

Testimony before the Committee on Energy and Commerce, Subcommittee on Health, United States House of Representatives

Chairman Burgess, Ranking Member Green, members of the sub-committee, thank you for holding this hearing and for the opportunity to present testimony. My name is Kirsten Moore; I direct the Health Care Products project at The Pew Charitable Trusts. Pew is a nonprofit, nonpartisan research and policy organization with a longstanding interest in drug quality and safety. Today I am here to relay Pew's strong support for reforming the regulatory framework for over-the-counter (OTC) drug products. Modernizing the OTC monograph system is necessary to enhance efficiency, improve safety, promote innovation, and ensure that FDA has adequate resources – all of which ultimately help consumers.

Scope of Problem

OTC products range from antiperspirant and deodorant to sunscreen to cough and cold medication and pain relievers. The OTC drug marketplace includes over 300,000¹ unique products and has annual sales of \$32 billion.² FDA's monograph review framework for evaluating OTC ingredients is cumbersome, inefficient, and outdated – having not been revised since its inception in 1972. The multi-step rulemaking process is lengthy, and the agency's lack of resources hinders FDA's ability to ensure the safety and effectiveness of OTC products and to promote innovation.

Most over-the-counter drugs are not regulated like prescription medications. Manufacturers of prescription drugs must submit clinical data to FDA to show they are safe and effective for their intended use and population before marketing them. These data are submitted in the form of a new drug application that FDA can approve, deny, or make a request for additional data. The process is drug-product specific, and FDA approves the formulation and what goes on the label (for example, intended uses, warnings, and directions for the consumer). New OTC products can be reviewed through this process, either as nonprescription drugs or as prescription drugs that may be sold over the counter later. Examples include certain allergy medications, antacids, and fluoride toothpastes.

In contrast, the majority of OTCs rely on a "monograph" system, which entails evaluating the safety and effectiveness of active ingredients in the product rather than the product itself. A monograph is a published "recipe" used by product manufacturers that is typically organized into therapeutic classes or product categories, such as topical antimicrobials. The monograph for each category includes active ingredients, dosage form (for example, tablet or ointment), doses and dosage instructions, concentration, and mandatory labeling, and is published as a final rule in the Federal Register and codified in the Code of Federal Regulations. If a manufacturer follows the recipe exactly for an existing monograph, the company is not required to seek FDA approval for a new product. Many ingredients in OTC products have been on the market since before 1962, when Congress first required that new drug products be shown to be effective, as well as safe, before they were marketed. FDA, recognizing in the 1970s that it needed a way to evaluate the many ingredients in products that were already on store shelves, initiated a scientific review of all active ingredients in them. Advisory committees, composed of physicians, pharmacists, consumers, and industry representatives, recommended that each active ingredient be in one of three categories: Category I includes ingredients which have been subject to adequate clinical investigations and testing, and experts generally agree that they demonstrate safety and efficacy for intended use. Category II includes ingredients that are not generally recognized as safe and effective, but may continue to be marketed until a monograph is finalized, which can take years. Category III includes ingredients for which there is not enough information to determine whether they are generally recognized as safe and effective. Again, the product can remain on the market until FDA finds that there is enough evidence to make a final determination.

Making changes to a monograph is a multi-step process. All proposed changes to monographs are reviewed by FDA and the Department of Health and Human Services, and often the White House Office of Management and Budget, which estimates the cost and benefit of the change to the economy and consumers. FDA also receives and must respond to public comment throughout the monograph revision process. In contrast, new drug applications are reviewed solely by FDA on the basis of whether the product is safe and effective. The additional review steps for monographs add considerable time, and they risk prioritizing economic considerations over consumer health and safety. There is no deadline by which monographs must be finalized, and several have been under review for decades.

Public Health Implications of Outdated OTC Monograph System

Approximately 240 million people, including infants and the elderly, use OTC products annually.³ FDA's limited resources and authority to regulate OTC products in a timely and streamlined fashion hinder its ability to oversee their safety and effectiveness. This can lead to critical adverse events, and create unreasonable discrepancies between the agency's response to the same risks in OTC products versus prescription drugs.

In 2002, FDA held an advisory committee meeting to discuss the problem of liver injury related to the use of OTC acetaminophen products.⁴ The advisory committee recommended a specific liver toxicity warning and changes to OTC packages so that products containing acetaminophen could be more easily identified.⁵ It took the agency seven years to finalize a rule amending the labeling requirements for OTC drugs in order to inform consumers about the risk of liver injury when using acetaminophen (and four years even to issue an initial proposed rule).^{6,7} In contrast, it took FDA only two years to convene an advisory committee and require new Boxed Warning on all *prescription* drug products that contain acetaminophen.^{8,9}

Similarly, FDA was able much more quickly to address the risks of prescription anti-inflammatory drugs compared with the identical active drug sold as an OTC product. In 2002, FDA held an advisory committee meeting to discuss the gastrointestinal (GI) and renal toxicity risks associated with the use of OTC nonsteroidal anti-inflammatory drugs (NSAIDs).¹⁰ The advisory committee agreed that a change to the current label was necessary to address these risks, but again, it took the agency seven years to publish a final rule requiring the change.¹¹ It took the agency less than a year to require a Boxed Warning for prescription NSAIDs.¹²

More recently, in April 2017, FDA required companies to add the strongest form of warning to children's prescription cough and pain medications containing codeine, a controlled substance. The agency was responding to concerns that the drug can cause potentially fatal breathing problems, especially in children younger than 12 years.¹³ In 2015, an FDA advisory committee identified 24 deaths and 64 cases worldwide of serious breathing problems in the previous 50 years among children who took medications containing codeine. Twenty-one of those who died were children younger than 12.¹⁴ Despite the evidence, FDA has not yet made the change to remove codeine from the monograph for OTC children's cough and cold products.

These examples illustrate the unnecessary delay incorporated into a multi-step rulemaking system, which compromises FDA's ability to respond swiftly to address new safety information and protect consumers. This is particularly concerning as there is no presumption of a health care professional intermediary in an over-the-counter environment, so consumers lack vital information about safe or appropriate use of products. FDA, industry, and public health stakeholders are united in their conviction that OTC monograph reform is critical to protect public health, and are in strong support of this proposed legislation.

OMUFA Draft Language Improves FDA's Ability to Prioritize Public Health

Earlier this year, Pew joined with the American Academy of Pediatrics, the American Academy of Allergy, Asthma & Immunology, American Academy of Dermatology Association, the American Public Health Association, the National Association of County and City Health Officials, Society for Maternal-Fetal Medicine and March of Dimes to issue a set of principles for over-the-counter monograph reform.¹⁵ These principles call for:

- (1) replacing the cumbersome rulemaking process with a more efficient mechanism for creating and updating monographs;
- (2) allowing FDA to act promptly to address emerging safety issues; providing FDA with sufficient resources to accommodate OTC drug innovation;
- (3) creating an efficient data collection system for FDA; and
- (4) establishing FDA as the final arbiter of scientific evidence on the safety and effectiveness of ingredients and changes to monographs.

These principles are broadly reflected in both the House and Senate language which have been circulated. We will highlight several significant improvements under the proposed legislation.

Efficiency

OTC monograph reform will enhance efficiency by replacing the cumbersome rulemaking process with an administrative order process, aligning the decision-making authority FDA has for OTC products with the authority the agency already has for prescription drugs. Under the proposed system, agency scientists would be able to make important safety and effectiveness decisions about OTC ingredients. Monograph reform would also expedite the review process by giving the Secretary authority to standardize the content and format for electronic data submissions and set forth a procedure for collecting and analyzing such data. This improves on the current system, in which reviewers must sort through and then systematize a volume of disorganized, often fragile, paper documents into a package that can be properly reviewed.

Safety

Monograph reform will improve FDA's ability to respond to safety threats and ensure the agency has complete information about OTC products. Allowing the agency to change the rules for OTC products by administrative order would allow it to react rapidly to emerging safety issues regarding the use and misuse or abuse of OTC drug products. Currently, products for which FDA has insufficient information remain on the market, but OTC reform would allow FDA to complete its review and remove products from the market if sufficient evidence of safety and effectiveness is lacking. Furthermore, requiring firms to submit all information in their possession, including negative data (as is required for prescription drug submissions), would enhance safety by ensuring that FDA is the final arbiter of scientific evidence on the safety and effectiveness of ingredients and changes to monographs, as is already the case for prescription drugs and medical devices. To ensure safety, any new exclusivity provisions should not apply to safety-related changes, enabling universal adoption of such changes and, user fees should not be assessed for adding new safety information, so that firms are likely to update products accordingly.

Innovation

With an improved regulatory regime, FDA would more quickly be able to accommodate innovation in OTC drug products, permitting new ingredients, and new indications and new formulations for existing ones, potentially giving patients who are unable to take pill forms to access medications through other routes of administration.

Resources

Achieving these potential commercial and public benefits will require additional FDA resources. Establishing a user fee program for OTC products will significantly enhance FDA's ability to effectively oversee this marketplace. Approximately 18 scientific reviewers oversee about 800 active ingredients for over 1,400 distinct therapeutic uses,¹⁶ with more than half of these reviewers dedicated to review of sunscreen ingredients.¹⁷ For context, FDA dedicates approximately 18 FTEs to review one application to market a new prescription drug.¹⁸ The proposed agreement would provide FDA with the resources required to substantially expand the OTC review and oversight capacity – from 31 FTEs (this number includes legal, policy and support staff as well as scientific reviewers) in 2018 to 110 FTEs in FY2022. This boost in personnel will enable FDA to clear up the monograph review backlog, address safety concerns for products currently on the market, and review future applications for innovative products in a timely manner.

OMUFA is a Compromise

Pew supports this bipartisan proposed legislation as written, because it will lead to improvements in public safety and administrative efficiency. However, it is noteworthy that the new exclusivity provided to certain OTC products that do not undergo clinical trials under this measure would exceed the 6-months' additional exclusivity that Congress provided to companies that carry out tests of their drugs in a pediatric population. Pew also recommends incorporating language authorizing the Secretary to require packaging to be redesigned if needed to resolve safety concerns.

Other concerns with this legislation may be resolvable as stakeholders gain experience in a new system, thus Pew recommends incorporating a mechanism that facilitates future negotiations between industry and FDA, so that they can resolve remaining inefficiencies without the need for new legislation. For example, the proposed process for dispute resolution over OTC ingredients requires multiple notifications and potential delays and is more complex than the process for resolving disputes over prescription drugs. Industry and FDA should have an opportunity to agree to a more streamlined dispute resolution process than is contemplated by the current legislation. In addition, the proposed language allows a manufacturer to file an application over protest, even when FDA has already reviewed and deemed that file insufficient with regard to evidence. These provisions undermine the goal of increased efficiency, both by requiring FDA to use resources on review of insufficient applications and by delaying the agency's ability to turn to applications from sponsors who have submitted complete files.

Conclusion

The current monograph system, unchanged since 1972, has had detrimental effects on consumers and compromises FDA's ability to ensure the safety and effectiveness of OTC products. We applaud this subcommittee for its bipartisan work on the current proposal. The Pew Charitable Trusts urges Congress to capitalize on this momentum and pass this legislation as soon as possible.

¹ Food and Drug Administration, "Drug Applications for Over-the-Counter (OTC) Drugs," accessed Aug. 25, 2017, <http://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/over-the-counterdrugs/default.htm>.

² Consumer Healthcare Products Association, "OTC Retail Sales 1964-2015," accessed Aug. 25, 2017, http://www.chpa.org/PR_OTCRetailSales.aspx.

³ Approximately 240 million people in the United States use OTC products annually in the seven categories (allergy, analgesics, anti-fungals, cough/cold/flu, upper and lower gastrointestinal, and medicated skin) that represent the significant majority of OTC products purchased in the United States. Consumer Healthcare Products Association, “The Value of OTC Medicine to the United States,” (2012).

⁴ U.S. Food and Drug Administration, “Non-prescription Drugs Advisory Committee; Notice of Meeting,” 67 Fed. Reg. 161 (August 20, 2002).

⁵ U.S. Food and Drug Administration, “June 29-30, 2009: Joint Meeting of the Drug Safety and Risk Management Advisory Committee with the Anesthetic and Life Support Drugs Advisory Committee and the Nonprescription Drugs Advisory Committee: Meeting Announcement,” last modified July 30, 2013, <https://wayback.archive-it.org/7993/20170722143526/https://www.fda.gov/AdvisoryCommittees/Calendar/ucm143083.htm>.

⁶ U.S. Food and Drug Administration, “Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use; Proposed Amendment of the Tentative Final Monograph; Required Warnings and Other Labeling,” 71 Fed. Reg. 77314 (Dec. 26, 2006).

⁷ 21 CFR § 201.326.

⁸ U.S. Food and Drug Administration, “June 29-30, 2009: Joint Meeting of the Drug Safety and Risk Management Advisory Committee with the Anesthetic and Life Support Drugs Advisory Committee and the Nonprescription Drugs Advisory Committee: Meeting Announcement,” last modified July 30, 2013, <https://wayback.archive-it.org/7993/20170722143526/https://www.fda.gov/AdvisoryCommittees/Calendar/ucm143083.htm>.

⁹ U.S. Food and Drug Administration, “FDA Drug Safety Communication: Prescription Acetaminophen Products to be Limited to 325 mg Per Dosage Unit; Boxed Warning Will Highlight Potential for Severe Liver Failure (January 13, 2011),” last modified July 31, 2017, <https://www.fda.gov/Drugs/DrugSafety/ucm239821.htm>.

¹⁰ U.S. Food and Drug Administration, “Nonprescription Drugs Advisory Committee; Safety Issues Related to ASA and NSAIDs, September 20, 2002,” accessed September 8, 2017, <https://www.fda.gov/ohrms/dockets/ac/02/transcripts/3882T2.pdf>.

¹¹ 21 CFR § 201.326.

¹² U.S. Food and Drug Administration, “Public Health Advisory - FDA Announces Important Changes and Additional Warnings for COX-2 Selective and Non-Selective Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) (April 7, 2005),” last modified Aug. 16, 2013, <https://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm150314.htm>.

¹³ U.S. Food and Drug Administration, “FDA Drug Safety Communication: FDA Restricts Use of Prescription Codeine Pain and Cough Medicines and Tramadol Pain Medicines in Children; Recommends Against Use in Breastfeeding Women” last modified April 20, 2017, <https://www.fda.gov/Drugs/DrugSafety/ucm549679.htm>.

¹⁴ U.S. Food and Drug Administration, “FDA Briefing Document: Joint Pulmonary-Allergy Drugs Advisory Committee and Drug Safety and Risk Management Advisory Committee Meeting; The Safety of Codeine in Children 18 Years of Age and Younger” Dec. 10, 2015, <https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Pulmonary-AllergyDrugsAdvisoryCommittee/UCM475975.pdf>.

¹⁵ The Pew Charitable Trusts, “Pew and the American Academy of Pediatrics Outline Principles for Over-the-Counter Drug Regulation Reform,” accessed Sept. 11, 2017, <http://www.pewtrusts.org/en/research-and-analysis/analysis/2017/05/05/pew-and-the-american-academy-of-pediatrics-outline-principles-for-over-the-counter-drug-regulation>.

¹⁶ Renu Lal, Pharm.D., “User Fees and the Future of the OTC Monograph System,” *FDA/CBER SBIA Chronicles*, July 6, 2016, <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/UCM510074.pdf>.

¹⁷ U.S. Food and Drug Administration, “Report in Response to the Sunscreen Innovation Act (P.L. 113-195) Section 586G,” accessed Sept. 11, 2017, <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/UCM503441.pdf>.

¹⁸ Renu Lal, Pharm.D., “User Fees and the Future of the OTC Monograph System.”