316] *Id.*

[317] *Id.*

[318] *Id.*

V. OTC MONOGRAPH REFORM UNDER THE CARES ACT

This section describes the current law, as revised by the CARES Act. This section also describes how the current law intersects with the Goals Letter negotiated between industry and FDA, which establishes timeframes for reviewing and acting on industry-initiated submissions, response times for industry-requested meetings, and other administrative actions.

A. Regulatory Status of OTC Drugs

1. Scope

Under current law, section 505G broadly applies to "nonprescription drugs marketed without an approved drug application under section 505" of the FDCA.[319] The term "nonprescription drug" means "a drug not subject to the requirements of section 503(b)(1)" of the FDCA, which can be dispensed only upon prescription of a medical practitioner.[320]

Certain nonprescription drugs marketed without an approved drug application are explicitly excluded from regulation under section 505G of the FDCA. A drug subject to an investigational new drug application (IND) is not subject to section 505G.[321] Homeopathic drugs, as described in 37 Fed. Reg. 9466, paragraph 25, are also excluded from regulation under section 505G. That paragraph states:

> The American Institute of Homeopathy requested that homeopathic medicines be excluded from the OTC review. Because of the uniqueness of homeopathic medicine, the Commissioner has decided to exclude homeopathic drugs from this OTC drug review and to review them as a separate category at a later time after the present OTC drug review is complete.[322]

Homeopathic drugs will continue to be regulated the same as before enactment of the CARES Act. FDA would continue to regulate homeopathic drugs under enforcement discretion, outlined in the agency's draft guidance, "Drug Products Labeled as Homeopathic."[323] Manufacturers of homeopathic drugs are not subject to OTC monograph user fees if they do not otherwise manufacturer OTC monograph drugs.

2. Regulatory Status of Drugs with Active Ingredients Under the OTC Drug Review

Section 505G(a) changes the regulatory status of OTC monograph drugs on the date of enactment of the CARES Act. These changes became effective on March 27, 2020 and do not require FDA action to effectuate the provisions.

---

[319] FDCA § 505G(a).

[320] FDCA § 505G(q)(1).

[321] FDCA § 505G(n).

[322] Procedures for Classification of Over-the-Counter Drugs, 37 Fed. Reg. 9464, 9466 (May 11, 1972).

[323] U.S. FOOD & DRUG ADMIN., DRAFT GUIDANCE, DRUG PRODUCTS LABELED AS HOMEOPATHIC (Oct. 2019), https://www.fda.gov/media/131978/download [perma.cc/7GYS-NQ38].

A drug is deemed to be GRASE, not a new drug, and is a nonprescription drug if it 1) contains an active ingredient that is GRASE in a final monograph or is classified as category I "for safety and effectiveness" in a TFM; 2) complies with the relevant monograph and the rules of general applicability for OTC monograph drugs; and 3) is in a dosage form that, immediately prior to the enactment of the CARES Act, was used to a material extent and for a material time, except as otherwise permitted under section 505G.[324] This last provision effectively changed the date of the material time and extent provision from May 11, 1972 to March 27, 2020, so that, for example, a dosage form introduced to the market during the intervening years could potentially meet the time and extent requirement. Section 505G(a)(1)(B) effectively finalizes the TFMs for drugs with category I active ingredients.

There are special provisions for drugs marketed under the stayed sunscreen monograph under 21 C.F.R. Part 352. Sunscreen drug products will be GRASE, not a new drug, and OTC if they comply with the applicable requirements of 21 C.F.R. Part 352, as published on May 21, 1999, except that the requirements governing effectiveness and labeling will be those in 21 C.F.R. § 201.327.[325] FDA had issued a proposed rule for OTC sunscreen drug products on February 26, 2019, and that rule, if finalized, would have proposed to set the maximum label SPF at 60+ and cap the actual SPF for such products at 80.[326] The CARES Act explicitly states that sunscreen drug products will not be governed by FDA's 2019 proposed rule and will instead be governed by 21 C.F.R. Part 352 and the labeling requirements in 21 C.F.R. § 201.327. If FDA wishes to finalize its 2019 proposed rule, it will need to reissue its proposal as a proposed administrative order and then follow the procedures under section 505G(b) to issue a final administrative order.

Certain OTC drugs are not GRASE but can continue to be marketed under the existing monograph before FDA makes a final GRASE determination. A drug can continue to be marketed as an OTC drug without an approved NDA if it is not described in paragraph (1), (2), or (4) and contains an active ingredient that is classified as category III for safety or effectiveness in the most recently applicable TFM or classified as category I in the most recently applicable ANPR.[327] As with drugs with category I active ingredients in a TFM, these drugs must also comply with the relevant monograph and the rules of general applicability for OTC monograph drugs.[328] Further, the drug must also be in a dosage form that, "immediately prior to the enactment of the [CARES Act], has been used to a material extent and for a material time under section 201(p)(2)."[329] Unlike GRASE drugs, drugs with active ingredients in category III in a TFM or category I in an ANPR are not eligible to rely on the "minor changes" provision to introduce new dosage forms into the market.[330]

Other OTC drugs may no longer be marketed. A drug that contains an active ingredient classified as category II for "safety or effectiveness under a tentative final monograph or that is subject to a determination to be not generally recognized as safe

---

[324] FDCA § 505G(a).

[325] FDCA § 505G(a)(2).

[326] 84 Fed. Reg. 6204, 6206 (Feb. 26, 2019).

[327] FDCA § 505G(a)(3).

[328] *Id.*

[329] FDCA § 505G(a)(3)(A)(iii).

[330] FDCA § 505G(c).

and effective in a proposed rule that is the most recently applicable proposal issued" under 21 C.F.R. part 330 will be deemed a "new drug" and cannot be marketed without an approved NDA on September 23, 2020.[331] FDA can extend the period during which these drugs can be marketed if FDA "determines that it is in the interest of public health to extend the period during which the drug may be marketed without such an approved new drug application."[332] FDA does not need to issue an administrative order or notice for this provision to go into effect.

These provisions anticipate how FDA would regulate drugs with different category classifications for safety and effectiveness. A drug must be classified as category I for safety *and* effectiveness in a TFM in order to be considered GRASE.[333] A drug classified in category I for safety but category III for effectiveness in a TFM could still be marketed without an NDA but would not be deemed GRASE.[334] A drug classified in category II for safety and category III for effectiveness in a TFM could no longer be marketed on September 23, 2020 because it would be governed by section 505G(a)(4), which covers drugs "classified in category II for safety *or* effectiveness."[335]

Drugs that FDA has determined not to be GRASE under the procedures in 21 C.F.R. Part 330 are deemed new drugs, misbranded, and subject to the requirement of an approved NDA. Further, a drug is deemed to be a new drug if it is intended for OTC use and not described in any of the other paragraphs of FDCA § 505G(a). That said, section 505G should not affect the treatment of drugs that are marketed without an NDA as of March 27, 2020 and that do not fall within one of the first five paragraphs in subsection (a) and that are not the subject of an order issued under the section. In other words, drugs that were on the market as of March 27, 2020 and do not contain an ingredient classified in a monograph, TFM, or ANPR and are not the subject of an administrative order will continue with the same regulatory status as before March 27, 2020. If, for example, these products were marketed under enforcement discretion before the CARES Act, these products could continue to be marketed with the risk that FDA could enforce against these products if its enforcement policy changes.

B. Administrative Order Process

Section 505G(b) establishes a new process for drugs marketed under OTC monographs. Section 505G(b) allows FDA to issue monographs through "administrative orders" rather than through notice-and-comment rulemaking. With the enactment of the CARES Act, all final monographs and TFMs for category I active ingredients are deemed to be administrative orders.[336] All other TFMs and ANPRs will not automatically be deemed to be administrative orders but will continue to exist in the Federal Register until FDA issues a proposed administrative order to finalize these monographs.

Section 505G(b) envisions three pathways for the issuance of administrative orders: 1) FDA-initiated administrative orders; 2) expedited FDA-initiated administrative

---

[331] FDCA § 505G(a)(4).

[332] *Id.*

[333] FDCA § 505G(a).

[334] *Id.*

[335] FDCA § 505G(a)(4).

[336] FDCA § 505G(b)(8).

orders; and 3) industry-initiated administrative orders. The timelines for finalizing administrative orders through each pathway can be found in the OTC Monograph User Fee Goals Letter and differs depending on which pathway is used to issue the administrative order. We discuss each pathway below.

1. FDA-Initiated Administrative Orders

Section 505(b)(2) allows FDA to issue, on its own initiative, administrative orders specifying the conditions under which an OTC drug is GRASE. These administrative orders may modify or finalize an existing monograph or propose a new monograph for a category of drugs. Section 505(b)(2) sets forth the procedures under which FDA can issue administrative orders in the ordinary course on its own initiative.

If FDA wants to change a monograph, FDA must issue a proposed administrative order. Before issuing the proposed administrative order, FDA must first "make reasonable efforts" to informally notify, no later than two business days before the proposed order, sponsors of drugs that would be affected and listed in FDA's registration and listing database.[337] FDA must provide a comment period of no less than forty-five calendar days to accept comments on the proposed order. There are special provisions if FDA issues a proposed order on its own initiative proposing to determine that a drug with an ingredient in category III in a TFM or category I in an ANPR is not GRASE.[338] In that instance, the proposed order must include notice of the data necessary to establish that the drug would be GRASE and the format for submissions by interested persons to prove that the drug is GRASE.[339] The comment period for such a proposed administrative order will be no less than 180 days.[340] FDA can issue a final administrative order after the statutorily mandated comment period.[341]

The final administrative order cannot take effect until the completion of procedural rights afforded to sponsors affected by the order. At the time FDA issues a final administrative order, sponsors of drugs that will be subject to the order can request formal dispute resolution up to the level of the CDER Director.[342] Sponsors must request formal dispute resolution forty-five calendar days after the issuance of the final order and within thirty calendar days of the prior decision.[343] The formal dispute resolution procedure and timelines will be very similar to the procedure for drugs under other user fee programs, as described in the guidance "Formal Dispute Resolution: Sponsor Appeals Above the Division Level."[344]

---

[337] FDCA § 505G(b)(2)(A).

[338] FDCA § 505G(b)(2)(B).

[339] *Id.*

[340] *Id.*

[341] *Id.*

[342] FDCA § 505G(b)(2).

[343] *Id.*

[344] The Formal Dispute Resolution Guidance lays out timelines for each level of the formal dispute resolution procedure. The deciding officer should provide an interim response or decision within thirty calendar days from receipt of accepted formal dispute resolution request (FDRR). If the initial response is transmitted by telephone, the deciding official will follow-up with a written confirmation within fourteen calendar days. An interim response can either request additional information or a meeting before making a decision on appeal. A request for clarifying information should be sent within thirty calendar days from receipt of the FDRR. If a meeting is needed, a meeting request should be sent within thirty calendar days from receipt of the sponsor's FDRR. Where a deciding official needs to discuss an FDRR with an advisory

Sponsors who completed the formal dispute resolution procedure would also have an opportunity for a hearing. These hearing procedures are not outlined in FDA's regulations but incorporate elements of existing FDA hearing procedures. For example, parties to a hearing will have the right to present testimony and cross-examine witnesses.[345] If multiple parties submit a request for a hearing, FDA may decide to consolidate these requests into a single hearing.[346] At the conclusion of the hearing, a presiding officer will issue a final decision on the issues presented at the hearing.[347] If a person disagrees with the final decision, the person would then have sixty days to seek judicial review.[348]

FDA's final administrative order and any final decision from the hearing would not take effect until at least the end of the sixty-day period to seek judicial review, and possibly much later.[349] For example, FDA could grant an administrative stay delaying the effectiveness of any administrative order while a sponsor seeks judicial review. A sponsor could also seek a stay from a district court. A court would evaluate the request based on the likelihood of success on the merits, irreparable harm in the absence of a stay, the balance of hardships, and the public interest.[350]

In certain circumstances, FDA can deny a hearing after the end of a dispute resolution procedure. FDA can deny a hearing when the order relates to a drug with active ingredients in category III in a TFM or category I in an ANPR for which no new safety data have been submitted since the publication of the most recent relevant determination.[351] FDA can also deny a hearing if it determines that there is "no genuine and substantial question of material fact."[352] In that case, the sponsor would have sixty days after the denial of a hearing to seek judicial review before the administrative order could take effect.[353]

2. Expedited FDA-Initiated Administrative Orders

FDA may use expedited procedures to issue an administrative order in special contexts.[354] Expedited orders can be issued in final form by FDA before an opportunity

committee, CDER will need to inform the requestor that the deciding official is seeking additional input thirty days from receipt of the FDRR. A sponsor can also request a meeting, including an advisory committee meeting, as part of the FDR process. U.S. FOOD & DRUG ADMIN., GUIDANCE, FORMAL DISPUTE RESOLUTION: SPONSOR APPEALS ABOVE THE DIVISION LEVEL (Nov. 2017) https://www.fda.gov/media/126910/download [https://perma.cc/3ZZB-BFAG].

345 FDCA § 505G(b)(3)(C)(iv).

346 FDCA § 505G(b)(3)(C)(ii).

347 FDCA § 505G(b)(3)(C)(v).

348 FDCA § 505G(b)(3)(D).

349 FDCA § 505G(b)(3)(C)(iv).

350 *See, e.g.*, Cigar Ass'n of Am. v. FDA, 317 F.Supp.3d 555, 560 (D.D.C 2018) (stating that to obtain an injunction pending appeal, the moving party "must establish [1] that he is likely to succeed on the merits, [2] that he is likely to suffer irreparable harm in the absence of preliminary relief, [3] that the balance of equities tips in his favor, and [4] that an injunction is in the public interest"); *see also* Winter v. NRDC, 555 U.S. 7, 20 (2008).

351 FDCA § 505G(b)(3)(B).

352 *Id.*

353 FDCA § 505G(b)(3)(D)(ii)(II).

354 FDCA § 505G(b)(4).

for comment, dispute resolution, and a hearing.[355] Under this procedure, FDA can issue an interim final administrative order no less than two days after it uses "reasonable efforts" to informally notify sponsors that would be affected by the order. The interim final order would take effect "on a date specified" by FDA.[356] After the interim final order, FDA would provide the public with opportunities for public comment, formal dispute resolution, and hearing, if applicable, potentially after the interim final order has already taken effect.

There are two situations where FDA can use the expedited procedure to issue an administrative order. First, FDA can use the expedited procedure when FDA has determined that "a drug, class of drugs, or combination of drugs" subject to section 505G "poses an imminent hazard to the public health."[357] The "imminent hazard" standard is the same standard for the suspension of an approval for an NDA.[358] FDA's regulations consider an "imminent hazard to the public health" to exist when a product or practice "pos[es] a significant threat of danger to health, creates a public health situation (1) that should be corrected immediately to prevent injury and (2) that should not be permitted to continue while a hearing or other formal proceeding is being held."[359] The Secretary of the United States Department of Health and Human Services (HHS) has rarely used the "imminent hazard" provision under section 505 of the FDCA to withdraw approval of an NDA.[360]

Second, FDA can use the expedited procedure when FDA determines "that a change in the labeling of a drug, class, of drugs, or combination of drugs . . . is reasonably expected to mitigate a significant or unreasonable risk of a serious adverse event associated with use of the drug."[361] The second type of change is limited to "labeling changes," which "may provide for new warnings and other information required for safe use of the drug."[362] However, FDA may not include requirements for "the packaging of a drug to encourage use in accordance with labeling" under the safety labeling changes provisions in section 505G(b)(4).[363] In other words, FDA could not use the expedited procedures to require manufacturers to change the packaging of a drug to unit dose packaging under the safety labeling standards. Changes to the packaging of a drug using expedited procedures are permissible if the drug presents an "imminent hazard to the public health."[364]

---

[355] *Id.*

[356] FDCA § 505G(b)(4)(C).

[357] FDCA § 505G(b)(4)(A)(i).

[358] FDCA § 505(e)(5).

[359] 21 C.F.R. § 2.5(a).

[360] To our knowledge, the Secretary of HHS has invoked the "imminent hazard" provision in section 505(e) of the FDCA only once when it suspended approval of NDAs for phenformin, a drug indicated for use in diabetes. FDA and HHS received evidence that phenformin can produce a fatal reaction known as lactic acidosis in some patients and that the cases of lactic acidosis had increased after the drug's approval. *See* 42 Fed. Reg. 40959, 40959 (Aug. 12, 1977) (describing the suspension of approval of NDAs for phenformin on July 25, 1977).

[361] FDCA § 505G(b)(4)(B)(i).

[362] FDCA § 505G(b)(4)(B)(ii).

[363] See FDCA § 505G(b)(7), which allows an administrative order under paragraphs (2), (4)(A), or (5) to include requirements for the packaging of a drug, such as unit dose packaging. This provision explicitly excludes paragraph (4)(B), pertaining to the safety labeling change provision.

[364] *Id.*

3. Industry-Initiated Administrative Orders

a) Procedures for Industry-Initiated Administrative Orders

Industry can initiate proceedings to change an administrative order. A sponsor can submit an OMOR asking FDA to determine that a drug, class of drug, or combination of drugs is GRASE or that a change to a condition of use of a drug is GRASE.[365] The request may ask FDA to evaluate a new active ingredient, new dosage forms of existing active ingredients, and new indications, among other changes to currently marketed products.[366]

The sponsor should submit the request "in the form and manner as specified" by FDA.[367] Section 505G(l) requires FDA to issue guidance specifying "the format and content of data submissions" and the "format of electronic submissions" to FDA under section 505G.[368] If FDA determines that the OMOR is "sufficiently complete and formatted to permit a substantive review," FDA will file the request and initiate the same administrative order proceedings as FDA-initiated administrative orders.[369] FDA would evaluate the request and issue a proposed administrative order in response to the request.[370] As with FDA-initiated orders, sponsors would have an opportunity for public comment, dispute resolution after issuance of a final administrative order, an administrative hearing, and judicial review.[371]

FDA is not required to review a request for a change if it determines that there is an "inadequate basis" to find the drug is GRASE and issues a final order announcing that determination.[372] FDA can refuse to file a request for a drug with an active ingredient not previously incorporated in a monograph drug if the request does not demonstrate either 1) "information sufficient for a prima facie demonstration that the drug subject to such request has a verifiable history of being marketed and safely used by consumers in the United States as a nonprescription drug under comparable conditions of use"; or 2) information that the drug has been marketed in Australia, Canada, Israel, Japan, New Zealand, Switzerland, South Africa, the EU, or a country in the European Economic Area under comparable conditions of marketing and use "for such period as needed to provide reasonable assurances concerning safe nonprescription use of the drug" and for a period where it was "subject to sufficient monitoring by a regulatory body considered acceptable by the Secretary," including for adverse events associated with nonprescription use of the drug.[373] FDA can also determine that the marketing information described above is not needed to provide a "prima facie demonstration" and other information is sufficient for such purposes.[374] If FDA refuses to review a request due to lack of prima facie information, a sponsor could resubmit an OMOR

---

[365] FDCA § 505G(b)(5).

[366] *Id.*

[367] FDCA § 505G(b)(5)(B).

[368] FDCA § 505G(l).

[369] FDCA § 505G(b)(5)(A).

[370] *Id.*

[371] *Id.*

[372] FDCA § 505G(b)(5)(B)(ii).

[373] FDCA § 505G(b)(6)(C).

[374] FDCA § 505G(b)(6).

only if 1) the drug is marketed as an OTC drug under comparable conditions of use for no more than five years under an NDA or abbreviated new drug application (ANDA); and 2) during such a period, 1 million retail packages have been distributed for retail sale.[375]

Whether manufacturers would have an incentive to introduce a new active ingredient through the OMOR pathway will depend on how FDA implements the provision. Section 505G(b)(6)(D) indicates that FDA will generally expect a drug to be marketed as an OTC drug for up to five years with significant OTC sales before it would consider a request under the OTC provisions.[376] A product with five years of OTC marketing experience in the United States would likely face competing products on the market under ANDAs at the time the manufacturer files an OMOR. At that point, it is unclear what incentive the manufacturer would have to introduce the product as an OTC monograph drug. If a product does not have marketing experience in the United States and intends to rely on EU marketing experience, the attractiveness of this pathway will depend on what data FDA will require to determine GRASE status. If FDA decides that the data requirements under an OMOR would be similar or slightly less burdensome than the requirements under an NDA, the regulatory incentives under an NDA will likely be more attractive. If, however, the data requirements for introducing an active ingredient through an OMOR are significantly less burdensome than under an NDA, the OMOR pathway may be an attractive option to introduce OTC products marketed in foreign countries into the United States.

b) Timelines for OMORs

OMORs are subject to user fees, and FDA has associated timelines and performance goals associated with reviewing OMORS and issuing administrative orders for industry-initiated administrative orders. The legislation and the Goals Letter divide OMORs into two tiers: Tier One OMORs and Tier Two OMORs. Most OMORs will be Tier One OMORs. Tier Two OMORs will be limited to the following changes to monograph drugs: reordering existing information in the Drug Facts Label, standardization of the concentration or dose of a specific finalized ingredient, an ingredient or nomenclature change, addition of an interchangeable term, modification to the directions of use for the Drug Facts label to be consistent with FDA guidance, addition of information in the "Other Information" section in the Drug Facts Label, and other specific items added by FDA. All other OMORs will be Tier One OMORs.[377]

The Goals Letter provides timelines for different types of industry-initiated administrative orders. For all industry-initiated administrative order requests, FDA would make a fileability determination within sixty calendar days after receipt of the request.[378] For Tier One industry-initiated administrative orders, FDA would issue a proposed order twelve months after receipt of the order request.[379] FDA would issue a final order 17.5 months after receipt of the order request.[380] The same timeline applies

---

[375] FDCA § 505G(b)(6)(D).

[376] *Id.*

[377] FDCA § 744L(9).

[378] GOALS LETTER, *supra* note 219, at 13.

[379] *Id.*

[380] *Id.*

to industry-initiated administrative orders to finalize a category III ingredient in a TFM or category I ingredient in an ANPR.[381] For Tier Two industry-initiated administrative orders, FDA would issue a proposed order ten months after receipt of the order request.[382] FDA would issue a final order 15.5 months after receipt of the order request. Industry-initiated administrative orders related to a specified safety change would take less time from OMOR receipt to issuance of the final administrative order.[383] FDA would issue a proposed order six months after receipt of the order request and issue the final order 11.5 months after receipt of the request.[384]

The timelines in the Goals Letter are subject to assumptions related to OMOR activities and performance goals associated with each assumption. Based on these assumptions and goals, few OMORs would likely be completed in the first five years after CARES Act enactment. For example, FDA assumes that there would be no industry-initiated order requests submitted in the first three years after OTC monograph reform, five requests in FY 2024, and ten requests in FY 2025.[385] Performance goals for industry-initiated OMORs would not apply until FY 2024.[386] For the first three years, FDA will review OMORs in order of receipt, but timelines and performance goals would not apply.[387] In FY 2024, FDA intends to issue 50% of industry-initiated order request final orders by the specified goal date.[388] The performance goal increases to 75% in FY 2025.[389]

C. Exclusivity

Sponsors can receive exclusivity for certain OTC monograph drugs determined to be GRASE through the OMOR process. Sponsors can receive eighteen-month exclusivity for an OTC monograph drug that is subject to a final administrative order issued in response to certain types of OMORs.[390] The final administrative order would have the effect of solely authorizing the requestor to lawfully market the drug pursuant to the new order.[391] Exclusivity would begin "following the effective date of such final order and beginning on the date the requestor may lawfully market such drugs pursuant to the order."[392] Because manufacturers cannot "lawfully market" a drug unless the drug is properly registered and listed in FDA's drug registration and listing database, exclusivity should begin on the date the manufacturer lists the drug.[393]

Exclusivity is available when an administrative order issued in response to an OMOR provides for 1) a drug "to contain an active ingredient (including any ester or

---

381 *Id.*

382 *Id.*

383 GOALS LETTER, *supra* note 219, at 24.

384 *Id.*

385 *Id.* at 14.

386 *Id.*

387 *Id.*

388 *Id.*

389 *Id.*

390 FDCA § 505G(b)(5)(C)(i).

391 *Id.*

392 *Id.*

393 *Id.*

salt of the active ingredient)" not previously incorporated in an OTC 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 (or for which the requestor has an exclusive right of reference) were essential to the issuance of such order."[394] The "active ingredient" language mirrors the language in section 505(c)(3)(E) granting five years exclusivity for an NDA approved for a drug with a new chemical entity. Exclusivity for "a change in the conditions of use of a drug" is available for an administrative order that relied on "new human data" provided by the requestor.[395] "New human data" means "clinical trials of safety or effectiveness (including actual use studies), pharmacokinetics studies, or bioavailability studies," the results of which have not been relied on by FDA or duplicate a study that was used to support a proposed or final determination for a monograph drug or approval of a drug approved under section 505 of the FDCA.[396] Unlike the understanding of "new clinical investigations" required for three-year exclusivity under section 505(c)(3)(E)(iii) of the FDCA, the definition of "new human data" includes pharmacokinetics and bioavailability studies.[397]

Exclusivity under section 505G will not always prohibit a company from marketing a similar drug during the exclusivity period. Section 505G exclusivity would not exclude a manufacturer from marketing the identical product under an ANDA. For example, if a company marketing an OTC drug under an NDA wanted to market the drug under the OTC monograph system and submitted an OMOR to FDA, identical OTC drugs could remain on the market under an ANDA during the period of exclusivity. Further, it is not clear how FDA would enforce the eighteen-month exclusivity provision. Because the final administrative order would be publicly available after finalization, another company could rely on the monograph and manufacture a drug in accordance with the monograph. The drug would be misbranded, but it is not clear whether FDA would prioritize enforcement against products intruding on another company's eighteen-month exclusivity.

It remains to be seen whether eighteen-month exclusivity will become an attractive incentive. If FDA applies virtually the same requirements in determining GRASE status as it applies for approval of NDAs, companies wishing to introduce new active ingredients for OTC use based on a history of use outside the United States might find it more attractive to file NDAs rather than pursue an OMOR. Such an ingredient, if never used in an approved drug in the United States, would be entitled to new chemical entity (NCE) exclusivity and receive five years of protection, which greatly exceeds eighteen-month exclusivity under OTC monograph reform. Similarly, manufacturers that wish to market modified versions of GRASE monograph drugs for which other clinical studies are needed might prefer to follow the 505(b)(2) pathway, which could provide three years of exclusivity instead of eighteen months, without the risk that FDA could fail to enforce against companies intruding on the exclusivity period.

---

394 FDCA § 505G(b)(5)(C)(ii).

395 *Id.*

396 FDCA § 505(b)(5)(C)(v).

397 *Id.*

D. Minor Dosage Form Changes

Section 505G(c) establishes a procedure to allow manufacturers to implement minor changes in dosage forms without the issuance of a new administrative order permitting the dosage form change. First, FDA must publish an administrative order specifying requirements for determining whether a minor dosage form change would affect the safety or effectiveness of a drug. FDA would issue the order together with guidance applying the order to specific dosage forms.[398] The administrative order-guidance pair should "take into account relevant public standards and standard practices for evaluating the quality of drugs and may take into account the special needs of populations, including children."[399]

Once FDA issues the administrative order-guidance pair, manufacturers could make changes to dosage forms in accordance with the requirements of the applicable administrative order.[400] Manufacturers would need to carry out studies specified in the administrative order for the dosage form and keep these data available to FDA on request.[401] The sponsor would have to maintain information on file that demonstrates that the change will not affect the safety or effectiveness of the drug and will not "materially affect the extent of absorption or other exposure to the active ingredient in comparison to a suitable reference product."[402] If FDA requests records related to the minor change, the sponsor would have at least fifteen days to submit the information to FDA.[403] The sponsor would need to submit updated drug listing information within thirty days of the date that the drug with the new dosage form is marketed.[404]

Section 505G(c) is a limited provision and applies to only changes in dosage forms. A sponsor wishing to make other changes to an OTC monograph drug, such as changes to labeling not covered by an existing monograph or the general requirements for nonprescription drugs, would need to submit an OMOR requesting FDA's determination that the change would be GRASE. Further, the minor changes provision is available to only products covered under a final administrative order. A manufacturer marketing a drug containing a category III ingredient in a TFM, for example, would not be able to rely on the minor changes provision to make a change in the drug's dosage form. The manufacturer would first need to submit an OMOR and have FDA determine that the drug is GRASE before the minor changes provision would apply.

Section 505G(c) would not change the ability of manufacturers to make changes to a drug that is covered by the existing monograph and the general requirements for OTC monograph drugs. As was true before OTC monograph reform, a manufacturer can continue to make changes in the dosage form of a drug in accordance with the monograph or administrative order governing the drug. Further, a manufacturer can continue to make other changes to the drug in conformance with the monograph and the general requirements for OTC monograph drugs. For example, a manufacturer can

---

[398] FDCA § 505G(c)(3).

[399] FDCA § 505G(c)(3)(B).

[400] FDCA § 505G(c)(1).

[401] FDCA § 505G(c)(2).

[402] FDCA § 505G(c)(3)(A).

[403] FDCA § 505G(c)(2)(A).

[404] FDCA § 505G(e).

continue to make changes to inactive ingredients for an OTC monograph drug without needing to rely on the minor changes provision, provided the drug contains safe and suitable inactive ingredients, in compliance with 21 C.F.R. § 330.1(e).

It is unlikely that manufacturers would be able to use this provision to implement a dosage form change until five years after enactment of the CARES Act. The minor changes provision will be available only after FDA has adopted an administrative order establishing data requirements for a specific type of dosage form, together with guidance for applying the orders to specific dosage forms. FDA contemplates that a small number of such orders will be issued in the first five-year user fee cycle. The Goals Letter indicates that FDA will issue the proposed administrative order and draft guidance for minor change to solid oral dosage forms by April 1, 2022.[405] This would be the first administrative order-guidance pair for the minor changes provision.

E. Communication with External Stakeholders

1. Confidentiality

Section 505G explicitly prevents FDA from disclosing confidential information submitted by manufacturers. Section 505G(d) states that information submitted by a requestor in connection with "proceedings on an order under this section (including any minor change under subsection (c))" is a trade secret or confidential information under the Freedom of Information Act (FOIA) the Trade Secrets Act will not be disclosed, unless the requestor consents to the disclosure.[406] That said, certain information that is trade secret or confidential commercial information will be publicly available at certain points of the administrative order process. FDA would make publicly available any information submitted by a requestor in support of an OMOR on the date it issues the proposed order.[407] Information submitted by a person for public comment in response to a proposed or final administrative order would also be publicly available.[408] Whether in a meeting, an OMOR, or any other type of interaction with FDA, a sponsor should clearly identify what information is trade secret or confidential commercial information.

FDA will not make public four types of confidential or trade secret information under any circumstances, unless otherwise required by law. First, FDA will not make available "pharmaceutical quality information, unless such information is necessary to establish standards" under which a drug is GRASE.[409] For example, FDA could make publicly available final formulation effectiveness testing information necessary to ensure a drug is GRASE even if the tests could qualify as trade secret information. Second, FDA will not disclose information submitted in an OMOR if the requestor

---

[405] GOALS LETTER, *supra* note 219, at 17.

[406] 5 U.S.C. § 552(b)(4) (exempts from public disclosure "trade secrets and commercial or financial information obtained from a person and privileged or confidential"). The Trade Secrets Act prevents an agency from disclosing information that "concerns or relates to the trade secrets, processes, operations, style of work, or apparatus, or to the identity, confidential statistical data, amount or source of any income, profits, losses, or expenditures of any person, firm, partnership, corporation, or association; or permits any income return or copy thereof or any book containing any abstract or particulars thereof to be seen or examined by any person except as provided by law . . . ." 18 U.S.C. § 1905.

[407] FDCA § 505G(d)(2)(A).

[408] *Id.*

[409] FDCA § 505G(d)(2)(B)(i).

withdraws the request before FDA issues the proposed order.[410] Third, FDA will not disclose information obtained under the minor changes provision if the sponsor did not submit that information in relation to an administrative order.[411] If FDA obtains information through a review of information on file under the minor changes provision, that information would not be publicly disclosed unless the sponsor also submits that information for an administrative order. Finally, FDA will not disclose information "of the type contained in raw datasets."[412]

The confidentiality provisions mean that trade secret and confidential commercial information provided to FDA in meetings in support of a request would be kept confidential until FDA issues a proposed order that responds to the request. FDA would also be prevented from disclosing the submission of an OMOR request until FDA issues a proposed administrative order in response to the request unless the OMOR sponsor discloses the submission of the request. These confidentiality provisions are similar to those related to confidential commercial and trade secret information in INDs.

2. Meetings with FDA

Sponsors can meet with FDA "to obtain advice on studies and other information necessary to support submissions" of OMORs and to discuss other matters related to the regulation and development of OTC monograph drugs.[413] FDA will establish procedures to provide development advice and procedures "to facilitate efficient participation by multiple sponsors or requestors" in proceedings under section 505G, including meetings with multiple sponsors or requestors or "organizations nominated by sponsors or requestors to represent their interests in a proceeding."[414] Section 505G(l) requires FDA to issue guidance on "the procedures and principles for formal meetings" between FDA and sponsors or requestors subject to the section.[415] The term "sponsor" refers to "any person marketing, manufacturing, or processing" a listed drug or a drug that is or will be listed subject to an administrative order under section 505G.[416] The term "requestor" refers to "any person or group of persons marketing, manufacturing, processing, or developing a drug."[417] Because meetings are available to sponsors and requestors, a party would not be able to request a meeting under this provision if it does not or has no intention of marketing, manufacturing, or developing a nonprescription drug. As we note in the previous section, these meetings will remain confidential if sponsors intend to discuss trade secrets or confidential commercial information with FDA.

The Goals Letter provides more detail on the meetings available under section 505G. These meetings mirror those available to sponsors of other user fee programs, such as PDUFA. Type X meetings are necessary "for an otherwise stalled monograph drug development program to proceed" or meetings to address an important safety

---

[410] FDCA § 505G(d)(2)(B)(ii).

[411] FDCA § 505G(d)(2)(B)(iii).

[412] FDCA § 505G(d)(2)(B)(iv).

[413] FDCA § 505G(h).

[414] FDCA § 505G(i).

[415] FDCA § 505G(l).

[416] FDCA § 505G(q)(2).

[417] FDCA § 505G(q)(3).

issue.[418] FDA intends to respond to Type X meeting requests within fourteen calendar days and would schedule a meeting thirty calendar days from receipt of the meeting request.[419] Type Y meetings are intended for milestone discussions.[420] These meetings include data requirements meetings to discuss what information would be needed to support a GRASE determination or presubmission meetings to support an OTC monograph order request.[421] FDA intends to respond to Type Y meeting requests within fourteen calendar days and would schedule a meeting seventy calendar days from receipt of the meeting request.[422] Type Z meetings constitute any other type of meeting. FDA intends to respond to Type Z meetings within twenty-one calendar days and would schedule a meeting seventy-five calendar days from receipt of the meeting request.[423]

The Goals Letter also provides assumptions regarding the number of meetings requested per year and FDA's performance goals for timelines associated with the meetings. FDA assumes that there will be six meeting requests in the first year after enactment of OTC monograph reform, nine meeting requests in year two, twelve meeting requests in year three, twenty-four meeting requests in year four, and forty meeting requests in year five.[424] FDA would not have performance goals until the third year after CARES Act enactment. Performance goals for meeting timelines will be 50% for year three and will rise to 80% by the fifth year after enactment.[425]

F. User Fees

A user fee system funds activity related to OTC monograph drugs. The CARES Act adds sections 744L and 744M to the FDCA, which establish a user fee program to fund FDA's OTC monograph drug activities. Facility fees and OMOR fees fund OTC monograph activities.

Facility fees are paid by entities that manufacture or process finished OTC drug products, including OTC drugs that are also cosmetic products. Facility fees are paid annually by each facility identified as "an OTC monograph drug facility on December 31 of the fiscal year or at any time during the preceding 12-month period."[426] An OTC monograph drug facility is any facility, whether foreign or domestic, that is under one management and at one physical location, engaged in "manufacturing and processing the finished dosage form of an OTC monograph drug."[427] Separate buildings in one location under the same local management will count as one facility. An OTC monograph drug facility does not include a facility that is only manufacturing or processing "clinical research supplies, testing, or placement of outer packaging on

---

418 GOALS LETTER, *supra* note 219, at 17.

419 GOALS LETTER, *supra* note 219, at 18.

420 *Id.*

421 *Id.*

422 *Id.*

423 *Id.*

424 GOALS LETTER, *supra* note 219, at 21.

425 *Id.*

426 FDCA § 744M(a).

427 FDCA § 744L(10)(A).

packages containing multiple products."[428] A facility producing only active ingredients or components for OTC monograph drugs but does not produce or process any finished OTC monograph drug products would not be subject to a user fee. Further, a facility producing both NDA and OTC monograph drugs would be subject to fees from multiple user fee programs.

No single provision states the facility fee amount. Instead, facility fees will be calculated by totaling fee revenue targets described in section 744M(b) of the FDCA, with inflation and operating reserve adjustments. FDA would calculate the facility fee by dividing the total fee by all OTC monograph facilities for each fiscal year, except that the fee for a "contract manufacturing organization facility" will be two-thirds the amount of the fee for other OTC monograph drug facilities.[429] A "contract manufacturing organization facility" is an OTC monograph drug facility where the owner of the facility manufacturers the drug for another organization and does not sell directly to wholesalers, retailers, or consumers in the United States.[430] Facility fees for FY 2021 will be due the later of July 1, 2020 or forty-five days after FDA publishes the OTC monograph drug facility fees for FY 2021 in the Federal Register. Failure to pay a facility fee would render the OTC monograph products produced in the facility to be misbranded.[431]

OMOR fees are for submission of industry-initiated administrative order proceedings. A "Tier 1 OTC monograph order request" (any request that is not a Tier 2 request) will be $500,000, adjusted for inflation.[432] A "Tier 2 OTC monograph order request" (request for certain, minor modifications of a monograph) will be $100,000, adjusted for inflation.[433] An OMOR fee is not needed for OMORS for certain safety labeling changes (i.e., OMORs to change the Drug Facts Labeling of an OTC monograph drug to add or strengthen "a contraindication warning or precaution," a "statement about risk associated with misuse or abuse," or "an instruction about dosage and administration that is intended to increase the safe use" of the drug).[434] Fees are due on the date of submission of an OMOR.[435]

G. Sunscreens

1. Regulatory Status of Sunscreen Products

The CARES Act included significant changes to FDA's regulations of sunscreens and the SIA. As we discussed in Section V.A.2, section 505G of the FDCA changed the regulatory status of sunscreens marketed as an OTC monograph drug. In order for a sunscreen product to be GRASE, it would need to comply with FDA's stayed monograph on sunscreens, except the effectiveness and labeling requirements will be those in 21 C.F.R. § 201.327. The CARES Act also affects FDA's prior positions on sunscreens marketed as an OTC monograph drug. On February 26, 2019, FDA issued

---

[428] FDCA § 744L(10)(A).

[429] FDCA § 744M(a)(1)(B).

[430] FDCA § 744L(2).

[431] FDCA § 502(ff).

[432] FDCA § 744M(a)(2)(A)(i).

[433] FDCA § 744M(a)(2)(A)(ii).

[434] FDCA § 744M(a)(2)(C).

[435] FDCA § 744M(a)(2)(B).

a proposed rule on sunscreen products. Due to the CARES Act, FDA would need to reissue the proposed rule as a proposed administrative order under the 505G procedures if it would like to change the requirements for sunscreen drugs regulated under section 505G.

The CARES Act mandates FDA to issue a revised administrative order to the stayed sunscreen monograph and provides statutory deadlines for when FDA would need to issue a new proposed administrative order. FDA would need to issue a proposed administrative order no later than September 27, 2021. The CARES Act does not set a deadline for when FDA would need to finalize the proposed administrative order, and because the order would be an FDA-initiated administrative order, there are no user fee timelines associated with finalization of the proposed order. That said, the order cannot come into effect less than one year after the date FDA issues the final, revised administrative order on sunscreens.[436]

2. Sunscreen Innovation Act

The CARES Act harmonizes OTC monograph reform with the SIA. Most significantly, the SIA will sunset on September 30, 2023.[437] Until then, the SIA and OTC monograph reform will run in parallel, subject to a number of changes to the SIA.

A sponsor of a nonprescription sunscreen active ingredient that is the subject of a "proposed sunscreen order" under the SIA may choose to continue review under the SIA provisions or may choose review under the new administrative order process for monograph drugs.[438] If a sponsor chooses review under the administrative order process, the proposed sunscreen order will turn into a request for an administrative order that has been accepted for filing.[439] FDA will continue to review active ingredients subject to a proposed sunscreen order in accordance with the SIA provisions.[440] If FDA finalizes the proposed sunscreen order, the determination will no longer be incorporated into the final sunscreen monograph.[441] Instead, a final sunscreen order will automatically be deemed to be a final administrative order.[442]

In order to ensure that sponsors continuing under the SIA will not be disadvantaged compared to sponsors continuing under the administrative order process, a final sunscreen order under the SIA will provide the sponsor exclusivity for a period of eighteen months, beginning on the date the requestor may lawfully market the sunscreen ingredient, if the sunscreen order permits a sunscreen active ingredient not previously marketed as a sunscreen monograph ingredient.[443] The CARES Act also allows sponsors under the SIA to request confidential meetings with respect to a proposed sunscreen order under the SIA.[444]

---

[436] CARES Act § 3854(c)(1)(B).

[437] CARES Act § 3854(b)(4).

[438] CARES Act § 3854(a)(1).

[439] *Id.*

[440] *Id.*

[441] CARES Act, § 3854(b).

[442] *Id.*

[443] FDCA § 586C(f).

[444] FDCA § 586C(b)(7)(B).

VI. CONCLUSION

The history of the OTC monograph system and the legislative history reveal several conclusions about OTC monograph reform. First, OTC monograph reform was a direct response to the challenges of the OTC Drug Review. OTC monograph reform did not intend to replace the existing OTC monograph system and attempted to address specific challenges identified with the Review. It is important to understand not just what OTC monograph reform changed, but also what reform retained to understand the regulatory regime for OTC monograph drugs. As an example, the administrative order procedures replaced the burdensome notice-and-comment rulemaking provisions within the OTC Drug Review. Similarly, the minor changes provision resulted from manufacturers' difficulties making dosage form changes to drugs marketed under the prior OTC monograph system. On the other hand, OTC monograph reform did not alter the data requirements and standards established under the OTC Drug Review and did not impose new safety or effectiveness standards on OTC monograph drugs. It would be difficult to interpret the provisions of OTC monograph reform without first understanding the history behind the OTC Drug Review and where OTC monograph reform modified, retained, or expanded on the Review.

Second, every provision of final legislation had been publicly vetted for several years and consensus on significant parts of the legislation had existed for several years before enactment. A variety of approaches to key issues were drafted, considered, and debated in the process and should be considered when implementing and interpreting OTC monograph reform. For example, FDA had proposed imposing new notification requirements for OTC monograph drugs, but that proposal was rejected in draft legislation and never seriously discussed after FDA's public hearing. Stakeholders extensively discussed data standards for the minor changes provision, and the end result was a provision that requires FDA to "take account of standard procedures and practices for evaluating the quality of drug products," including applicable provisions of the USP.[445] The reference to "standard procedures and practices" was intentional and represents the result of considerable discussions between stakeholders on OTC monograph reform.[446]

Finally, as was true of other FDA user fee legislation, OTC monograph reform represented a meaningful compromise between Democrat and Republican members of Congress, industry, FDA, physician groups, consumer groups, and other interests. Final decisions on key issues were the subject of bipartisan agreement and represented a middle ground between different stakeholder interests. As an example, the eighteen-month period of exclusivity was the subject of extensive debate, with shorter and longer alternatives under consideration. Some stakeholders would have preferred shorter or no exclusivity, but the end result was a provision that provided exclusivity with the expectation that exclusivity be meaningful. To provide another example, FDA's authorities under the expedited administrative order procedure were also extensively debated, with the final language reflecting bipartisan agreement about the scope of FDA authority. These compromises should be considered as FDA implements OTC monograph reform.

---

[445] FDCA § 505G(c)(3)(B).

[446] *Id.*